CONSORTIUM FOR RADIOLOGIC IMAGING STUDIES OF POLYCYSTIC KIDNEY DISEASE (CRISP) II

MANUAL OF PROCEDURES

February 20, 2008

See the online version for the most recent updates at:
https://www.crisp2.pitt.edu

Sponsored by
The National Institute of Diabetes &Digestive
&Kidney Diseases (NIDDK)
The National Institutes of Health (NIH)
U.S. Department of Health and Human Services

TABLE OF CONTENTS

Chapter 1. Purpose of the CRISP II Manual of Procedures

The purpose of the CRISP II Manual of Procedures (MOP) is to provide study investigators with one all-encompassing source to use as a guide in carrying out CRISP II studies. The CRISP II MOP includes sections on study organization and administration; subject recruitment; protection of human subjects; publications and communications; study design; screening, enrollment, and follow-up; data management (forms, web-based data entry system, quality control/assurance, statistical design and analysis, and reporting); and personnel. The complete MOP will remain posted on the CRISP II website (private access) for the entire length of the study and will be updated as necessary.

Study investigators will also be able to print complete copies of the CRISP II MOP directly from the website, as needed. The Data and Safety Monitoring Board will also have private access to the web-based CRISP II MOP.

The online version of the MOP is the most recent and complete. The DCIAC will add changes as necessary and will notify study personnel when changes have been posted. It is the responsibility of PCC personnel to ensure that all paper versions of the MOP are kept up to date.

1.1. Revision History

Chapter 2. Introduction and Background

2.1. Preface

The Division of Kidney Urology and Hematology Disease (DKUHD) of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) funded a cooperative agreement (UO1) for a consortium of participating clinical centers (PCCs) and a data coordinating and imaging analysis center (DCIAC) to develop and implement studies to test whether imaging techniques can provide accurate and reproducible markers of progression of renal disease in patients with polycystic kidney disease.

The awarded participating clinical centers are Emory University, University of Kansas, and Mayo Foundation (with a subcontract to the University of Alabama). The awarded DCIAC is Washington University in St. Louis. Due to the relocation of the DCIAC P.I. from Washington University to the University of Pittsburgh, the DCIAC for CRISP II is currently located at the University of Pittsburgh.

The goal of the CRISP Study is to conduct a prospective, longitudinal trial to evaluate the accuracy and validity of magnetic resonance imaging to determine disease progression in ADPKD defined as a change in both renal and renal cyst volumes and renal function over time.

2.2. Background and Rationale

2.2.1. Autosomal Dominant Polycystic Kidney Disease

Autosomal dominant polycystic kidney disease (ADPKD) is a major cause of disabling morbidity and is the fourth leading cause of end-stage renal failure in the world, affecting more than 500,000 U.S. citizens and millions more worldwide. It is the most common single-gene disorder that is potentially lethal. Annual costs to treat ADPKD exceed 1 billion dollars for dialysis, renal transplantation and regular management of other complications secondary to the disease (1).

ADPKD is caused by mutations within either of two genes, PKD-1 and PKD-2. Both genotypes are characterized by the progressive enlargement of innumerable cysts derived from tubules that lead to an overall progressive increase in the size of the kidneys. Over the past decade knowledge of the molecular and cellular pathogenesis of ADPKD has significantly increased. The PKD genes have been identified and the functions of their protein products have been defined (2).

ADPKD is a bilateral condition, although the absolute changes in kidney size may be asymmetric. The progressive increase in kidney size is associated with considerable morbidity throughout the life of individual patients, and include 1) abdominal pain, 2) gross hematuria, 3) hypertension at an early age, 4) renal stones, 5) renal infections, 6) cosmetic deformity of the abdomen and 7) renal insufficiency in those older than 50 years of age (3-11). ADPKD is in fact a systemic illness. In addition to the kidney, cysts are frequently found in the liver, pancreas, arachnoid and less frequently in the spleen and testis. Aneurysms of the cerebral arteries occur in approximately 5 - 10 % of patients with ADPKD, and abnormalities of the heart valves are detected in approximately one-fourth of patients.

The hallmarks of ADPKD are innumerable fluid-filled cysts scattered throughout both kidneys that cause the total renal size to increase many times greater than normal. In affected individuals, enlargement of the kidneys generally progresses steadily culminating in renal insufficiency in more than 50 %, although the age of onset of renal failure is highly variable. Examples of end-stage renal disease (ESRD) in the first year of life have been reported, but it is also common knowledge among nephrologists that patients with well-developed ADPKD may live beyond 80 years of age without serious impairment of renal function. Consequently, it is impossible to predict from clinical information the long term course of the disease in young, asymptomatic patients.

In patients with a positive family history, the diagnosis of ADPKD is established by the demonstration of bilateral renal cysts defined by ultrasound, computed tomography, magnetic resonance imaging or direct surgical inspection. The disease exhibits a dominant mode of genetic transmission with complete penetrance. Genetic linkage to markers on chromosomes 16 and 4 have been used in relatively large families to determine those without renal cysts who may be at risk for ADPKD and more recently mutation analysis has become commercially available.

Although all patients who inherit ADPKD develop cysts within the kidneys, there is substantial variability in the occurrence of renal failure. Several groups of investigators in North America and Europe have explored the age of onset of ESRD (12-19). Patients with ADPKD most commonly develop ESRD in the sixth decade of life. In the Modification of Diet in Renal Disease study (MDRD), ADPKD subjects with GFR values between 25 and 55 mL/min per 1.73 m2 lost GFR at a rate of 5.8 mL/year, whereas in non-ADPKD participants (chronic glomerulonephritis, hypertensive renal disease, etc) GFR decreased 3.1 mL/min per year. Once the GFR begins to decrease the typical course is one of inexorable decline in filtration culminating in death from uremia, unless the patient is rescued with dialysis and/or renal transplantation. The rate of functional decline can be highly variable among unrelated individuals with ADPKD as well as between members of the same family. This suggests that factors in addition to the inherited mutations determine the rate of functional decline.

As for many other chronic, progressive disorders, GFR is a poor marker of renal function in ADPKD. GFR levels remain at levels well within the normal range for many years during which time renal cysts occupy progressively increasing fractions of total renal volume (12-19). Compensatory adjustments in glomerular filtration and tubular reabsorption help to maintain the GFR on a nearly even keel until the loss of filtering units falls below the minimum required to maintain the filtration rate normal. At this juncture, GFR falls in a linear, precipitous decline.

2.2.2. ADPKD Disease Progression

Cysts have been found in the kidneys of first trimester fetuses that carry one of the ADPKD mutations. More typically, the disease goes unnoticed until it is discovered in the course of a physical examination or by ultrasound or computed tomographic testing. Dissection studies of kidneys in the early stage of disease development indicate that the cysts may arise in all segments of the nephron and collecting ducts. More recent studies using immunohistochemistry or hormonal responsiveness in cyst-derived cultured cells suggest a predominant origin from collecting ducts. Close examination of the cysts by light and electron microscopy has revealed evidence that adjacent parenchyma is compressed along with infiltration into the interstitium of mononuclear cells in association with fibrosis. It is important to emphasize that the cysts appear to develop in only a small fraction of the nephrons and collecting ducts, perhaps fewer than 1% (20). The distribution of the cysts may be highly asymmetric within and between the kidneys.

The tubule basement membrane surrounding the individual cysts are typically thickened and laminated. In early stages of the disease examined by light microscopy, the adjacent renal parenchyma appears to be uninvolved. On the other hand, studies of cell proliferation and apoptosis markers indicate that the adjacent non-cystic renal tubule cells may respond to a proliferative stimulus similar to that observed within the epithelial cells lining the cysts.

As the disease progresses, the size of the individual cysts increases, but whether the number of cysts increase is not known. There is a progressive decrease in non-cystic parenchyma which has led researchers to suggest that the enlarging cysts crowd out the normal parenchyma in the same way that solid neoplasms displace and erode tissues in which they arise. As the cysts enlarge and the total kidney size increases, the volume of non-cystic parenchyma, on which the function of the kidneys depend, declines. There is evidence of accelerated apoptosis in the renal cysts and the adjacent non-cystic parenchyma. In later stages the interstitium expands owing to the accumulation of collagenous material

and frank fibrosis together with foci of mononuclear cells. The distortion of the interstitium involves the peritubular capillaries, veins and arterioles, in association with the sclerosis of small and medium-sized arteries (20).

In the terminal stages of the disease, glomeruli are commonly globally sclerotic which more typically reflects an antecedent scarring process within afferent arterioles in contrast to the focal sclerosis pattern of glomeruli subjected to abnormal transcapillary hydrostatic pressure. Non-sclerotic glomeruli appear enlarged, reflecting compensatory hypertrophy. Mild to moderate proteinuria is observed in ADPKD and appears to be a harbinger of poor prognosis for overall renal function. At the end-stage, polycystic kidneys are typically enlarged, sometimes more than 10 times greater than normal. The end-stage polycystic kidney is comprised primarily of fluid trapped in cysts varying in size from a few microliters to more than 100 mL. The surface of the kidney is typically laced with bands of fibrotic material. On the cut surface, the cysts stand out as distinct cavities between strands of scar tissue. Normal parenchyma is rarely seen.

Alterations in the interstitium adjacent to cysts can be observed early in the course of the disease in human patients. Several studies have suggested that tubulo-interstitial changes may be important in the development of renal insufficiency in human ADPKD (21-23). ADPKD is associated with polycystic liver in the majority of patients. The liver cysts are usually not detected until late in the course of the disease, but in some women the livers may reach a very large size. In these unfortunate patients partial hepatectomy or liver transplantation may be required to achieve an acceptable quality of life.

2.2.3. Future Approaches to Therapy of ADPKD

Signal transduction pathways and pathophysiologic mechanisms have been defined to the point that therapeutic trials are being planned to investigate the potential effects of novel molecules to slow the rate of disease progression (24). The use of these new compounds is dependent upon the development of accurate measures of disease progression that can be used for prospective studies.

In the broad field of Nephrology, the preservation of GFR is held to be the major goal of treating most progressive renal disorders. It is important to note, however, that a disease like ADPKD has morbidities that diminish the quality of life of patients long before kidney function declines to the point that requires renal replacement therapy. Several major morbidities (hypertension, pain, gross hematuria, stone, abdominal distension, renal infection) appear to be linked to the progressive enlargement of the kidneys due to the cysts. Consequently, goals of ADPKD therapy include relieving the suffering caused by enlarged kidneys by limiting the growth of cysts. As noted previously, verifiable changes in GFR occur relatively late in ADPKD after major damage has been done by the cysts and fibrotic mechanisms have been activated. Thus, GFR is not a useful indicator of therapeutic effectiveness in the early stages of the disease if a major goal of therapy is to prevent the growth of the cysts to prevent their secondary effects to destroy renal structure and ultimately, reduce renal function. In order to treat the disease before irreversible damage is done, a more sensitive and pertinent marker of disease progression is needed.

2.3. CRISP I Study: Objectives and Observations

2.3.1. Study Objectives

In 2000, PKD researchers at the University of Alabama, Emory University, University of Kansas, Mayo Clinic and Washington University St. Louis joined together to create the Consortium for Radiologic Studies of Polycystic Kidney Disease (CRISP I). This consortium of Participating Clinical Centers (PCCs) and a Data Coordinating and Imaging Analysis Center (DCIAC) developed and implemented studies to

test whether imaging techniques could provide accurate and reproducible markers of progression of renal disease in patients with PKD. The Steering committee, comprised of principal investigators from the PCCs and DCIAC, developed initial study protocols for the imaging studies and proceeded to collect and analyze radiologic and clinical data over the last 5.5 years.

The primary objectives of this investigation were to: (1) to develop and test the accuracy and reproducibility of imaging techniques to monitor changes in renal cyst size and parenchymal involvement in well characterized cohorts of patients with PKD to assess their utility as surrogate markers of disease progression, (2) to establish and maintain a database of uniformly and accurately collected information including renal functional parameters and other selected markers of disease progression identified by the DCIAC and the PCCs, to correlate parenchymal involvement with renal functional changes in PKD patients with various rates of progression, and (3) to maintain and make available such data to facilitate the planning and implementation of clinically appropriate interventions in the near future.

The goals of CRISP II are to extend the observations of CRISP I in order to: 1) draw unequivocal linkage between the rate of kidney/cyst enlargement and qualitative (signs and symptoms) and quantitative (declining renal function reflected in iothalamate clearance and albuminuria) end-points; 2) to provide a marker of disease progression (kidney volume) sensitive and accurate enough to be used as a primary outcome marker in clinical trials aiming to forestall disease progression; 3) to develop and test other biomarkers of disease progression.

2.3.2. CRISP I Study Observations

The CRISP I consisted of a cohort of 241 individuals (145 women, 96 men) with ADPKD screened from a total of 289 eligible subjects; 235 subjects remained in the study at the end of the 3rd year of study, a remarkable rate of retention. The cooperation and synergies evinced among investigators of diverse scientific backgrounds in the Patient Coordinating Centers (PCCs) and Data Coordinating and Image Analysis Center (DCIAC) has been remarkable. Accomplishments of the group effort are listed below:

2.3.2.1. Method to Determine Total Kidney and Total Cyst Volumes

A novel MR-based method to measure and to quantify total renal volume (TKV) and total renal cyst volume (TCV) was developed and rigorously tested in subjects with ADPKD (25, 26). MRI-based morphometric methods were shown to reproduce total kidney and cyst volumes in phantoms with reliability coefficients of 99.9% and 89.2%, respectively. The coefficient of variation of total kidney volume measurements by stereology in 4 subjects studied at each of the 4 PCCs was 3.5%. Statistical models for describing the changes over time have been developed and used for analytic purposes. The longitudinal measurements can, and have, been used for planning intervention trials with imaging endpoints, allowing quantitative information about the tradeoffs of the number of participants, the length of follow-up and the frequency of assessment.

2.3.2.2 MR- versus Ultrasound-based Volumetry

Ultrasound was determined to be sufficiently accurate to determine renal cystic involvement for screening and enrollment into CRISP I and could determine very large differences in total renal volume utilizing both the ellipsoid formula and longitudinal length measurements. Within and between observer variability of total renal volume measures were significantly greater with ultrasound vs. MR. Ultrasound was of insufficient accuracy for longitudinal measurements of change in renal volume in contrast to MR. Thus, although ultrasound will be an important tool for screening individuals at risk for ADPKD prior to enrollment in therapeutic trials, it is not useful as a measurement tool to quantify progression of renal volume over relatively short intervals of time.

2.3.2.3. Asymmetry of Renal Enlargement

Cyst development was frequently found to be asymmetric, although on the whole the average left kidney volume exceeded right kidney volume by 19.3%. The greatest asymmetry was 163%, left > greater than right; by contrast the right kidney volume maximally exceed that of the left by 48%. The median Left vs. Right ratio of 1.091 reflects the fact that 163 left kidneys were larger than the matched right kidney. The biologic implications of this renal volume asymmetry are not clear, but the finding does suggest that the germ cell mutation, which is found in all of the renal cells, is probably not the sole determinant of how fast kidney cysts may enlarge.

2.3.2.4. Hypertensive versus Normotensive Subjects

Sixty four participants were normotensive at enrollment into CRISP I. Twenty two have subsequently developed hypertension at a mean time 2 years after enrollment into CRISP I. Age, body mass index, weight and serum creatinine concentrations were significantly greater in those who developed hypertension in comparison to those who remained normotensive. At this time we have insufficient power to determine if renal or cyst volume enlargements are greater in those who develop hypertension. Hypertensive subjects demonstrated a significant increase in total renal volume, cystic volume and % change in renal volume from baseline that was not detected in the normotensive or newly hypertensive CRISP participants (Figure 2.1.). Systolic and diastolic blood pressure levels measured throughout the three year follow up of CRISP I were directly related to the rate of renal enlargement in both treated hypertensive ($r=0.21$, $P<0.03$) and untreated normotensive ($r=0.38$, $P<0.02$) individuals. Hypertensive subjects demonstrated a significant decline in renal function determined by both iothalamate clearance (Figure 2.2.) and serum creatinine measurements (Figure 2.3.), while no change in renal function occurred in the normotensive individuals or those who became hypertensive in the course of the study.

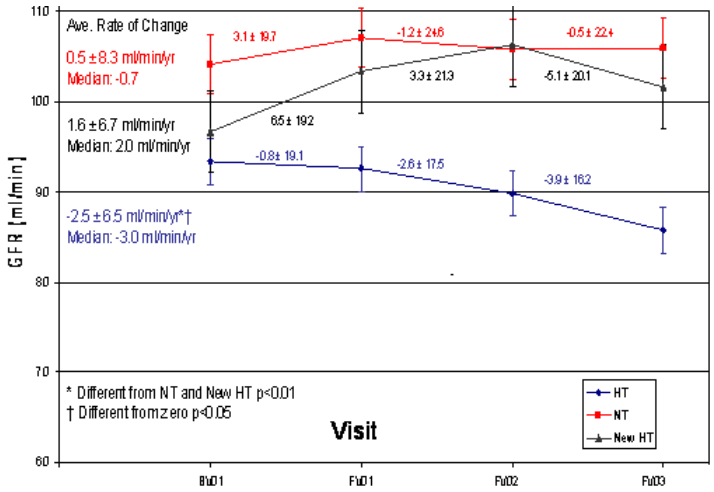


Figure 2.1. GRF by Visit

Annual rate of change in glomerular filtration rate measured by iothalamate renal clearance in normotensive (squares), new hypertensives (triangles) and hypertensives (diamonds) in CRISP I. A significant decline in glomerular filtration rate was found in the hypertensive (-3.0 mL/yr/1.73m^2) subjects that was significantly different from both normotensives and new hypertensives.

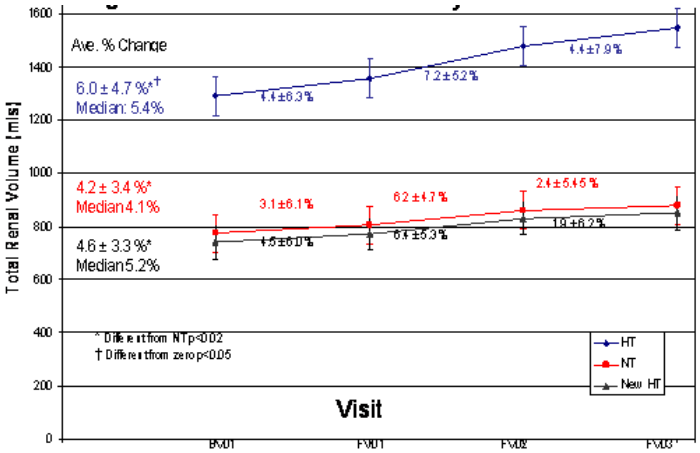


Figure 2.2. **Total Renal Volume by Visit**
Annual rate of change in renal volume in normotensive (squares), new hypertensives (triangles) and hypertensives (diamonds) in CRISP I. A significant increase in renal volume from baseline was found the hypertensive subjects and a significantly greater rate of change in renal volume than in normotensive subjects.

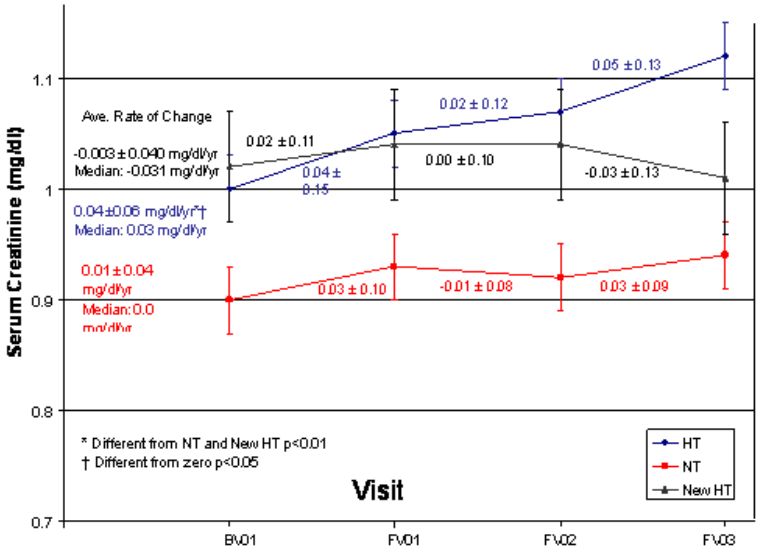


Figure 2.3. Serum Creatinine by Visit
Annual serum creatinine levels in normotensive (squares), new hypertensives (triangles) and hypertensives (diamonds) in CRISP I. The average annual rate of change was significantly increased only in the subjects who were hypertensive at baseline.

2.3.2.5. Kidney and Cyst Volumes Increase Continuously in ADPKD

There was an increase in total kidney and cyst volume from year to year in over 80 % of ADPKD subjects although the apparent rate of increase varied widely from subject to subject (27). This is illustrated in Figure 2.4. Shown are TKVs (in milliliters) for individual subjects who were female (open squares) or male (closed circles). Four sequential measurements of TKV were available for most of the individuals. As shown in Figures 2.4.-2.6., some individuals demonstrated rapid rates of increase in TKV, whereas in others renal volume increased by only a few per cent over a period of 4 years. This striking data set illustrates the clinical course of ADPKD in dramatic terms. Total kidney volume was generally less in the younger subjects than in those over age 30. The line in Figure 2.4. represents an

approximation of the upper limit of total kidney volume (TKV) in this cohort (slope =slope 100 mL/year; intercept = 0. It is important to add that total kidney volume measurements in all nineteen ADPKD subjects from the Mayo and Kansas CT volumetric studies (28, 29) fell within the maximal limit of the CRISP I cohort. A random coefficient model on log10 TKF gives a mean (SD) intercept (baseline visit) of 2.96 (0.25) and a slope of 0.022 (0.014) corresponding to 910 mL and an average 5.2% growth.

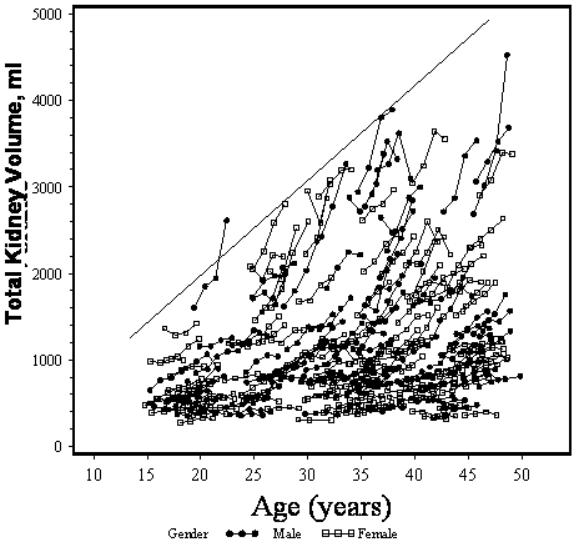


Figure 2.4. Time-course plot of TKV growth curves.

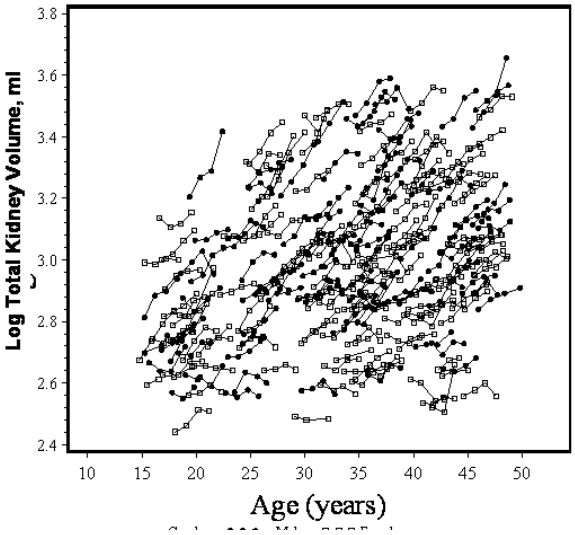


Figure 2.5. Time-course plot of TKV growth curves.

2.3.2.6. Patterns of Renal Volume Change

The general pattern of kidney and cyst enlargement in ADPKD patients gave the impression that the rate of kidney enlargement was non-linear (Figure 2.4.). Indeed, in a semi-log plot total kidney volume appeared to increase as a logarithmic function of age (Figure 2.6.) in those cases with the most

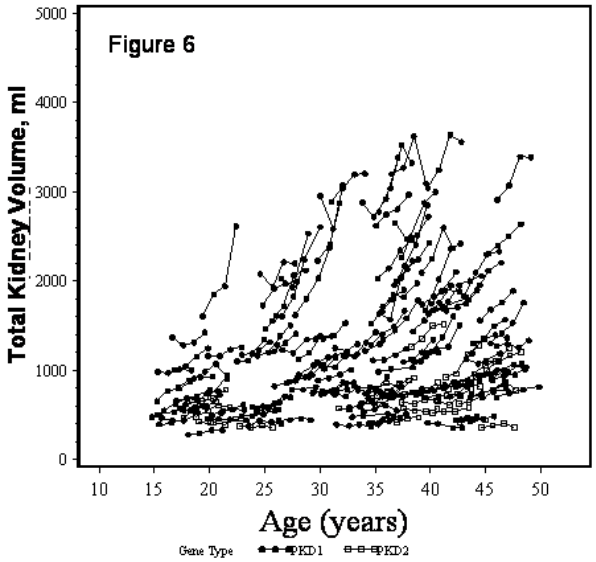


Figure 2.6. Semi-log plot of TKV growth curve.

rapid rates of volume increase. This observation is consistent with the view that mural epithelial cell proliferation within cysts progressively increases the potential cyst volume. Fluid accumulates within this potential volume by net trans-epithelial secretion of salt and water to fill and further expand the potential space created by proliferation of the mural epithelial cells. Pumping of fluid into closed compartments leads to hydrostatic pressures within the cysts that are higher than the surrounding parenchyma, a factor that may be of importance in the crowding of adjacent non-cystic parenchyma and for the propensity of these cysts to rupture and to cause hemorrhage.

It is interesting to find that each patient seemed to follow a prescribed rate of kidney volume increase from year to year. It seems reasonable to suppose that each person may exhibit a "signature" rate of kidney and cyst growth that reflects the underlying germ-line and acquired mutations. Fitting jointly a random coefficient model for each kidney provides an estimated correlation of 0.91 between the rate of growth on the right kidney to that in the left kidney. If this observation is confirmed over a longer time period, then more refined analysis might yield an instrument of great clinical utility for determining prognosis in individual patients relatively early in the course of the disease and in the selection of subjects for clinical trials.

There was considerable overlap between males and females in respect to the rate of kidney enlargement (Figures 2.4. and 2.5.), although males overall had larger kidneys at baseline.

2.3.2.7. Cyst Number Not the Rate of Growth Is Associated with the Mutated Gene

The significance of gene type to disease progression is analyzed in this study of the CRISP cohort. Gene type was determined in 183 families (219 cases); 156 (85.2%) had PKD1, and 27 (14.8%) had PKD2. PKD1 kidneys were significantly larger (Figure 2.6.), but the rate of cystic growth (PKD1 5.68%/yr; PKD2 4.82%/yr) was not different ($P = 0.24$). Cyst number increased with age, and more cysts were detected in PKD1 kidneys ($P < 0.0001$). PKD1 is more severe because more cysts develop earlier, not because they grow faster, implicating the disease gene in cyst initiation but not expansion (30).

2.3.2.8. Renal Volume and Kidney Function

Most nephrologists who work in the field think that the expanding cysts cause secondary structural and functional changes in polycystic kidneys. To examine this possibility we separated individuals in the CRISP I cohort by gender and sorted them into 5 renal volume categories at baseline (in mL) : < 500, 501 - 1000, 1001 - 1500, 1501 - 2000, and >2000 in order to survey the potential effects of renal enlargement on outcomes (Table 1).

Mean age tended to increase in both male and female cohorts in association with kidney volume. There was a striking trend in kidney volume in subjects with the PKD2 genotype. No PKD2 individuals had kidneys larger than 1500 mL and most were less than 1000 mL. This fact is also illustrated in Figure 2.6. The PKD2 subjects (open squares) clearly exhibited lower values for TKV than age-matched PKD1 subjects. Approximately 90% of the CRISP I cohort has been successfully genotyped. It has been established that PKD2 patients develop ESRD approximately 16 years later than patients with PKD1 (31). This fact, together with the new data in Figure 2.3. that PKD2 subjects have smaller (less cystic) kidneys than age-matched PKD1 subjects strongly supports the hypothesis that total kidney and total cyst volume have dominant roles in promoting ESRD in these patients.

Table 1

Males TKV	Age	%PKD2	% Hypertensive	Corrected IOTH base	Change in GFR Baseline - Year 3 Ioth	Coc-Gault	cr UV/P	Ualb ug/d	UMCP-1 ng/mg crea
<500	22.9	40.0	35.7	116.1	8.5	-15.5	0.8	39.6	223
501-1000	32.1	34.5	45.9	123.3	12.6	-3.0	-11.1	23.6	347
1001-1500	35.1	0.0	80.0	109.0	-7.7	-11.2	-2.5	44.0	456
1501-2000	32.0	0.0	92.3	108.5	-2.9	-10.4	-2.4	58.7	799
>2000	37.6	0.0	100.0	101.7	**-24.2**	**-25.6**	**-20.8**	120.9	711
Females									
<500	29.5	25.0	15.4	112.3	2.8	3.0	0.0	21.5	376.3
501-1000	31.6	23.1	60.3	103.4	-4.4	-2.5	-3.0	34.1	487.6
1001-1500	33.5	10.0	76.9	94.9	-6.3	-4.8	12.2	37.6	771.0
1501-2000	37.9	0.0	75.0	83.4	-11.1	**-12.7**	-8.2	63.7	1264.1
>2000	35.0	0.0	92.9	80.6	**-23.2**	-9.6	**-8.9**	68.5	1185.3

Bold changes P < 0.05

The data in Table 1 are averages. Age, %PKD2, % hypertensive, Corrected Iothalamate Clearance, Ualbumin and UMCP-1 were measured at enrollment (Baseline). Changes in GFR (Iothalamate Clearance, Cockcroft-Gault creatinine clearance, and measured creatinine clearance over a 24h interval are differences between Baseline and Year 3 (an interval of 3 years).

At enrollment, GFR (Iothalamate) appeared to correlate inversely with TKV in males and females, a finding that was reported in a previous publication from this study (32) and is illustrated in Table 1. Table 1 also indicates that clear-cut changes in GFR, reflected by significant decreases in Iothalamate, Cockroft-Gault and measured creatinine clearances, occurred in relation to the increase in renal volume. In the >2000 mL TKV groups, significant paired decreases in iothalamate, Cockroft-Gault estimated creatinine clearance and measured creatinine clearances were observed in the fourth year of observation. Declines in relation to increasing renal volume were also found in relation to urinary albumin excretion and the excretion of the chemokine, Monocyte Chemotactic Protein-1 (MCP-1). Urine albumin and MCP-1 excretion appear to rise above normal levels (> 26 ug/d; > 263 pg/mg creatinine, respectively) relatively early in the course of the disease and may be alternative markers of disease progression before changes in GFR can be detected.

These preliminary findings suggest that further refinement of the renal volume indicator of disease progression may yield even more powerful predictive tools for managing this disease. Moreover, based on the CRISP I and the combined Mayo-Kansas University CT studies reported previously (28, 29), it is clear that sequential measurements of Total Kidney and Total Cyst volumes reliably portray disease progression.

2.3.2.9. Developing a Marker of Disease Severity

We have made a step toward the goal of developing an age-adjusted index of total renal volume progression (Progression Severity Index, PSI). In preliminary calculations, the TKV of each subject in the CRISP I cohort was compared on enrollment to that of the most advanced cases in the combined CRISP I and Mayo-Kansas University cohorts (28, 29). The PSI was determined from the ratio of the measured TKV (subject)/ Maximal TKV in the CRISP I cohort (estimated from the equation for the line defining Age vs. Maximum TKV in Figure 2.4.) determined for each subjects age at baseline. When multiplied by 100, the PSI is the percentage of maximal kidney volume for the stated age of the subject. We found in a

preliminary analysis that PSI was directly correlated with a) declining GFR, b) increased urine albumin excretion and c) onset of hypertension.

This, or an index based on a regression on age, is a promising new way to select subjects with minimal, moderate or severe ADPKD for clinical trials and possibly to judge prognosis.

2.3.2.10. Disease Severity in African Americans

African Americans (n=28) demonstrated significantly smaller renal (896 vs. 1178 ml) and cyst volume (423 vs. 565 mL) than their non-African American (n=215) counterparts. AA and non-AA were similar with regard to age, gender distribution, weight, body mass index, and age of diagnosis of ADPKD. A similar inverse relationship between total renal volume and GFR was present: AA: r= -0.43, P<0.004, non-AA: r=-0.40, P<0.0001). In those with confirmed PKD1 and PKD2 mutations, PKD1 AA demonstrated significantly smaller renal and cyst volumes than their non-AA counterparts. Two findings need to be explored further: 1) the prevalence of the PKD2 genotype appears to be greater in AA than in non-AA and mutation identification needs to be completed in all participants and 2) measurements of the renin-angiotensin-aldosterone system (Approved Ancillary Study in CRISP I and proposed in this application) to determine if activation of the RAAS is relatively suppressed in this African American cohort. Further studies are needed to clarify this potentially important racial difference in disease severity.

2.3.2.11. Validation of MR-based Renal Flow Measurement

An MR-based method to measure renal blood flow was developed and validated in phantoms, healthy controls and ADPKD individuals at Mayo College of Medicine and Emory University. Steady-flow measurements with a PVA phantom that has mechanical and magnetic properties reflecting those of vessel wall and internal diameters ranging from 3 to 11 mm demonstrated close agreement between actual and MR estimated flows (r=0.991) with an average overestimation of 0.9$\pm$4.9%. Pulsatile-flow measurements showed 0.6–4.1% errors of estimated flow rates, using 14 or 20 cm FOVs, a 5 mm tubing and actual flow rates of 315 or 540 mL/min. Reproducibility was evaluated through blinded repeated analysis by two radiologists of data sets from 19 patients. Average intra-reviewer CVs were 1.4% and 1.2%. Intra-class correlation coefficients were 0.987 and 0.983. The average inter-reviewer CV was 2.5% with a reliability coefficient of 0.983 (31).

Further validation studies have been performed in healthy volunteers to assess the reproducibility of the measurements using independent acquisitions and the effect of gadolinium administration. Immediate repetition of a flow scan showed a standard deviation of 17.5 mL/min on average, corresponding to a mean CV of 2.9%. Repetition of the scan including the plane scouting process showed a standard deviation of 34.2 mL/min on average, corresponding to a mean CV of 6.0%. The mean flow following gadolinium administration was on average 6.64 mL/min higher than pre-contrast flow.

2.3.2.12. Cross-sectional Study of RBF

One hundred twenty-seven participants, forty-six male and eighty-one female (32.9±8.2 years of age) had MR RBF measurements at baseline at the Mayo Clinic or Emory University. Forty of them (31.5%) had multiple renal arteries. Left kidneys were larger than right kidneys and had more severe disease. RBF was lower in the left kidneys. Right and left kidney volumes, cyst volumes, and percent cyst volumes were inversely correlated with the ipsilateral RBF. Iothalamate clearances were inversely correlated with age and kidney volume and positively correlated with RBF. When considered alone, age, diagnosis of hypertension, kidney volume and RBF were all significant predictors of GFR. In the multiple-variable model, however, only age and RBF were significant independent predictors (31).

2.3.2.13. Longitudinal Analysis and Predictive Value of RBF

To determine whether RBF changes over time, participants at Mayo Clinic and Emory University underwent determinations of RBF at 1, 2, and 3 years after the baseline studies. After 3 years of follow-up, RBF had significantly declined and TKV and TCV had significantly increased, while GFR had remained stable. Correlation and multiple regression analysis were used to examine the effects of age, gender, body mass index, hypertension status, mean arterial pressure (MAP), TKV, RBF, GFR, serum uric acid, HDL and LDL cholesterol, urine sodium excretion (UNaE) and UAE on GFR and TKV slopes. TKV, TCV, RVR, serum uric acid, UAE, UNaE, age, BMI, MAP, and estimated protein intake were positively and RBF and GFR negatively correlated with TKV and TCV slopes. TKV, TCV, RBF, RVR, UNaE, and UAE were independent predictors of TKV and TCV slopes. TKV, TCV, and MAP were negatively and RBF positively correlated with GFR slopes. Regression to the mean confounded the analysis of GFR slopes. TKV, TCV, and RBF were independent predictors of GFR decline. These results suggest that RBF reduction a) parallels TKV increase, b) precedes GFR decline, and c) predicts the structural and functional disease progression of ADPKD (33).

2.3.2.14. Monocyte Chemotactic Protein-1, a Disease Severity Marker

Urinary MCP-1 excretion appeared to be a marker of disease severity (Table 1). This chemokine is synthesized by renal cyst epithelial cells and may reflect a phenotypic transformation in tubular epithelium that becomes cystic (34). The CRISP I study confirms that urinary MCP-1 may increase above normal levels early in the course of the disease and may be a marker of inflammation or interstitial irregularities that are a serious consequence of cyst expansion. Since MCP-1 is synthesized by the mural epithelial cells and accumulates to very high levels in cyst fluid. To find its way into the final urine, however, cysts must be in direct communication with the urinary collecting system. Since most macroscopic cysts larger than a few millimeters in diameter have no connections to the urinary collecting system, the major source of MCP-1 in the final urine may be relatively small cysts that remain hydraulically connected to the tubules from which they derived. Thus, it is tempting to speculate that urinary MCP-1 may reflect the contributions of relatively small cysts that may have been newly formed. If that hypothesis can be confirmed, MCP-1 might be useful as a surrogate marker of disease activity early in the course of the disease in individuals with relatively small cysts.

2.3.2.15. Liver Cysts

Hepatic cysts were found at greater prevalence than previously reported in all age groups: 83% overall, and 58% in 15 to 24, 85% in 25 to 34, and 94% in 35 to 46 age groups; 85% in women (57%, 91%, and 95% from the younger to the older subgroups, respectively); and 79% in men (60%, 75%, and 93%, respectively). The high prevalence of hepatic cysts in the current study cohort of relatively preserved renal function indicates that the relatively late onset of the liver abnormality in some subjects is not the consequence of a uremic environment. The detection of cysts in relatively young subjects exemplifies the superiority of MRI over ultrasound for imaging small cysts, and probably accounts for the larger prevalence in early stage disease than published previously. The prevalence of hepatic cysts was directly related to renal volume ($\chi 2 = 4.30$, $P = 0.04$) and to renal cyst volume ($\chi 2 = 5.59$, $P = 0.02$). A wide range of hepatic cyst burden was observed (0 to 4673 mL, a logarithmic transformation mean of 3.20 mL). Furthermore, we found that hepatic cyst volume was significantly greater in women than in men (5.27 vs. 1.94 mL) ($P=0.003$). The average hepatic cyst volume was 0.25, 5.75, and 22.78 mL in sequential age groups, respectively ($P < 0.0001$). Hepatic cyst volume and renal volume correlated ($r = 0.22$, $P = 0.001$). Mean renal volume was greater in subjects with than those without hepatic cysts (1004 vs. 712 mL) ($P =0.0005$) (35).

2.3.2.16. Complex Renal Cysts

Complex renal cysts, a marker of renal complications including cyst hemorrhage, developed in over 80% of the CRISP I cohort and were significantly associated with the total renal volume (r=0.67) and renal cyst volume (r=0.66). These findings demonstrate a potential renal imaging marker to predict structural disease severity. In our preliminary study of 70 subjects with complex cysts, we found the mean complex cyst volumes were 5 mL in 15 to 24, 21 mL in 25 to 34, and 21 mL in 35 to 46 age groups. The youngest age group was significantly different from the other two groups. Women had larger complex cyst volume than men (mean 20 vs. 12 mL), but without statistical significance. No statistically significant difference (p=0.47) in complex cyst volume was observed between the subjects with and without a history of hematuria.

2.3.2.17. Comparison Between GFR Methods

To study the natural history of ADPKD, accurate assessment of changes in GFR over time (GFR slope) is needed. A study in patients with baseline moderate to severe hypertensive chronic kidney disease (GFR < 65 mL/min per 1.73 m2) found equivalent results between iothalamate clearance and the MDRD equation. However, subjects in CRISP had normal or near normal renal function at baseline (creatinine clearance >70 mL/min). Furthermore, several recent studies have suggested that estimated GFR with serum creatinine based equations is not accurate in populations with predominantly normal renal function.

Table 2

	Odds ratio for a decline in GFR (-5% or lower annually)		
Predictor	Iothalamate Clearance	MDRD Equation	Creatinine Clearance
Cyst Volume			
> 500 mL	4.1 (2.3 to 7.4)*	2.3 (1.3 to 4.0)*	1.5 (0.8 to 2.6)
≤ 500 mL	1	1	1
Hypertension			
Present	3.5 (1.9 to 7.1)*	2.7 (1.5 to 5.1)*	1.1 (0.6 to 2.0)
Absent	1	1	1
ACR			
> 30 mg/g	3.1 (1.7 to 5.6)*	1.9 (1.1 to 3.4)*	1.4 (0.8 to 2.6)
≤ 30 mg/g	1	1	1
Age Group			
> 40 years	2.6 (1.1 to 6.0)*	1.3 (0.6 to 2.9)	1.2 (0.5 to 2.7)
25 to 40 years	1.5 (0.7 to 3.2)	1.4 (0.7 to 2.9)	1.1 (0.5 to 2.3)
< 25 years	1	1	1

To investigate this further, we compared GFR slope by different methods with respect to baseline predictors in the CRISP cohort (n=241) (36). Each subject had up to four annual GFR measures by three different methods: a 2 hour iothalamate clearance, a 24 hour creatinine clearance, and the abbreviated MDRD equation. For each individual, lothalamate GFR was regressed on time from baseline to generate a percent slope (annual percent change in GFR). A decline in GFR was defined as a slope of -5% or lower annually. Predictors for a decline in GFR were compared between methods. These baseline predictors included kidney cyst volume, hypertension, urine albumin to creatinine ratio (ACR), and age. As shown in the following table, associations were stronger between predictors and a decline in GFR by iothalamate clearance slope than by the MDRD equation slope. There were no statistically significant associations by creatinine clearance slope. Based on these findings, continued measurement of GFR by

iothalamate clearance is needed to understand the natural history of ADPKD. Changes in muscle mass or dietary protein over time may confound a serum creatinine based equation slope and lead to erroneous conclusions.

2.3.2.18. Genotyping Studies of CRISP Subjects

Mutation screening has been completed on 239 CRISP patients (including inferred information on two family members from which we do not have samples) from 202 families, 32 of which are multiplex within the study. It involved amplifying the coding regions of PKD1 and PKD2 as 82 fragments and analysis of the products by DHPLC. Mutation negative samples, ones with missense, in-frame deletions or atypical splicing changes, and controls were sent to Athena Diagnostics for sequencing (total 150). Large deletions were also screened in persistent mutation negative cases. An algorithm was developed to predict the pathogenicity of missense and atypical splicing changes including the chemical significant of substitutions, evolutionary conservation in orthologs to fish and in homologous proteins, and population data, including segregation in pedigrees and analysis of normal controls.

Using this comprehensive screening approach, mutations were determined in 182 pedigrees (90.1%), representing 213 patients. Linkage identified this disease gene in three further families (8 patients). One hundred and fifty seven families are PKD1 (85.2%) and 27 PKD2 (14.8%), similar ratios to previous studies of clinical ADPKD populations.

For the PKD1 population, 107 (66.5%) have truncating mutations (frame shifting, nonsense or splicing), 43 (27.7) were missense changes and 9 (5.8%) in-frame deletions/insertions. In the PKD2 families, 22 (84.6%) were truncating, 3 (11.1%) missense, and 2 in-frame deletions (7.4%). Although the majority of changes were unique to a single family, 53 (29.1%) were due to a recurrent mutation.

Comparisons of PKD1 and PKD2 patients showed that baseline kidney and cyst volumes are significantly larger in PKD1 than PKD2. However, the rate of growth of kidney and cyst volume as measured at a Log10 was not significantly different between the two genotypes. Counting of cysts shows that PKD1 kidneys have more cysts and so indicate that the milder disease in PKD2 is due to less cyst development rather than slower cyst growth.

2.3.2.19. Determinants of Renal Volume in ADPKD

CRISP showed that progressive renal enlargement in ADPKD mimicked exponential-like growth. In our recent study (27), we explored the basis of this renal enlargement by determining the selective and combined effects of cyst initiation rate, total cyst number and cyst growth rate on the time-dependent change of total cyst volume (TCV). We used dynamic models of spherical cysts composed of proliferating mural epithelial cells and fluid-filled cavities together with enabling equations incorporating cyst surface area, cyst volume and an invariable growth rate constant to compute the time-dependent change in volume of solitary spherical cysts or of multiple cysts swelling collectively. The volume of individual cysts increased exponentially. Multiple expanding cysts enlarged TCV in an exponential-like pattern even when individual cysts formed at different rates, thereby leading to different numbers of cysts, or exhibited different but invariable growth rate constants. TCV depended on the rate of cyst initiation and on the total number of cysts; however, the compounding effect of exponential-like growth was the most commanding determinant of long-term TCV expansion. Extrapolation of TCV data plots for individual CRISP subjects back to age 18 years predicted rational TCV values.

We conclude that: 1) cysts initiated early in life contribute most to TCV; 2) cyst growth rate determines renal size primarily, although the tempo of formation and the ultimate number of cysts contribute as well; 3) there is similarity in the patterns of expansion of renal cysts and the growth of solid tumors; and 4) the good fit between the exponential models and the extrapolated CRISP data indicates that the TCV growth rate is a defining attribute for individual patients.

2.4. CRISP II Study: Overview and Specific Aims

2.4.1. Overview of Study Design

The CRISP II Study is a prospective, observational study that is an extension of CRISP I. CRISP I was also a prospective, observational study that enrolled 241 ADPKD subjects between the ages of 15 and 45 years and was designed to determine if novel imaging techniques such as magnetic resonance (MR) imaging could reliably and accurately detect change in renal structure early in the course of APDKD. It is anticipated that 220 CRISP I subjects are available to enroll in CRISP II. CRISP II is designed to include all CRISP I individuals including those who enroll simultaneously in other clinical trials. In this respect, HALT, an ongoing interventional trial of the PKD Clinical trials network may maximally enroll up to 105 subjects in Study A (which includes MR imaging identical to that proposed in this submission) and 32 subjects in Study B (no MR imaging). Importantly, the Principal Investigator (Dr. Ty Bae) and personnel for the Imaging Center (now at the University of Pittsburgh) for both HALT and CRISP II are the same. The CRISP/HALT liaison committee has reviewed and approved dual participation in both CRISP II and HALT and the CRISP and HALT Steering Committees have approved the development of CRISP II.

To minimize subject burden and to maintain retention throughout CRISP II, those CRISP II individuals who also participate in HALT will not undergo duplicate imaging, blood pressure measurements or blood sampling. They will, however, complete the necessary studies of CRISP II that are not included in HALT.

The goals of CRISP II are to extend the observations of CRISP I in order to: 1) draw unequivocal linkage between the rate of kidney/cyst enlargement and qualitative (signs and symptoms) and quantitative (declining renal function reflected in iothalamate clearance and albuminuria) end-points; 2) to provide a marker of disease progression (kidney volume) sensitive and accurate enough to be used as a primary outcome marker in clinical trials aiming to forestall disease progression; 3) to develop and test other biomarkers of disease progression.

2.4.2. Specific AIM 1

Extend the preliminary observations of CRISP I to ascertain the extent to which quantitative (kidney volume and hepatic and kidney cyst volume) or qualitative (cyst distribution and character) structural parameters predict renal insufficiency and develop and test new metrics to quantify and monitor disease progression. Hypotheses to be tested in this aim are:

a) Increased renal volume in general and all renal volumes > 750 mL adjusted for age and other significant covariates in CRISP I predict rate of loss of renal function as well as progression to specific endpoints, e.g. KDOQI Stage IV, ESRD, and/or death.
b) Baseline medullary vs. non-medullary cyst volume and cyst number in CRISP I predict loss of renal function over time.
c) Prediction models (formulas) utilizing age and renal volume at baseline in CRISP I will effectively predict loss of renal function over time.
d) Baseline liver cyst volume adjusted for the appropriate variables predicts rate of increase in liver cyst volume in CRISP I participants.

2.4.3. Specific AIM 2

Extend the preliminary observations of CRISP I to ascertain the extent to which age and sex-adjusted measurements of renal blood flow by MR technology predict the rate of renal growth; and, renal blood flow and kidney volume predict the rate of renal function decline in ADPKD**.** Hypotheses to be tested in this aim are:

a) Baseline renal blood flow predicts the rate of increase in renal volume in CRISP I participants
b) Baseline renal blood flow, independent and in addition to baseline renal volume, predicts loss of renal function in CRISP I participants
c) Combining longitudinal measures of renal blood flow and renal volume may enhance the capacity to predict loss of renal function in CRISP I participants.

2.4.4. Specific AIM 3

Collect DNA samples and clinical information from CRISP family members known to have ADPKD for use to examine genotype-phenotype relationships and by independently funded studies to identify genetic modifiers. Hypotheses to be tested in this aim are:

a) Genetic heterogeneity and mutation type and/or location affect disease severity in the CRISP population.
b) Genetic factors that modify the renal and hepatic phenotypes will be detected by a genome-wide association study employing a high resolution SNP array (this hypothesis will be examined using the CRISP population by an ancillary study to be submitted as a separate RO1 application in February 2007).

2.4.5. Specific AIM 4

Maintain and expand a database of uniformly and accurately collected information including renal structural and functional parameters and a repository of biological samples which can be used by ancillary or independently funded studies initiated by CRISP or non-CRISP investigators. An ancillary study that during CRISP I began to examine whether urine MCP1 (a product of cyst formation and growth excreted in increased amounts in baseline urine collections) concentrations predict clinical renal imaging patterns and disease course will continue during CRISP II. Hypotheses to be tested in this aim are:

a) The pattern of urinary excretion of MCP1 in individual patients remains consistent over time.
b) Baseline urinary excretion of MCP-1 predicts total kidney volume and total cyst volume and number, loss of renal function, and progression to specific endpoints, e.g. KDOQI Stage IV, ESRD, and/or death.
c) Urinary excretion levels of periostin and other potential markers identified by micro-array screening of human ADPKD tissues will also predict total kidney volume and total cyst volume and number, loss of renal function, and progression to specific endpoints, e.g. KDOQI Stage IV, ESRD, and/or death.

Chapter 3. Study Organization and Administration

3.1. Overview

The Consortium for Radiologic Imaging Studies of PKD (CRISP) includes four Participating Clinical Centers (PCCs), the Data Coordinating Image Analysis Center (DCIAC), the Project Office at the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK), a Steering Committee, and a number of subcommittees. Principal investigators and their staffs participate in the activities of the CRISP subcommittees, as does the NIDDK Program Director. An External Advisory Committee (EAC) has been formed and reports directly to NIDDK.

3.2. CRISP II Study Steering Committee

The CRISP Steering Committee is responsible for developing and implementing study procedures and protocols. The Steering Committee consists of principal investigators from the participating clinical centers (PCC) and the Data Coordinating Image Analysis Center (DCIAC), and staff physicians from NIDDK. The CRISP PCC's and principal investigators (PI's) are the Mayo Clinic in Rochester, Minnesota (Vicente Torres) and University of Alabama at Birmingham (Lisa Guay-Woodford) as a single center, Emory University in Atlanta, Georgia (Arlene Chapman), and University of Kansas Medical Center in Kansas City, Kansas (Jared Grantham). The DCIAC has been relocated from Washington University in St. Louis to currently at the University of Pittsburgh, Pittsburgh, Pennsylvania, where K. Ty Bae is the Principal Investigator and James Bost leads the Data Center-Biostatistics core. William M. Bennett from Oregon Health Science University is the Chair of the Steering Committee.

All major scientific decisions are determined by majority from the voting members of the Steering Committee. The Steering Committee has formed a number of subcommittees, made up of investigators and staff. Each PCC PI, the DCIAC PI, the Steering Committee Chair, and Dr. Catherine Meyers (NIDDK Program Director) are voting members of the Steering Committee. Principal investigators attend all Steering Committee Meetings, with co-investigators invited at the discretion of PI's. Study coordinators and other ancillary staff may also be invited to attend Steering Committee meetings at the discretion of the PI's. Contact information for Steering Committee members can be found on the CRISP website, https://www.pitt.CRISP2.edu.

3.3. National Institute of Digestive & Diabetes & Kidney Diseases (NIDDK)

Dr. Catherine Meyers serves as the NIDDK Project Director for CRISP and is a voting member of the Steering Committee. In her role as Project Director, Dr. Meyers provides scientific support for the activities of the investigators. These activities include protocol development, quality control, interim data monitoring, final data analysis and interpretation, preparation of publications, and overall performance monitoring. Dr. Meyers is also responsible for forming and coordinating the activities of the CRISP External Advisory Committee and subsequent Data Safety and Monitoring Board. Dr. Laura Moen joined the CRISP study in March, 2006, as NIDDK Project Officer, and will work with Dr. Meyers in carrying out these activities.

3.4. External Advisory Committee

An External Advisory Committee (EAC) has been selected by NIH/NIDDK to review the protocol and is made up of nephrologists, who have expertise in PKD and/or have past experience in conducting randomized clinical trials, statisticians, and radiologists. The CRISP protocol requires EAC approval before the study can begin. Once recruitment is underway, members of the EAC will serve on the Data Safety and Monitoring Board (DSMB).

The members of the CRISP EAC are as follows:

Katherine Freeman, PhD (Chair)
Director, Biostatistics
Montefiore Medical Center
111 East 210th Street
Bronx, NY 10467
Phone: 718-231-6704
Fax: 718-515-8514
Email: Kfreeman@montefiore.org

David A. Bluemke, MD, PhD
Clinical Director, MRI
Russel H. Morgan Dept. of Radiology
Johns Hopkins Medical Institutions
Baltimore, MD 21287
Phone: 410-955-4062
Fax:
Email: dbluemke@jhmi.edu

Harold Feldman, MD, MSCE
Director, Clinical Epidemiology and Biostatistics
Associate Professor of Medicine and Epidemiology
Renal-Electrolyte and Hypertension Division
University of Pennsylvania
720 Blockey Hall
423 Guardian Drive
Philadelphia, PA 19104-6021
Phone: 215-898-0901
Fax: 215-898-0643
Email: hfeldman@cceb.med.upenn.edu
njones@cceb.med.ipenn.edu

Martin Pollak, MD
Brigham & Women's Hospital
Department of Medicine
77 Ave. Louis Pasteur, HIM543
Boston, MA 02115
Phone: (617) 525-5840
Fax: (617) 525-5841
Email: mpollak@rics.bwh.harvard.edu

Terry J. Watnick, MD
Johns Hopkins University School of Medicine
Nephrology Division
720 Rutland Ave.
Ross 954
Baltimore, MD 21205
Phone: (410) 614-1650
Fax:
Email: twatnick@jhmi.edu

3.5. Data Safety and Monitoring Board

Once participant recruitment for CRISP begins, the External Advisory Committee (EAC) will become the Data Safety and Monitoring Board (DSMB). The charge of the DSMB is to regularly monitor study data, review and assess study performance, and make recommendations, as appropriate, to NIDDK in regard to: 1) performance of individual centers; 2) issues related to participant safety and informed consent, including notification of and referral for abnormal findings; 3) adequacy of study progress in terms of recruitment, quality control, data analysis, and publications; 4) issues pertaining to participant burden; 5) impact of proposed ancillary studies and sub-studies on participant burden and overall achievement of the main study goals; and 6) overall scientific direction of the study. NIDDK is responsible for organization and scheduling of DSMB meetings, while the Data Coordinating Image Analysis Center is responsible for providing the DSMB with the materials needed to complete its reviews. The DSMB will carry out its responsibilities for the duration of the CRISP studies.

3.6. Data Coordinating Image Analysis Center

The CRISP Data Coordinating Image Analysis Center at the University of Pittsburgh has operational responsibility for the design, implementation, coordination and monitoring of all aspects of the study. Specific responsibilities of the coordinating center include:

1. Developing data collection forms, manuals, and recruitment and other study materials.
2. Developing and implementing study data management and communication systems.
3. Developing and implementing protocols for MR imaging acquisition, transfer, and analysis.
4. Tracking recruitment and adverse events.
5. Performing data management and quality assurance of study data.
6. Preparing data files and documentation for use by CRISP investigators and the larger renal community.
7. Developing and maintaining both the study and public web sites for CRISP.
8. Coordinating activities of central laboratories and repositories.
9. Reporting study benchmarks and results to the Steering Committee and DSMB.
10. Arranging and coordinating study teleconferences and meetings.
11. Providing technical supports and trouble-shooting for all aspects of imaging at PCC's.
12. Collecting, evaluating, storing, and analyzing the imaging data generated by the PCC's.
13. Managing imaging data and providing image measurements for statistical analysis.
14. Providing biostatistical expertise to CRISP investigators and other users of study data.
15. Performing central training of study personnel and monitoring clinic performance.
16. Collaborating with CRISP investigators in producing, submitting, and tracking manuscripts to report CRISP study results.

3.7. Participating Clinical Centers

Responsibilities of Participating Clinical Centers include:

1. Collaborating in designing and monitoring of the study, including regularly attending Steering Committee meetings.

2. Recruiting a specified number of participants for the study according to inclusion and exclusion criteria as stated in the study protocol.
3. Performing all study procedures according to protocol and collecting data in a standardized fashion.
4. Ensuring the safety, confidentiality and ethical treatment of study participants.
5. Collaborating in analysis and dissemination of study results.

Subjects are evaluated in person at one of four participating clinical centers (PCC's), three led by CRISP principal investigators and one led by CRISP co-investigator. Each individual PCC is listed below.

- Mayo Clinic, Rochester, Minnesota
- Emory University, Atlanta, Georgia
- Kansas University Medical Center, Kansas City, Kansas
- University of Alabama at Birmingham, Birmingham, Alabama

Contact information for each PCC may be found in the CRISP website, https://www.pitt.CRISP2.edu.

3.8. Subcommittees

The Steering Committee has established six subcommittees and has appointed Chairs for each of them. These subcommittees have been established to address specific aspects of CRISP study and to provide information and recommendations to the Steering Committee in regard to the study. Additional subcommittees will be formed by the Steering Committee as required. All recommendations made by subcommittees will be submitted to the Steering Committee for review and approval within a specified timeframe. All Subcommittee recommendations must be approved by the Steering Committee prior to implementation.

3.8.1. Clinical Protocol and Recruitment – Vicente Torres, Chair

The charge of the Clinical Protocol and Recruitment Subcommittee is to deal with operational issues of the protocol from the perspective of the clinical staff. Particular attention will be paid to issues related to recruitment and retention of CRISP participants.

3.8.2. Imaging – Ty Bae, Chair

The Imaging Subcommittee is charged with developing and implementing CRISP Study Imaging protocol and analysis. The Imaging Subcommittee will also serve as the initial forum for decisions and appeals of imaging-related issues, and its recommendations will be referred to the Steering Committee for final decisions.

3.8.3. Forms – Arlene Chapman, Chair

The charge of the Forms Subcommittee is to develop CRISP study forms. All proposed forms, as well as revisions to existing forms, must be reviewed and approved by the Forms Subcommittee and, subsequently, the Steering Committee prior to implementation.

3.8.4. Genetics – Peter Harris, Chair

The charge of the Genetics Subcommittee is to develop policies to govern the use of genetic data or samples from CRISP study.

3.8.5. CRISP/HALT Liaison – Arlene Chapman and Robert Schrier

The CRISP/HALT Liaison Subcommittee was formed to address issues affecting both the CRISP and HALT studies. Its members include the NIDDK Project Manager, the Steering Committee chair from each study, and three investigators who participate in both studies.

3.8.6. Publications – Vicente Torres, Chair

The responsibility of the Publications Subcommittee is to establish policies and procedures for assigning working groups and approving CRISP-associated abstracts, presentations, and publications prior to submission. All proposed publications in which any CRISP resources will be used must first be reviewed and approved by the Publications Subcommittee and then forwarded to the CRISP Steering Committee for approval. The CRISP Publications Policy is listed in Chapter 6.

3.8.7. Ancillary Studies – Jared Grantham, Chair

The responsibility of the Ancillary Studies Subcommittee is to establish policies and procedures for assigning working groups and approving CRISP-associated ancillary studies. All proposals for ancillary studies in which any CRISP resources will be used must first be reviewed and approved by the Ancillary Studies Subcommittee and then forwarded to the CRISP Steering Committee for approval. No ancillary study may be implemented without having received prior approval from the Steering Committee. The CRISP Ancillary Studies Policy is listed in Chapter 5.

3.8.8. Data Management/Quality Control – James Bost, Chair

The Data Management/Quality Control Subcommittee meets weekly and as needed to discuss issues concerning:

- Requested modifications to the CRISP II website
- MOP updates
- Missing data and/or incomplete submissions
- Tracking and other report generation
- Data quality (both form and imaging)
- Data security
- Data analysis

The subcommittee includes Dr. James Bost and Dr. Ty Bae as well as key data management and imaging staff and the CRISP II data coordinator. Issues requiring PI input are presented for discussion at the next Steering Committee meeting.

3.9. Revisions to Study Policies and Procedures

The CRISP Manual of Procedures was developed according to the study protocol. As CRISP moves forward, it is likely that revisions to the protocol may, on occasion, be necessary. Any proposed changes to the study protocol require Steering Committee approval. Once a proposed change to the study protocol is approved by the Steering Committee, the DCIAC will incorporate such change into the MOP. Revisions to the MOP that do not affect the protocol should be addressed as follows:

Minor revisions or minor changes to the MOP will be made by the DCIAC and communicated to study personnel via email. Minor revisions are items such as a change in a lab address or a change in study personnel.

Significant revisions - As study investigators gain experience and determine best practices, suggestions for changes in study policies or procedures are likely to be made that will result in significant

revisions to the MOP. The steps involved in proposing and making a significant revision to the MOP are listed below: To suggest a change in study policies or procedures that does not necessitate revision to the study protocol, forward a draft of the proposed change, by email, to the Project Manager, Johana Schafer.

1. Ms. Schafer will circulate the draft to the members of the Steering Committee and study coordinators for review.
2. Steering Committee members and study coordinators are to review the draft of the proposed change in study policy or procedure and forward their comments and suggestions to Ms. Schafer within two weeks.
3. Ms. Schafer will revise the draft proposal, based on comments and suggestions from Steering Committee members and study coordinators and forward the final proposal to the Steering Committee for approval.
4. Once Steering Committee approval has been granted, Ms. Schafer will make the appropriate revisions to the MOP.

3.10. Laboratories

Blood and urine samples are to be collected, processed and analyzed at participating clinical sites (PCCs), local (hometown) labs, and a central laboratory (Cleveland Clinic Foundation). Additional samples are to be collected and shipped to NIDDK Repositories at Fisher BioServices and Rutgers University.

3.10.1. Required Lab Assessments

Laboratory assessments and specimen samples required for CRISP II study are as follows:

1. Serum Creatinine – Serum samples will be obtained in duplicate, one processed at the local lab and the other frozen and batch shipped to the Cleveland Clinic Laboratory
2. Total Electrolyte Panel – Sodium, potassium, chloride, total CO2
3. Lipid Panel – Total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol
4. B-HCG qualitative urine pregnancy test, for any woman who has missed a period or for whom pregnancy may be suspected.
5. Urine Tests – Albumin, creatinine, designated biomarkers (MCP-1).
6. Specimen Banking – Send serum, plasma and urine to repository at Fisher Bioservices
7. Genetic Sample – Send whole blood for consented family members or for any CRISP I participant who consents and for whom a sample is not already in storage.

3.10.2. Instructions for Participants

Study participants should be instructed to avoid medications that may alter renal hemodynamics or with potential nephrotoxicity (NSAIDS, antibiotics), or that alter serum creatinine independent of GFR (trimethoprim [Bactrim], cimetidine), for 1 week prior to all clinic visits. However, participants taking low dose aspirin (81 or 325 mg once daily) will be allowed to continue on this dose throughout the study as effects on renal hemodynamics are minimal. For a visit in which MR imaging will be done, the participant should be instructed to hold morning does of all antihypertensive medications until the imaging exam has been completed. If the participant is on any second-line antihypertensive medications that require twice daily dosing, those medications should also be held the night prior to the MR visit. The purpose for holding the antihypertensive medications prior to the imaging exam is to reduce the hemodynamic effects of medications on renal blood flow measurement. For the list of medications that should be avoided, please refer to the appendix ‘List of Medications that should be avoided’.

3.10.3. PCC Laboratories

PCC laboratories are those laboratories that are physically located at each of the four clinical sites. All clinical sites utilize GCRCs when possible and appropriate.

Each PCC is responsible for reporting lab normal ranges to the DCIAC at least annually, as well as forwarding any updates as they occur. A copy of the latest laboratory accreditation must also be sent to the DCIAC.

3.10.4. Cleveland Clinic Foundation Reference Laboratory– Serum Creatinine

The Reference Laboratory at the Cleveland Clinic Foundation in Cleveland, Ohio will receive and analyze serum specimens for creatinine. The samples will be collected and stored at the PCC and then shipped to the laboratory on a quarterly basis.

3.10.4.1. Supplies

The PCCs are to provide sample collection supplies (tubes, needles).

The CCF Reference Laboratory will provide all necessary shipping supplies to the PCCs. These include Styrofoam-insulated mailing containers with cardboard outer mailing boxes, cold packs, cryogenic serum mailing tubes, mailing tube labels, Ziplock plastic bags and packing tape. To order supplies from the CCF Reference Lab, email clientservices@ccf.org or call 800-628-6816. The contact person is: Ingrid Raulinaitis at 216-444-8108. Supply order forms will be included with shipping boxes each time the boxes are mailed to the PCC.

3.10.4.2. Labeling

Each tube is to be labeled with the CRISP ID number and a unique accession number. This accession number will be generated when the Shipping Manifest (Form 50) is printed.

3.10.4.3. Sample collection/processing

Seven to ten (7-10) mLs of blood are to be drawn in a single serum separator tube (SST), allowed to clot for 30 minutes, and centrifuged for at least 10 minutes in the usual manner. Following this, 1 mL of serum is to be transferred to a 2 mL tube and labeled with the CRISP ID number and a unique accession number.

3.10.4.4. Storage

At the time of collection, the CCF Shipping Manifest (Form 50) is to be completed to function as a storage log until the time of shipment. Samples are to be frozen at -20 degrees Celsius and batch shipped on a quarterly basis (being allowed to thaw enroute).

3.10.4.5. Packaging/Shipping

Shipping information needs to be completed on only the first page of the manifests that accompany each shipment. Retain a copy of the completed manifests at the PCC and include the original manifests with each shipment. Information from this form is to be entered in the WDES to serve as an inventory of all samples shipped.

For shipping, serum samples must be placed in a Ziplock bag. Place two paper towels in the bag to absorb any leakage that might occur. The bags should be flattened by hand to remove excess air and then sealed and placed with a frozen coolant pack into the Styrofoam mailing container. Completed shipping manifests may be placed in the Styrofoam box, in which case they should be inserted into an

individual Ziplock bag for protection from leakage or condensation. The inner lid is put on, and the Styrofoam box is slipped into the cardboard outer mailing box. The box is sealed with packing tape. Pre-addressed FedEx Airbills have been provided for the shipment of samples. All samples should be sent by next-day express service to the following address:

Cleveland Clinic Foundation Reference Laboratory
9500 Euclid Avenue, L 15
Cleveland, OH 44195
216-444-4835
Attention: Christina Thiery

Samples must not be shipped on a Friday or on a day prior to a holiday.

PCCs are to notify Tina Thiery (thieryc@ccf.org) or Kathy Leonhardt (leonhak@ccf.org) at the CCF Reference Laboratory that a shipment is on its way. PCCs must freeze the cold packs prior to use in shipping.

CCF Reference Laboratory will verify that all samples have been received in suitable condition and will send confirmation to the clinical sites via email. Information about missing or damaged samples will be communicated via secure website. Study coordinators will be notified of any problems by email and provided with a hyperlink to the pertinent information.

The DCIAC will be billed centrally for the analysis of all specimens.

3.10.5. Hometown Laboratories

For non-local participants who are unable to return to the PCC for FV07 and FV09, a blood sample may be obtained in duplicate at a local facility. The duplicate serum samples will be shipped to the PCC, one for processing and creatinine measurement at the PCC and the other sample will stored at the PCC and then be batched shipped quarterly to the Cleveland Clinic Foundation Reference Laboratory.
There is no central billing for such labs, and each PCC is responsible for reimbursing the participant, the ordering physician, or the hometown lab for the cost of obtaining the sample.
For standardization purposes, the local labs will be contacted directly with the procedure to be followed.

3.10.5.1. Ordering

Generally, PI will order the collection of blood samples. If PIs are unable to order, the study coordinator is to contact the primary care physician (PCP) and ask him or her to order.

3.10.5.2. Participant Instructions

The coordinators need to arrange to have the procedure ordered and instruct patients accordingly. For the sample shipment, participants are to be given a FedEx airbill to complete and be given instructions on how to ship.

3.10.5.3. Obtaining Serum Samples

The coordinator is to contact the participant's PCP to confirm that samples can be processed per protocol (centrifuged within one hour of collection). If this is not possible, a local facility that is able to process the samples, per protocol, must be identified and the participant instructed to go to that facility

for sample collection and processing. A sample collection kit, including shipping materials and prepaid airbill, is to be shipped to the participant to bring to the lab. The participant must be instructed to ship the sample to the PCC on the day of collection. No measurements or tests will be performed at the local lab.

3.11. NIDDK Central Repositories

The NIDDK Central Repositories are made up of three separate, contract-funded components that work together to store data and samples from significant, NIDDK-funded studies. The three components are: 1) Biosample Repository (Fisher); 2) Genetics Repository (Rutgers); and 3) Data Repository (RTI). Dr. Rebekah Rasooly is the NIDDK Project Manager for the Central Repositories. Her email address is <rasoolyr@extra.niddk.nih.gov>. NIDDK has developed model language for informed consent forms that describes the repository and explains what will happen to samples and data that are collected. Informed consent for biosamples may be obtained in the overall study consent, but a separate, written, informed consent document is recommended in order to draw genetic samples. The Repositories will not contain any personal identifiers on samples or in datasets.

3.11.1. Biosample Repository

3.11.1.1. Biosample Repository – Supplies

Fisher BioServices will supply all labels, collection tubes and materials for sample shipment as well as the FedEx airbill. The contact person at Fisher BioServices is:

Heather Higgins
NIDDK Repository
Fisher BioServices
20301 Century Blvd. Bldg. 6, Suite 400
Germantown, MD 20874
Phone: (240) 686-4703
Fax: (301) 515-4049
Email: bio-niddkrepository@thermofisher.com

3.11.1.2. Biosample Repository - Blood Collection/Processing

During the FV06 and FV08 clinic visits a maximum of 36 mL of whole blood should be collected, processed and sent to the NIDDK Biosample Repository at Fisher BioServices. Samples are to be centrifuged and shipped refrigerated (on frozen cold packs) to the NIDDK Biosample Repository at Fisher Bioservices **on the day of collection**, where they will be aliquotted into 1 mL tubes and archived.

- Serum samples: Draw 2 SST Tubes (tiger-top, 10 mL draw volume serum separator tubes), containing gel separation layer and appropriate for shipping centrifuged samples (no decanting).
- Plasma samples: Draw 2 PST tubes (green/grey-cap, 8 mL draw volume plasma preparation tubes containing heparin appropriate for shipping centrifuged samples (no decanting).
  1. Gently invert tubes (but do not shake). Invert SST tubes 5 times and PST tubes 8-10 times.
  2. Let SST tubes clot in a vertical position for a minimum of 30 minutes. Note: PSTs contain an anticoagulant (heparin), so there is no need for clotting time.
  3. Centrifuge all tubes, ideally within one hour of collection, but certainly within two hours. *Spin SST tubes at 1300 RCF (g) for 15 minutes. Spin PST tubes at 1300 RCF (g) for at least 10 minutes. No decanting is necessary.

*If centrifugation is not possible within 1-2 hours of collection, refrigerate samples until centrifugation is possible. Allow tubes to acclimate to room temperature prior to centrifugation (approximately 10

minutes) as cool temperatures may prevent proper separation. If serum/plasma samples are hemolyzed, or otherwise lost or destroyed, they should be redrawn if the participant lives locally and then shipped to Fisher BioServices.

3.11.1.3. Biosample Repository - Urine Collection/Processing

A freshly voided urine sample will be also collected during the FV06 and FV08 clinic visits. Ship samples to Fisher BioServices on a **quarterly** basis including the required shipping manifests.

1. Freshly voided urine specimens will be centrifuged in 50 mL PP tubes at 500 g for 5 minutes as soon as possible, with volume, processing times, and voiding times noted (processing times should be no longer than 20-30 minutes from the time of acquisition). Tubes will be kept in ice throughout this process.
2. The bottom 250 µL pellet (sometimes barely- or non-visible) will be transferred with a 1.0 mL pipette to a 1.5 mL eppendorf tube previously prepared with 750 µL of TriReagent (Molecular Research Center, Inc. Cincinnati, OH) and inverted several times and put on ice prior to freezing at -80 degrees Celsius for future RNA/DNA retrieval.
3. The remaining urine sample will then be transferred to 10 mL polypropylene (not polystyrene) Falcon culture tubes, stored in six 5 mL aliquots, and sent to the NIDDK Repository.
4. Urine samples for MCP-1 analysis will be sent annually from the NIDDK Repository to KUMC.

3.11.1.4. Biosample Repository – Specimen Labeling

The labels for the vials will be provided by Fisher BioServices. With a Sharpie write the visit number or date of collection on the label. Following are direction for applying the labels to the cryovials:

1. Attach the label to the vial when the vial is at room temperature.
2. Leave the cap on the vial when labeling; the inside of the vial is sterile.
3. Apply the label to the vial so that the long edge of the label is parallel to the floor when the vial is held in an upright position. The label should not trail off the bottom of the vial or over the cap.
4. While holding the vial in an upright position, affix the white portion of the label to the vial first, aligning the short edge just to the right of the graduations on the vial, with the human readable text to the right of the barcode. Approximately half of the clear tail will overlap the white ink patch on the vial when labeled correctly. Text printed on the clear tail is easier to read over the white background.
5. Wrap the clear tail around the perimeter of the vial. The end of the clear tail should overlap the white portion of the label by approximately 1/4".
6. Verify that all edges of the label adhere to the vial.

3.11.1.5. Biosample Repository – Storage/Packing/Shipping

If it is not possible for the repository to receive samples within one day of collection, centrifuge tubes and store in a refrigerator (4 degrees Celsius) until they can be shipped in order to be received by the lab within one day of shipping.

For information on assembling the refrigerated laboratory shippers to be used for shipping blood samples to Fisher BioServices, please refer to the documents in the Appendix: Assembling the Refrigerated Laboratory Shipper and Assembling the STP 320 Repository Shipper.

Prior to shipping, complete the necessary shipping manifest. Verify the collection date and number of tubes per sample. Complete the shipping information on the first page per shipment. Retain a copy of the completed manifests at the PCC and include originals with shipment. The three digit site code must be completed at the top of the page on each shipping manifest. The site codes are listed below:

230 Emory
231 UAB
232 Kansas
233 Mayo

3.11.2. Genetic Repository

All CRISP II participants from whom a sample is not already in storage at the NIDDK Genetic Repository at Rutgers, are to be asked if they are willing to provide blood specimens for DNA extraction and the establishment of EBV transferred lymphoblastoid cell-lines. The participants must be informed that the specimens will be sent to the NIDDK Genetic Repository to be saved for use in future studies related to kidney disease. In addition, we plan to collect more exhaustive family histories of all CRISP I patients and draw an electronic pedigree for each family (Progeny). Identified affected family members who agree to participate will be consented into the study and a blood sample will be collected for DNA extraction and the establishment of EBV transferred lymphoblastoid cell-lines, employing the NIDDK Center for Genetic Studies, Rutgers University Cell and DNA Repository.

3.11.2.1. Genetic Repository – Supplies

Rutgers will supply all materials for sample collection and shipment. Supplies are to be ordered using the RUCDR Web Portal. Allow three weeks for delivery. The FedEx shipping label will be provided by Rutgers. Any other necessary FedEx supplies should be ordered by the coordinator. The plastic pouches will need to be ordered through FedEx as the shipping label needs to be placed inside the plastic pouch and then affixed to the box. FedEx supplies are free and can be ordered online or by calling 1-800-463-3339.

3.11.2.2. Genetic Repository – Sample Collection/Labeling/Shipping

The site number you are assigned must be used as the first three digits of the ID number followed by a hyphen and then the CRISP ID number. The site code for each site is noted below:

230 Emory
231 UAB
232 Kansas
233 Mayo

The alternate ID number serves as a secondary cross-reference between the collection site and the RUCDR for resolving potential labeling discrepancies during collection. The alternate ID number can be any number or sequence of numbers. It can be a combination of the draw date and time such as: 0719071047. The alternate ID is completely up to the site to decide but a record must be kept of the number used.

Attach ID labels to the tubes. Information on the label must include: NIDDK-CRISP ID# and Alternate ID#. If space allows include gender and age. Do not write the participant's name or any other identifying information on the label. Labels must not wrap entirely around the circumference of the tube making it impossible to see the full length of the specimen through the tube.

Collect blood specimen in the 3 yellow top tubes with ACD. Be sure to invert each tube gently 8-10 times to mix blood with additives and keep them at room temperature. Whole blood samples should be sent to the Genetic Repository on the day of collection.

Complete, date and sign the NIDDK Phlebotomy Collection Form in the "To Be Completed by Phlebotomist" area. A copy should be kept at the clinical site and the original sent with shipment.

Double check NIDDK ID#, verify that ID information on tube matches that on the enclosed NIDDK Phlebotomy Collection Form.

Place tubes with labels facing down in Styrofoam container. Package the blood tubes in the safety mailer following the enclosed instructions. Be sure to seal the Styrofoam container with the red water resistant tape.

Place the NIDDK Phlebotomy Collection Form in the mailer box outside the plastic bag. Tape cardboard box closed when assembly is complete.

Use the enclosed FedEx shipping label to ship the sample to the Rutgers University Cell Repository. Be sure shipping label is marked for priority overnight delivery.

Ship samples to: Dr. Douglas Fugman
Rutgers University Cell and DNA Repository
604 Allison Road, Room C120A
Piscataway, NJ 08854-8082
(732) 445-1498

For routine shipments be sure the outside of the box is labeled "Diagnostic Specimen Packed in Compliance with IATA Packing Instruction 650".

Call Federal Express (1-800-463-3339) for pickup, and a courier will be dispatched to pick up the samples. **Do not, under any circumstance, put the mailer into a FedEx drop box.**

Notify Dana Witt at the Rutgers University Cell and DNA Repository that blood is being shipped and provide the FedEx tracking number and the NIDDK ID#. This can be done by email witt@biology.rutgers.edu, fax (732-445-1149), or phone (732-445-1498). This can also be done through the Web Portal at http://rucdr.rutgers.edu/shippingblood.

3.11.2.3. Genetic Repository – How to Use the RUCDR Web Portal System

Establishing a Username and Password

http://rucdr.rutgers.edu/scripts/up.exe?AIMACTION=vnewaccountconiddk&enforce_color=ON&skey=1092563715108250079 5

Go to the URL listed above and then just follow the directions on the top of the page. You can sign up for multiple NIDDK sites (if you are associated with more than one) at once. (Phlebotomists performing off-site draws will send a notice from http://rucdr.rutgers.edu/shippingblood.)

Logging in to the System

The URL for the RUCDR Web Portal is http://rucdr.rutgers.edu. Click on the square for NIDDK to get to your login screen. Enter your newly created username and password. If you ever forget your username or password there is an option on this screen to "Retrieve Lost Password". You will need to remember what email address you used to create your account to use this function!

Announcement Board

When you enter the web portal you will see announcements from the RUCDR. The dates of future holiday closings will be listed here.

Navigating the Web Portal

Click the tabs on the top of the screen to access the different parts of the web portal. The functions accessible from each tab are listed below.

Request Functions

From the "Request Functions" tab you can do two things: "Submit Request" or "Look Up Status of Request".

1. **Submit Request**
   To get to these options, pick a function from the drop-down menu: Shipping Blood, Request Mailers, or Question.
   Next, pick a site number from the drop-down menu.

Fill out the section of the form corresponding with the function you chose. Even if your function choice was not "Question", you can add information to any request in the textbox under the heading "Special Notes/Special Instructions/Questions".

Good thing to know! If you choose "Shipping Bloods" you can only enter one FedEx tracking number per submission, but if you have more than one sample in the box you can list all the NIDDK ID numbers separated by commas. As always, do not over pack the mailers and enclose a separate piece of paperwork for each sample.

In Section 2: Attachments (a light grey area towards the bottom of the page) you can add a file.

2. **Look Up Status of Request**

   You can search your recent requests to see their status in multiple ways. These are self-explanatory. If you just hit the search button without selecting any search criteria all the requests you have made will be shown.

   There are 4 different status assignments a request can have:

   - Open
   - Assigned
   - Pending
   - Closed

   Open: This status signifies that a request has been submitted, but is not yet assigned.

   Assigned: This status signifies that an open request is assigned to a particular staff person.

   Pending: This status signifies that a request has been assigned and a staff person is working on it, but hasn't yet completed the job.

   Closed: When a request is completed the status is set to closed.

Self Help Resources

This tab is a holding area for useful documents.

1. **FAQ** – If you have a question, hopefully it is already answered here.
2. **Download Center** – These instructions are here! Also, any paperwork enclosed with mailer kits is here in case you need to print off extras.
3. **View Announcements** – In case you missed the announcement page when you first logged in to the web portal you can read it again.
4. **Support Resources** – Links that may be of interest to visit.

Account Management

From this tab you can "Modify Your Profile" or "Change Password".

Important Information Regarding Blood Shipments

When a package is received, a mailer request is filled or a question is answered, you will receive an email from us and the status will be changed to "closed". The NIDDK Cell Line # will be sent in a separate email only to those individuals that have been designated to receive that information.

3.11.2.4. Genetic Repository – Storage

Ideally genetic samples should be shipped the day of collection, but must be shipped within 4 days of collection and must be received no later than the morning of the fifth day after collection. Samples must remain at room temperature until processed and must not be frozen or refrigerated at any time.

3.11.3. Data Repository

The NIDDK Data Repository at Research Triangle Institute (RTI) will gather, store and distribute incremental or finished datasets from CRISP. It will also be responsible for helping the DCIAC prepare databases and incremental datasets for archiving and for carrying out restricted queries of stored databases. In general, the Data Repository (RTI) will receive all data collected by the DCIAC, provided that subjects have consented to having his/her data included in the repository. No personal identifiers will be sent to the repository. Contact information for the Data Repository (RTI) may be found below. Phil Cooley RTI − NIDDK Database Repository Box 12194 Research Triangle Park, NC 27709 Tel: (919) 541−6509 Fax: (919) 541−6178 email: pcc@rti.org.

3.12. Iothalamate Clearance (GFR) Measurement Procedure

3.12.1. Principle

The short non-radiolabeled Iothalamate Clearance Test is a simple test that is done to obtain an estimate of a patient's glomerular filtration rate (GFR) without subjecting the patient to the more-expensive and time-consuming standard renal clearance (if an estimate of renal plasma flow is not needed).

3.12.2. Iothalamate Glomerular Filtration Rate (GFR) Procedure

A laminated copy of the *Iothalamate Glomerular Filtration Rate (GFR) Test* #81476, shown below, is provided to coordinators along with an instructional DVD [Iothalamate GFR Training Procedure DVD]. Coordinators can play the GFR training DVD available on the CRISP II website.

Iothalamate Glomerular Filtration Rate (GFR) Test #81476

TEST REQUISITION FORM

1. **Use** the requisition form supplied with the kit.
2. Before you begin the test, **enter** the patient's initials and collection date on each of the sample tubes.
3. **Explain** the GFR procedure to the patient.
4. **Confirm** that the patient has been fasting for **4** hours, or 2 hours if the patient is diabetic.
5. **Question** the patient to be sure that he/she has not participated in other contrast studies within the last 12 hours.
6. **Record** the patient's height and weight
7. **Ensure** that the patient does not have sensitivity to iodine.

SPECIMEN COLLECTION - Number 1

1. **Instruct** the patient to empty his/her bladder completely.
2. **Prepare** the contrast injection using a 1 cubic centimeter (cc) tuberculin syringe, consisting of 0.5 cc sterile water and 0.5 cc Iothalamate.
3. Remember, the **dosage** for pediatric patients weighing less than or equal to 40 kilograms is less.
4. **Record** the time the patient returns.
5. **Check** the patient's arms to determine which will be most suitable for blood collection. Then use the opposite arm to inject the Iothalamate dose and **record the time**.
6. **Return** the patient to the seating area and **instruct** him/her to wait for 1 hour and to drink 10 to 20 ounces of water. (The amount of water may be less if the patient is under physician orders to restrict fluid intake).
7. **Aliquot** 5 milliliters of urine into the tube designated for the urine zero (UO) sample.

SPECIMEN COLLECTION - Number 2

1. After 1 hour, **instruct** the patient to completely empty his/her bladder.
2. **Record** the time.
3. **Discard** this urine equilibration (VE) sample.
4. **Use** an ultrasound monitor to ensure the patient's bladder is empty. (If ultrasound is not available, ask the patient if his/her bladder is completely empty).
5. If patient is unsure, have him/her **void again**.
6. **Collect** 3 milliliters of blood from arm opposite of the injected arm. (It is critical to make this blood draw within 5 minutes of the patient's voiding.)
7. **Record** the time of this blood draw.
8. **Return** the patient to a seating area where he/she should be instructed to drink 10 to 20 ounces of water.

SPECIMEN COLLECTION - Number 3

1. After 45 minutes, **instruct** the patient to completely empty his/her bladder.
2. **Record** the time.
3. **Keep** the urine, making sure you have a minimum of 100 milliliters. If the patient is not able to provide enough urine at this time, have him/her return to the seating area and encourage more fluid intake. After 30 minutes, collect additional urine until at least 100 milliliters is reached.
4. **Collect** 3 milliliters of blood from arm opposite of the injected arm within 5 minutes.
5. **Record** time of blood draw.
6. The patient can be **dismissed**.

MEASURING THE SPECIMEN

1. Accurately **measure** or weigh the volume of the urine #1 (VI) sample and allocate 5 milliliters into the tube designated for the VI sample.
2. **Record** the volume.
3. **Verify** that all the spaces in the shaded area of the requisition form are filled in completely. The patient's first and second blood draws should be centrifuged for 10 minutes at 3,000 revolutions per minute (rpm).
4. **Aliquot** the first blood draw into the tube designated for the Patient Draw 1(P1) sample.
5. **Aliquot** the second blood draw into Patient Draw 2 (P2) allocated tube.
6. **Verify** that the collection times are written on each of the respective sample tubes.

TollFree:800-533-1710 Website: mayoreferenceservices.org Email: mml@mayo.edu

MC4091-23

3.13. Information for Study Personnel

3.13.1. Training

The Data Coordinating and Image Analysis Center (DCIAC) is responsible for training all CRISP II personnel in the correct procedures for carrying out the study. A two day training session for Study Coordinators was conducted on April 10 and 11, 2007 at the University of Pittsburgh. Principal investigators reviewed the CRISP II Protocol, updated forms and discussed the Manual of Procedures during the Steering Committee meeting on January 9, 2007, in Washington, DC. The DCIAC is responsible for assuring that procedures are carried out in a consistent, standardized manner and is also responsible for monitoring procedures at each PCC and proposing remediation measures for sites or individuals that do not meet acceptable performance levels.

3.13.2. Data Collection Forms Completion

Data collection forms may be completed by a certified study coordinator or by other designated personnel, defined as individuals having completed training and demonstrated proficiency in carrying out the policies and procedures applicable to the task(s) they are performing for the study. The signature of a study investigator must be included on the completed data collection forms to verify that he/she reviewed and approved the completed forms.

3.13.3. Communicating with the DCIAC

All communications with the DCIAC should be through email at CRISPII@pitt.edu. Responses are guaranteed within 48 hours. If the concern is urgent contact Johana Schafer the study coordinator at 412-641-2328 who will triage your call to the appropriate individual at the DCIAC.

3.13.4. Email Lists

Several email listservs have been established to facilitate communication between CRISP study personnel. When a message is emailed to one of these lists, a copy of it will be delivered to all study personnel who are subscribed to that particular list. In addition, all messages sent to a list are archived and can be easily accessed from the Archives page of the CRISP website. The following listservs are available:

CRISP Study Personnel
<crispall@list.pitt.edu>
CRISP Steering Committee
<crispsteer@list.pitt.edu>
CRISP Study Coordinators
<crispcoord@list.pitt.edu>
CRISP Imaging Committee
<crispimage@list.pitt.edu>
CRISP Genetics Committee
<crispgenetics@list.pitt.edu>

To add or remove an individual from one of the above lists, please email a request to crispii@pitt.edu.

3.13.5. Setting up New CRISP Personnel

When a new staff member joins the CRISP II team, the site coordinator should download the New Personnel Form, complete the form and fax to the Study Coordinator. The Study Coordinator will

enter the information into the Website. The DCIAC will generate a username and password for this individual. An email with the link to the CRISP II website and the username and password will be sent to the new staff member who will then have access to the website. The staff member can also use the website to change their password. Initial usernames and passwords will be sent to the Study Coordinator as well.

3.13.6. Departing Staff Personnel

If a member of the CRISP II team is leaving the study, the site coordinator should immediately notify the study coordinator who will notify the DCIAC. The DCIAC will disable that individual password which will make it impossible for her to access the CRISP II website. This individual will be immediately removed from all listservs as well.

Chapter 4. Protection of Human Subjects

4.1. IRB Requirements

The Institutional Review Board (IRB) at each PCC must approve the CRISP protocol, informed consent documents, and recruitment materials prior to recruiting participants to the study. All revisions to these materials must also be submitted to and approved by each site's IRB. Copies of the current IRB approval letters are in Appendix.

4.2. Informed Consent

In order to be eligible for the study, each participant must be willing to sign 1) a statement of informed consent consenting to annual visits and interim contact visits. This will document the agreement of the participant to participate in study activities. The participant will be queried in a sincere discussion prior to enrollment to insure continued willingness to be involved in the study and comply with the study protocol and follow up visit schedule. Copies of the signature of the signed informed consent forms will be kept at the Study Sites and the date that the consent was signed will be kept at the DCIAC. These will be stored apart from the other study forms since they contain confidential information, i.e., the participants' names. Copies of the current consent forms used at PCC are in Appendix.

4.2.1. Sequence of Consent Procedures

It is recognized that Clinical Center Institutional Review Boards (IRBs) have official responsibility for determining informed consent procedures. Prototype informed consent forms have been developed for the study, and each Clinical Center's IRB-approved consent form will be reviewed to make sure the essential material is included. Copies of all IRB approvals (including amendments and renewals) must be promptly sent to the DCIAC.

Consent occurs at the initial stage of study. Consent should be obtained at the time of the first visit whether it is the Screening, Enrollment or Baseline Visit, and will include description of the interaction with members of the study team, a complete medical history, a complete physical examination, blood and urine tests to be obtained, DNA to be obtained, GFR's obtained annually, follow-up visits, annual MR and ultrasound procedures. If a second genetics consent form is to be used, it will be obtained at one of the above mentioned visits.

4.2.2. Participant Examination

Although the CRISP study is not an interventional or therapeutic trial but an observational study, findings obtained throughout the study may provide important information for maintaining the standard of care for the participants in the study. All physical examinations must be performed by a physician, nurse practitioner, physician assistant or by a nurse coordinator supervised by a physician. Any abnormal findings by imaging, blood work or physical examination are required to be reported to the patient's primary treating physician within 3 weeks. Should subjects become acutely symptomatic during their annual or baseline visits or should medical conditions requiring immediate attention be identified, it is necessary that the primary treating physician be contacted immediately. Follow-up letters to treating physicians after patients have completed their baseline and annual visits including certain findings such as blood chemistries, and blood pressure levels are recommended. This not only

improves the chances of successful subject retention but maintains an awareness of the CRISP study in the medical community. All documents pertaining to these evaluations need to be kept at each PCC site for review at site visits throughout the study.

4.3. Regulatory Documents

All site coordinators are responsible for having on file the appropriate regulatory documents and for submitting necessary reapprovals on time. Regulatory documents include IRB approvals of the study protocol, amendments to the study protocol, informed consent documents, financial disclosure documentation, and recruitment materials. Copies of all IRB−approval letters must be sent to the CRISP Study Coordinator, Johana Schafer at the DCIAC. In summary, regulatory documents to be sent to the DCIAC include the following:

Required regulatory documents include the following:

1. Official documentation of the IRB registration number and assurance ID number.
2. IRB approval of the current CRISP II protocol.
3. A copy of all IRB−approved consent and assent forms required by the PCC.
4. Documentation of conflict of interest and financial disclosure of all investigators.
5. Documentation of the institution's normal ranges for required lab tests and a copy of the latest laboratory accreditation.

4.4. Participant Confidentiality

Participant confidentiality is protected thorough a multi−tiered approach to assure compliance with the requirements of the Privacy Act, the Privacy Rules of HIPAA, and with all other applicable laws that protect the confidentiality of health information. Each participant is to be informed of the purpose of the study and consented for participation in all aspects of the protocol through use of IRB−approved consent documents. Participants must sign an authorization (along with the informed consent document) for public release of their data. At the time of registration in CRISP I, each participant was assigned an identification number. This number will be source of identification for CRISP II as well. Participants are identified only by number in the study database and generated reports and, in general, only group data will be published. If individual participant data are published, no identifying information will be included. The data management system is highly secure with multiple levels of controls on access. The medical records of the participants in the CRISP study are confidential. Specific study−related information may be made available to the FDA, study sponsors, the NIH, or other regulatory agencies but will be de−identified.

4.4.1. HIPPA Compliance

Only individual PCCs and the CRISP II DCIAC have access to identifiable protected health information (PHI) for study participants. All participant data will be maintained in locked file cabinets and/or on secure, password−protected computers at each PCC and at the CRISP II DCIAC, with access limited to CRISP II researchers and staff. Each PCC will have access to PHI of only its own site-specific participants. The disclosure of individual health data to the general public or affiliated external researchers will comply with the provisions of the HIPAA Privacy Rule. Clinical data and images will be de−identified prior to disclosure, according to the rules and prescribed mechanisms for doing so in Sections 164.502(d), 164.514(a)−(c). Data values that have the potential for unmasking participant identity will not be available on the public−use data set or will be made available only as calculated

variables that cannot be uniquely mapped back to raw values. These include clinic locations, dates of hospital admission, information about parents or siblings, and rare medical conditions.

4.4.2. Data Transfer and Security

Data from the client machine and the web server are sent using 128 Bit encryption utilizing Verisign SSL certificates. Servers, both web servers and database servers are located behind network firewalls and use Windows security for restricted access. Backups are done on a daily basis. Daily backups are rotated on a monthly basis with weekly backups rotated on an annual basis. Weekly backups are stored in a local bank's safety deposit box. All servers are located in locked rooms with controlled authorized access. Servers are virus protected utilizing Symantec virus protection software.

4.5. Safety Monitoring

Because this is an observational study risk to patients in CRISP II will be minimal. We will however, conduct screening evaluations of CRISP I potential participants to determine whether it is safe for them to have imaging and to take part in the study We will also provide selected results from study assessments to participants and/or their physicians when there are health and safety implications.

4.5.1. Definition and Reporting of Serious Adverse Events (SAE)

4.5.1.1. Definition of an SAE

An SAE is defined as any undesirable experience meeting one or more of the following criteria, regardless of relatedness to study participation, occurring from the time a participant signs the informed consent (before the screening visit) until the end of the study.

- *Resulting in Death* − All deaths must be reported as SAEs.
- *Hospitalization* − All hospitalizations, elective and nonelective, must be reported as SAEs. If a hospitalization is prolonged due to an event related to this study, this is also considered an SAE.
- *Life−threatening* − If the patient is at substantial risk of dying at the time of the event, or if continued use of a study medication or study procedure would result in the patient's death.
- *Resulting in significant, persistent or permanent harm or disability.*
- *Exceeding the nature, severity or frequency of risk described in the protocol.*
- *Congenital anomaly* − If there is suspicion that exposure to a study procedure prior to conception or during pregnancy resulted in an adverse outcome in the child.
- Any other important medical event, including new cancer diagnosis, which may jeopardize the participant, or may require intervention to prevent permanent impairment or damage or other outcome listed above.

4.5.1.2. SAE Reporting Requirements

All SAEs must be reported *within 24 hours* of study personnel learning of the event to the local PI and to the DCIAC via data entry of SAE Report Form 13. Information not available at the time of the initial report should be submitted to the DCIAC within 5 business days of its becoming available. PIs at the clinical centers are responsible for fulfilling local IRB reporting requirements, which may vary by center. A copy of the local IRB stamped form should be sent to the DCIAC.

The DCIAC will prepare summary reports at least annually for the clinical centers, NIDDK, and the External Advisory Committee on SAEs. Principal investigators at the clinical centers are responsible for fulfilling local IRB reporting requirements, which may vary by center.

Chapter 5. Ancillary Studies Policy

5.1. General Policy

To enhance the value of the CRISP study, the Steering Committee welcomes proposals from individual investigators to carry out ancillary studies. In order to protect the integrity of the CRISP study and other derivative studies, the Ancillary Studies Committee and the Steering Committee must review and approve all proposed ancillary studies before their inception or submission of a proposal for external funding consideration.

5.2. Definition of an Ancillary Study

An ancillary study is one based on information from the CRISP study participants or study data in an investigation or analysis that is relevant to, yet not described in the Study protocol, and derives support from non-CRISP funds. Screening studies, i.e. to survey a microarray or proteomics database, will not be eligible. Rather, steering committee support of CRISP ancillary studies will require presentation of a clear hypothesis, rationale, specific aims and well-developed analytic tools based on preliminary studies.

Preferred ancillary studies will utilize the established database (standard blood and urine chemistries, DNA analysis, kidney and cyst volume measurements: see *Kidney Int. 64:1035-45, 2003; N Engl J Med. 354:2122-30, 2006*) together with samples of urine, plasma and serum stored in the NIH repository.

An ancillary study may propose the collection of additional data not collected or analyzed as part of the routine CRISP study data set provided that funds are available to the investigator to cover the costs.

Ancillary studies may be submitted by the investigators within the CRISP study or by investigators without a prior relationship to the CRISP study. Ancillary studies require external (non-CRISP) funding to cover all associated costs. Examples include studies funded by investigator-initiated NIH research awards (RO1s), grants from academic institutions (K12s) or private sources (e.g. private foundations, the PKD foundation, pharmaceutical companies). Any ancillary study must have sufficient funding to cover the costs incurred to process or ship samples and for tasks such as sample selection, preparing and documenting analysis files, participating in statistical analysis, and integrating the new ancillary data back into the combined CRISP database.

5.3. Requirements and Procedures for Approval of an Ancillary Study

5.3.1. Overview

Participation in, and approval of an ancillary study is subject to review by the CRISP Ancillary Studies Committee, and formal approval by the CRISP Steering Committee.

To facilitate application the investigator should send a preliminary draft of the proposal including brief background, hypothesis, rationale, specific aims and methodology to the chair of the Ancillaries Studies Committee. The chair will consult other members of the Ancillary Studies Committee to determine if the proposal fits within the guidelines and capabilities of the CRISP protocol. At this juncture hypothesis ‘overlap’ issues among competing applicants will be resolved.

Steering Committee – J.J. Grantham, V.E. Torres, A.B. Chapman, L.M. Guay-Woodford, K.T. Bae, C.M. Meyers, J.E. Bost, W. M. Bennett (chair)

Ancillary Studies Committee – J.J. Grantham (chair), J.E. Bost, A.B. Chapman, V.E. Torres, K.T. Bae, C.M. Meyers

All Ancillary Study must include at least one Steering Committee member as a collaborating investigator who will not participate in the final merit review of the proposal.

Under specific, selected conditions (e.g. an imminent funding deadline), the Steering Committee Chair may serve as the proxy for the Steering Committee, although this is expected to be a relatively uncommon situation. Approval by the Steering Committee requires four of 6 votes in favor of the proposal. Dissenting voters must provide the explicit reason for their dissent. Any issues of concern to dissenting voters are shared with the applicant and opportunities for clarification provided. All sites (PCC's, DCIAC, and NIDDK) agree to cooperate with approved ancillary studies regardless of their individual vote. Ancillary study investigators must receive approval of their concept, and then engage in detailed budget and scientific planning in cooperation with participating clinical center investigators and the DCIAC before submitting their grant to any funding agency. Potential ancillary investigators are encouraged strongly to communicate with the Chair of the Ancillary Studies Committee (In the absence of the Ancillary Studies chair with the chair of the Steering Committee) prior to submitting a preliminary proposal.

An ancillary study proposal submitted within the CRISP Study Steering Committee must include at least one CRISP investigator as a co-investigator. If other investigators wish to participate in a particular ancillary study, they may contact the proposing Investigator directly with the assistance of the Chair of the Ancillary Studies Committee, if needed.

5.3.2. Proposals for Ancillary Studies as Part of Training or Career Awards

The CRISP Study investigators and the NIH anticipate that the CRISP Study will be an important resource for career development and training among members of the academic community. Therefore, proposals for ancillary studies to be funded through training grants or career development awards through the NIH or other funding sources require special consideration. These funding mechanisms typically provide funding only for investigator effort, not additional data collection, and as such, these proposals will generally propose research questions and analyses that could be considered part of the core CRISP Study. In these cases, consideration of what analyses might be authorized could present a conflict of interest for the CRISP investigators. Therefore, the Ancillary Studies Committee will be specifically directed to consider the scientific gain to the CRISP study from the addition of the proposed ancillary analyses, as well as the training and career development opportunities afforded to the applicant by the proposed ancillary study.

Evaluation in the case of proposals to be funded through training grants is limited to trainees of CRISP study investigators, as the quality of the analyses will be greatly dependent on the mentor identified in the training grant. In the case of faculty career awards, evaluation of ancillary study applications will need to consider the anticipated scientific contribution of the applicant, including their ability to perform data analyses that may not be able to be performed at the DCIAC without additional funding. Further, willingness to adhere to the requirements of the Publications and Ancillary Committee with respect to authorship will be particularly important.

The review process will have several steps. The first step is registration of the proposal concept. This may occur up to one year before an anticipated submission date. Proposal concepts should be registered on the CRISP website. Once a concept proposal document is generated, the next step is review of the proposal concept and acceptability by the Publications and Ancillary Studies Committee. The proposal concept should be summarized in 2−4 pages.

5.3.3. Considerations for Approval

1. The proposed study must meet the standard of highest scientific merit.
2. The proposed study must not interfere with the completion of the main objectives of the CRISP Study.
3. Participant burden.
   - The proposed study must be acceptable to the participants (e.g. time, discomfort, privacy).
   - The proposed study must not interfere with other parts of the main CRISP Study.
   - The proposed study must not hamper continued participation in the main CRISP Study.
4. The proposed study must not adversely affect participant cooperation or compliance with the CRISP Study
5. The proposed study must put minimal demand on scarce CRISP Study resources such as blood samples.
6. The proposed study must require the unique characteristics of the CRISP Study cohort to accomplish its goals.
7. The investigators must have adequate resources to effectively complete the project, including:
   - Sufficient budget and personnel.
   - Staff having the requisite expertise to meet the objectives of the project.
8. The ancillary study investigators must agree to return the complete ancillary data set back to the CRISP Study if requested by the CRISP Study Steering Committee.
9. The proposed study must not create a serious diversion of study resources (personnel, equipment or study samples) or investigator/staff time, either locally or centrally.
10. The proposed study must not jeopardize the public image of the CRISP Study.
11. The investigator must pledge to abide by the rules and regulation for CRISP covered in the Manual of Procedures listed on the website.

5.3.4. Instructions for Preparation of Requests for Approval of an Ancillary Study

All proposed ancillary studies must be submitted to the CRISP Ancillary Studies Committee at least two months before submission to a funding agency. Under specific conditions (e.g. an imminent funding deadline) the CRISP Steering Committee Chair may serve as the proxy for the Steering Committee.

5.3.5. Proposal Format

A written request for approval of an ancillary study should be submitted to the Ancillary Studies Committee as a preliminary 2 to 3 page document containing the following information:

A. Identifiers

1. Initiating investigators, collaborators, potential CRISP Study co-investigator.
2. Planned starting date and project timeline.
3. Funding plans and estimated cost.

B. Design and Methods

1. Brief background and rationale.
2. Study questions or hypotheses.
3. Specific data collection methodology, including questionnaires and coding forms, if available.

C. Specific answers to the following questions

1. What are the potential burdens to participants?
2. What, if any, follow-up is needed? Specify length of time and events to be ascertained.
3. How many participants are required?

4. How will the ancillary study be funded? Would any additional un-reimbursed work be expected of the CRISP Study personnel? How will the ancillary study budget cover demands on CRISP Study personnel time and Study resources?
5. Where will the data analyses be conducted?
6. How will the confidentiality and other aspects of protection of human subjects be maintained?
7. When and in what form will a complete data set be provided to the CRISP Study?

D. Data or Specimen Requirements:

1. What CRISP Study core data and/or analyses are needed for the ancillary study?
2. Is blood or other biologic samples (either fresh or from the CRISP Study's repository of stored samples) required?
3. What quantity of specimens will be needed?

After preliminary review and provisional acceptance, more detailed information may be requested before final approval.

5.4. Changes to Proposed Study

Once an ancillary study is approved, if a change occurs in the structure or concept of the study, then a revised proposal must be submitted to the Ancillary Studies Committee, for review and approval. If the changes are substantial, the Ancillary Studies Committee may submit the proposal to the CRISP Steering Committee for approval.

5.5. Proposal Budget

The investigator applying for an ancillary study must supply all additional funds needed to successfully complete the study. The Ancillary Studies Committee will be concerned with both the obvious and the hidden costs to the CRISP Study entailed by an ancillary study. Provision of funds for these expenses is essential − an ancillary study that will generate CRISP expenses cannot begin without evidence of fiscal support to cover these costs. These costs must be stressed in research grant applications based on a CRISP Ancillary study and include, but are not limited to:

1. If work is to occur on site, rental of appropriate clinic, lab and office space.
2. If subject involvement outside of main exams is anticipated, subject coordinator time to arrange subject appointments must be reimbursed.
3. Personnel, equipment and supplies necessary to complete the project.
4. Statistical and data management staff for coordinating the additional data management and analyses.

5.6. Human Subjects/Data Confidentiality

Confidentiality of CRISP participants must be guaranteed. Individually identifiable data may not be released. If the data collection/request is not covered in the original informed consent process for the main CRISP Study a signed consent must be obtained from every participant in the ancillary study, However, IRB approval of the consent is not necessary in order to submit an application to the Ancillary Study Committee.

1. Key personnel of the ancillary study must be certified in the NIH OHRP or equivalent training course.

2. A copy of the IRB approval letter for the ancillary study is to be sent to the DCIAC. If a separate consent form is required for the ancillary study, a copy of the signed ancillary study consent form for each study participant must be included in the CRISP Subject Study record. A data file tracking all signed ancillary consent forms must be maintained by the ancillary study and an electronic copy of that file must be submitted to the CRISP DCIAC.

The principal investigator of an ancillary study is responsible for reports regarding the course of the study to the Ancillary Studies Committee or Steering Committee as appropriate, monitoring the study to assure continuing compatibility with CRISP Study and serving as a liaison to the CRISP Steering Committee. The CRISP Steering Committee monitors the development of the ancillary studies, receipt of funding, initiation dates, and progress. A written progress report on ancillary studies must be made annually to the Steering Committee.

5.7. Analysis and Publication of Results of Ancillary Studies

Analyses of ancillary studies within CRISP can be undertaken in three specific ways: i) analysis can take place at the DCIAC and be conducted under the supervision of its biostatistician-investigators, ii) datasets could be released for analysis by external investigators when approved by the Ancillary Studies Committee and the DCIAC; iii) ancillary studies funded as career or training awards, as well as studies taking place in a subset of clinical centers may be situations in which release of data for analysis deserves special consideration. Under these circumstances, the ancillary study investigator will provide interim reports on analyses to the DCIAC to ensure that all study data used in analysis of ancillary study results are consistent with data in the main study database and to ensure the quality of analytical approaches.

Proposals for manuscripts resulting from all ancillary studies shall be submitted for review to the Ancillary Studies Committee and require approval by the Steering Committee *before* establishment of a writing committee or submission for publication or presentation. It is anticipated that principal investigators of approved ancillary studies will generate at least one scientific paper based on the ancillary study analyses, as specified in the CRISP Publications Policy. Each manuscript and abstract would be expected to include a CRISP investigator. The phrase "CRISP Study" should be included in the title in all scientific presentations and manuscripts and listed as a key word whenever possible. Manuscripts will also contain an appendix listing CRISP investigators deemed appropriate.

5.8. Feedback of Results of Ancillary Studies to Participants

Results of ancillary studies shall be reported to participants and/or their physicians if medically useful. Such reporting should follow standard CRISP protocol for notification of participants.

5.9. Handling of CRISP Data and Specimens

At the time of distribution of CRISP specimens and/or information, the CRISP Collaborating Investigator, with help from the DCIAC, will make explicit arrangements with the ancillary study Principal Investigator for the security of these study materials, and for their final disposition at the conclusion of the ancillary study. The safety and confidentiality of the CRISP data at the collaborating institution is the responsibility of the ancillary study Principal Investigator, as is the appropriate disposition of these materials after the study has been completed. Leftover DNA and laboratory specimens are destroyed or

returned, and files of CRISP data are returned or deleted, as established at the outset of the collaboration. An archival copy of the newly collected data and/or laboratory results not already held at the DCIAC will be sent to the CRISP DCIAC at the conclusion of the data analysis and publication of the main (ancillary) study hypothesis. This transfer is the responsibility of the ancillary study CRISP Principal Investigators. Once transferred back to the CRISP DCIAC, these ancillary data will become part of the aggregate CRISP database. Subsequent access to these data will be governed by the Steering Committee.

5.10. Ancillary Studies Submissions – Training Grants

We recognize the need to both protect the integrity of the core hypotheses and yet provide for research training in junior members of our various institutions. The ancillary submission form includes a place to check for "Training Proposal" which will alter the philosophy of the review process within the Ancillary Studies Subcommittee as well as the Steering

When a Training proposal is submitted, the mentor(s) should briefly state their attributes as mentors in the proposed training area, and their commitment to the individual. The mentor's abbreviated 'NIH-style' CV should be attached.

Chapter 6. Publications and Communications

6.1. Publications Policy

The policy of the CRISP concerning publications and presentations is designed to achieve five objectives:

1. To assure timely publication of the results of the CRISP studies to the appropriate professional audiences.
2. To avoid premature publication of results that might compromise performance of the study (such as publishing trends before they become statistically convincing) or that might compromise the ability to publish results in high-quality peer-reviewed journals (such as premature release to the lay press).
3. To maintain high standards of quality of all materials published by the CRISP.
4. To guard against duplicate publication of results by assuring absence of overlap of materials prepared by various writing committees.
5. To assure attribution of credit to all professionals participating in studies within the CRISP.

To accomplish these ends, it is the policy of the CRISP that preparation of all publications or presentations, other than materials prepared for local publicity purposes, must be assigned by the Steering Committee Chairman, after consultation with the Publications Committee Chair, to specifically appointed writing committees, and that all such materials must be reviewed and approved by the Publications Committee and/or the Steering Committee prior to publication. A listing of the members of the Publications Committee can be found on the CRISP website.

6.1.1. Scope of Policy, and Exception for Local Publicity Materials

All materials to be presented orally or submitted for publication or dissemination by individuals associated with the CRISP or dealing with any aspect of a study within the CRISP must receive prior review and approval by the Publications Committee and/or Steering Committee.

6.1.2. Source of Suggestions for Publications

Suggestions for topics appropriate for preparation of abstracts, peer-reviewed papers, or chapters and reviews are made by the Publications Committee; in addition, all participants in the CRISP are invited to suggest topics appropriate for preparation as abstracts, peer-reviewed papers, or chapters and reviews from the studies within the CRISP. Such suggestions can be made and discussed during meetings or conference calls of the Steering Committee or be made in writing to the Steering Committee Chair, with copies forwarded to the Publications Committee Chair. The Publications Committee Chair shall review the request to be certain there is no overlap with material previously assigned to other writing committees. Where such overlap exists, the Publications Committee Chair may make recommendations to the Steering Committee Chair that the suggestion be referred to an existing writing committee, that additional study participants be added to existing writing committees, or make other suggestions to resolve the overlap. However, final decision in this matter rests with the Steering Committee Chair after consultation with the Publications Committee Chair.

It is the policy of the CRISP to encourage non-physician professionals to prepare scientific presentations to their own professional meetings and to prepare scientific papers for their own professional journals in addition to participating in the preparation of papers for medical journals. Since the subject matter of these reports and papers may well overlap with material being prepared by writing committees for medical journals, it is the policy of the CRISP that, under these circumstances, rather than forming a new writing committee, such non-physician processionals should be added to the

existing writing committee concerned with related matters, specifically for the purpose of preparing such reports. The authors of these presentations and reports will be the members of the writing committee, with first author being the individual added to the committee for this purpose, using the appropriate authorship style.

In addition, the Publications Committee will formulate and maintain a list of suggested topics that should be prepared for publication, to assure that all completed investigations of the CRISP studies are reported to the scientific community in a timely fashion.

6.1.3. Assignment of Writing Committees

The Steering Committee Chair, upon receipt of a recommendation for preparation of a topic for publication, and after confirming that the topic does not overlap with a previous assignment to another writing committee, and discussion with the Publications Committee Chair, will appoint the Chair of a new writing committee to prepare the publication. Appointments of writing committee chairmanships will be made in an equitable fashion to all professionals-physicians, clinical coordinators, statisticians, and others − in a fashion that recognizes the special contributions of each member of the CRISP study to its performance.

Upon appointment of the Chair of a new writing committee, the Publications Committee Chair will notify each collaborating center, including clinical centers, the DCIAC, the NIH, and the central laboratories, of the new writing committee, soliciting indications of interest to be on that writing committee. If more individuals express interest than is practical to assign to a committee, the Steering Committee Chair, after discussion with the Publications Committee Chair, shall make final assignments of the members of the committee.

In all cases, writing committees dealing with an issue that requires analysis of data by the DCIAC will have a member of the DCIAC assigned to it.

From time to time it may be expedient for the chairmanship of a writing committee to be reassigned to another member of that committee, or for members to be dropped from or added to a writing committee. The Steering or Publications Committee Chair is authorized to make such changes with the consensus of the members of the Writing Committee or on his/her own authority where there is clear cause.

6.1.4. Classes of Reports for the CRISP

There are four classes of reports for the CRISP II Study:

Class A

Reports of the major outcomes of the studies − It is assumed there will generally be only one or two such reports derived from each phase of the Study. Generally these reports will be prepared by the Writing Committee appointed by the Publications Committee Chair, with the Steering Committee Chair as Chair of the writing committee.

Class B

Reports addressing in detail one aspect of the CRISP Studies, but in which the data are derived from the entire study.

Class C

Reports of data derived from a subset of centers by investigators of the studies within the CRISP (e.g., sub-studies or ancillary studies) or originally conceived analyses of data from entire studies of the CRISP (original analyses).

Class D

Reports of investigations initiated outside of the CRISP, but uses data or samples collected by a study within the CRISP. The investigators may be CRISP or other investigators, but the source of the ideas and the funding for the study will have been derived outside of the CRISP itself.

6.1.5. Authorship

The authorship policy of the CRISP must achieve two somewhat conflicting goals. First, it is recognized that the findings of the study, especially the findings reported in Type A and B reports, are derived from the efforts of the entire CRISP professional staff. Thus, all reports, regardless of type, must give recognition to all the participants of the CRISP studies (e.g.: CRISP), and reports of Types A and B must give primary recognition to the entire study professional staff. On the other hand, it is recognized that the preparation of a manuscript places special demands on the assigned writing committee, especially on the Chair of the writing committee. Further, recognition of special effort and achievement is important in the professional careers of study staff, and specific listing as an author is a significant motivating factor that will help assure prompt completion of writing assignments and timely publication of results of the CRISP. The CRISP authorship policy attempts to recognize each of these goals. The authors of CRISP publications will be listed as detailed below for each type of publication.

6.1.5.1. Type A – Publications

Abstracts: From the CRISP, e.g. CRISP study, presented by XXXX. (This will usually be determined by the Steering Committee Chair).

Papers: From the CRISP (e.g. CRISP study[1]).

[1]The CRISP Participant Box, detailed below, must be included in these papers.

6.1.5.2. Type B – Publications

Abstracts and Papers: From the CRISP study[1], prepared by [Chair of the writing committee, other members of the writing committee listed alphabetically].[2]

[1]The CRISP Participant Box will be included in all papers if this can be arranged with publisher. Otherwise it will be referenced in one of the Type A papers. It will not be practical to publish the entire list of participants in abstracts.

[2]It will be stated in a footnote that the names of the writing committee are listed alphabetically after the name of the committee chair.

6.1.5.3. Type C and D – Publications

Abstracts and Papers: By [members of the writing committee in any order acceptable to them] and the CRISP study.[1]

[1]The Participant Box will be included in all Type C papers if this can be arranged with the publisher. Otherwise it will be referenced in one of the Type A papers. In type D papers, the list of participants will be referenced in all cases. It will not be practical to publish the entire list of participants in abstracts.

6.1.5.4. Listing of Professional Participants in the CRISP Participant Box

The CRISP Participant Box for each phase will list all professionals that have participated in a study within the CRISP for a minimum of one year in that phase. The participants for each participating center will be listed together, with the center Principal Investigator listed first, and identified as "PI" followed by the other center staff listed alphabetically. Each participant is to be listed only by his/her professional and academic degrees and not by the specific position that he/she holds in the study. The centers are to be listed in the following order:

1. NIH
2. Steering Committee Chair
3. Data Coordinating and Image Analysis Center

4. Clinical Centers (in alphabetical order)
5. Central Laboratories (in alphabetical order)

Prior to the publication of any papers from any phase of a study from the CRISP, each center will be asked to confirm and approve the listing of the personnel from that center in the CRISP Participant Box.

6.1.6. Acknowledgment of Support and Reprint Addresses

Acknowledgment of grant support is to be used in all papers reporting results of the CRISP study. (In the case of ancillary studies, additional sources of support should be cited as appropriate).

The CRISP is supported by the Division of Kidney, Urologic and Hematologic Diseases of the National Institute of Diabetes and Digestive and Kidney Diseases, NIH, through cooperative agreements.

The following information regarding reprint requests should be included in all papers prepared by the CRISP. The NKUD Clearing House will maintain an inventory of all CRISP publications and will actually mail out the reprints.

Requests for reprints should be addressed to: National Kidney and Urologic Diseases Clearing House Box NKUDIC Bethesda, MD 20892

6.1.7. Schedule for Completion of Writing Assignments and Resolution of Overlaps Between Writing Committees

At the time a writing committee is constituted by the Steering Committee Chair, the Publications Committee will establish a timetable for completion of the writing assignment that takes into account deadlines for publication, the amount of time required for data analysis, other commitments of the DCIAC, and priority of the publication. These deadlines may differ based on the complexity of data analysis; however, once the required analysis has been determined, these materials should be available to the writing committee within three weeks.

The Chair of the Writing Committee should provide the Chair of the Publications Committee with a general outline of the proposed publication, within a month of receiving its assignment, to permit the Publications Committee to identify any overlap with the assignments of other writing committees and to permit establishment of an appropriate timetable. Where overlaps of materials to be covered by different writing committees are detected, the Publications Committee Chair will attempt to resolve these informally with the chairs of the involved writing committees. In the event that this effort at mediation fails, the issue will be resolved by the Steering Committee Chair. The Publications Committee Chair will report at each meeting of the Steering Committee on the progress of the various writing committees.

6.1.8. Review of Abstracts and Presentations by the Publications Subcommittee

To expedite review of abstracts, oral presentations, and any other material for which there is an explicit deadline for submission, the following procedure will be used:

1. The writing committee that wants to submit an abstract, give a talk, or submit other material, for which there is an explicit submission deadline, shall contact the Publications Committee Chair. If data analysis is required by the DCIAC in order to submit an abstract or presentation, this notification must be made at least 6 weeks prior to the deadline. In the event that the Publications Committee Chair is unavailable, an Alternate Chair may be contacted. The Chair (or Alternate Chair) will name a subcommittee of three members of the Publications Committee to review the submitted material and will inform the submitter and this subcommittee of their appointment.
2. The submitted material should be mailed by the submitter directly to the subcommittee and the Steering Committee. This material must be submitted preferably two weeks and never later

than one week prior to the deadline for submission. Concerns by any member of the Steering Committee on the submitted material should be addressed to the Publications Committee Chair (or Alternate Chair) to be reviewed by the subcommittee members.

3. The members of the subcommittee shall review the material and notify the Chair solely of the approval or disapproval. If there is unanimous approval, the Publications Committee Chair (or Alternate Chair) shall inform the submitter that he/she has CRISP approval for the submission. In the event of a split vote for approval, the issue will be reviewed by the Publications Committee Chair (or Alternate Chair) with the Steering Committee Chair whose decision will be binding.
4. All materials submitted for approval in this fashion will be distributed by mail, together with notice of the disposition, to all members of the Publications Committee, the Publications Committee Chair and to the Steering Committee Chair. All approved materials will also be forwarded to the NIH Trial Coordinator and, for record purposes, to the Principal Investigator of the Data Coordinating and Image Analysis Center and will be distributed to the entire membership of the Steering Committee at the next meeting of that Committee as an Appendix to the report of the Publications Committee.
5. In the case of abstracts or other similar written material, the entire material to be submitted must be sent by the submitter for review by the appointed subcommittee.
6. In the case of an oral presentation, an outline of the talk and a copy of any slides to be used must be submitted for review.
7. Approval for submission of an abstract does not automatically grant approval of the material ultimately to be presented. This material must also be submitted for review and approval in accordance with the above rules at least seven (7) days prior to the scheduled oral or poster presentation. Normally this review will be done by the same subcommittee of the Publications Committee that reviewed the initial abstract.

6.1.9. Review of Papers by the Publications Subcommittee

All materials for which there is no explicit deadline, and all full papers that may result in a citable scientific reference, whether or not there is a deadline for submission, must be submitted to the Publications Committee Chair for formal review by the entire Committee. If there is a deadline for submission of a formal paper that does not require analysis by the DCIAC, it is the responsibility of the submitter to be certain it is submitted to the Publications Committee Chair or subcommittee, at least 30 days prior to the deadline, to permit such review. *If data analysis is required of the DCIAC prior to submission of the paper, the Publications Committee Chair must be notified at least 6 weeks prior to the 30 day-deadline to allow for adequate analysis*. This review will be conducted as follows:

1. The Publications Committee Chair shall appoint a panel of three primary reviewers, two of whom must be Publications Committee members, and one of whom may be any professional member of the CRISP with appropriate expertise. The Publications Committee Chair shall distribute the material to all members of the Publications Committee and to the Principal Investigator of each center participating in the CRISP. The three members of the review panel shall each prepare and send to the Publications Committee Chair a written critique of the submitted material for distribution to the entire Publications Committee. The PI's of the various clinical centers will be given a deadline of 14 days by which any comments or critiques that study participants at their center may wish to make to the Publications Committee Chair. This mechanism will assure that each professional participating in the CRISP will have an opportunity to review any materials that will be submitted for publication bearing his/her name as a participant and co-author.

2. The Publications Committee Chair shall schedule a meeting of the Committee (generally by conference call), including review of papers and other non-time critical materials as Agenda items. The reviews of the panel members and any comments received from the center PIs will be distributed to the Committee with the agenda.
3. While discussion of the submitted papers and other materials will be led by the three appointed reviewers, all members of the Committee will be invited to participate and all shall vote on final disposition.
4. In keeping with medical editorial traditions, there are three possible dispositions: approval of the material as submitted (possibly with some recommendations for revision that do not require re-review), non-acceptance of the material as submitted but with recommendations to the authors for revisions and resubmission, and disapproval of the material.
5. The Publications Committee Chair shall be responsible for communicating the decision of the Committee to the authors, together with a summary of suggestions for revision, if any. If the Committee has recommended non-acceptance of the material as submitted, but with suggestions for revision and resubmission, he/she and the writing committee may agree not to proceed with a report to the Steering Committee at that time, pending revision and resubmission.
6. If there is a recommendation for approval or final approval or final disapproval of submitted material, or if there is a recommendation for revision which is contested by the author(s), the Publications Committee Chair shall report this outcome in writing to the Steering Committee for final action. In the case of a dispute between the Publications Committee and the author(s), the Publications Committee Chair shall provide a copy of the submitted material and a summary critique to the Steering Committee, and the chair of the writing committee shall be given an opportunity to submit a rebuttal.
7. The authority to grant final approval for a formal scientific paper of the CRISP rests with the Steering Committee.
8. All materials submitted for approval in this fashion will be forwarded, together with notice of disposition, to the Steering Committee Chair. All materials receiving final approval by the Steering Committee will also be forwarded to the NIH Trial Coordinator and for record purposes to the Principal Investigator of the DCIAC.
9. In the event that editors of a scientific journal to which an approved CRISP scientific manuscript is submitted request a revision to a paper, the revisions should be submitted to the Publications Committee to review the revision, and every effort will be made to expedite such repeat reviews.

6.1.10. Criteria for Review of Materials by the Publications Subcommittee

All materials submitted to the Publications Committee will be reviewed for acceptability on two grounds:

1. Materials shall be evaluated for scientific accuracy, quality, importance, and style. The intent is to assure that all approved CRISP materials reflect well on clinical studies.
2. Materials shall be reviewed to assure appropriateness of the content. The material shall be reviewed to assure that it conforms to the assignment to the writing committee, addressing satisfactorily the assigned topics and not encroaching on material assigned to other writing groups. In addition, the material shall be reviewed to assure that it does not divulge prematurely the outcomes or findings of the studies within the CRISP or compromise the eventual publication of any findings in high-quality peer-reviewed journals. In this latter regard, it must be remembered that publication of reports of more than 400 words are generally taken to

constitute prior publication of a body of material and will generally preclude subsequent publication of the material in a peer-reviewed journal.

6.1.11. Maintenance of Records of Publications and Presentations

The DCIAC will maintain a record of all official publications and presentations of studies from the CRISP, separated into the following categories:

- Peer-reviewed papers accepted and published in professional journals.
- Invited editorials, reviews, chapters and books.
- Abstracts published in citable journals.
- Other presentations at regional or national meetings that do not result in a citable abstract.

This listing will be updated at least every six months and will be distributed to the PI of each center participating in the CRISP, together with reprints or copies of any papers, chapters, or abstracts accepted for publication since the last update. This is intended to facilitate the updating of curricula vitae and the timely submission of reports to GCRCs and other such organizations within the participating centers.

6.1.12. Acknowledgment and Acceptance of CRISP Policies on Publications and Presentations by the Professional Participants in the CRISP Studies

To assure that all professionals involved with the CRISP know and understand the policies governing CRISP studies and to preclude the possibilities of misunderstandings after initiation of any studies, each professional member will be given a copy of this document and asked to sign a Statement of Understanding, listing the major provisions of this document and attesting to his/her acceptance of these policies. The original of the signed Statement of Understanding is to be returned to the DCIAC for record purposes. A copy of the Publications Policy and signed Statement of Understanding is to be kept by the CRISP professional participant for reference.

6.2. CRISP Website

The Data Coordinating and Image Analysis Center (DCIAC) developed and maintains the CRISP II website, a password−protected content accessible to only study personnel. The address of the CRISP II website is: https://www.pitt.CRISP2.edu.

The CRISP website has several distinct components dedicated to management and coordination of the study: administrative resources, data−entry system support, forms tracking, querying and editing, and reporting. The administrative component of the web site includes the following features: study protocol, study personnel directory, meeting and conference call minutes, subcommittee minutes and reports, email lists archives, announcements and news, Manual of Procedures (MOP), data collection forms and a link to the web−based data−entry system. Multi−tiered support is provided for website users, including written procedures and technical support via email or telephone. Study documents (MOP, forms, reports, etc.) are available for download in various formats, including MS Word (.doc) and portable document format (.pdf).

Chapter 7. CRISP II Study Design and Protocol

7.1. Overview of Design

The CRISP II Study is a prospective, observational study that is an extension of CRISP I. CRISP I was also a prospective, observational study that enrolled 241 ADPKD subjects between the ages of 15 and 45 years and was designed to determine if novel imaging techniques such as magnetic resonance (MR) imaging could reliably and accurately detect change in renal structure early in the course of APDKD. It is anticipated that 220 CRISP I subjects are available to enroll in CRISP II. CRISP II is designed to include all CRISP I individuals including those who enroll simultaneously in other clinical trials. In this respect, HALT, an ongoing interventional trial of the PKD Clinical trials network may maximally enroll up to 105 subjects in Study A (which includes MR imaging identical to that proposed in this submission) and 32 subjects in Study B (no MR imaging). Importantly, the Principal Investigator (Dr. Ty Bae) and personnel for the Imaging Center (now at the University of Pittsburgh) for both HALT and CRISP II are the same. The CRISP/HALT liaison committee has reviewed and approved dual participation in both CRISP II and HALT and the CRISP and HALT Steering Committees have approved the development of CRISP II.

To minimize subject burden and to maintain retention throughout CRISP II, those CRISP II individuals who also participate in HALT will not undergo duplicate imaging, blood pressure measurements or blood sampling. They will, however, complete the necessary studies of CRISP II that are not included in HALT.

7.2. Study Timeline

STUDY CALENDAR

Time Line	Visit Number	Form Name	Form Number	Date Expected
Initial Clinic Visit	FV-06	Consent Form Family History Registration Biannual Med & Events Biannual Labs Quality of Life (SF-36v2) Pain Symptoms Physical Findings Women's OB-GYN GFR Collection GFR Reporting Archived Blood Sample Archived Urine Sample MR-RBF Checklist (PI signature)	Site Specific	
Interim Phone Visit	FV-06.6	Follow-Up Study & Events		Initial Visit + 6 months
Alternate Year Lab	FV-07	Alternate Year Labs Follow-Up Study & Events		Initial Visit + 12 months
Interim Phone Visit	FV-07.6	Follow-Up Study & Events		Initial Visit + 18 months
Clinic Visit	FV-08	Biannual Med & Events Biannual Labs Quality of Life (SF-36v2) Pain Symptoms Physical Findings Women's OB-GYN GFR Collection GFR Reporting Archived Blood Sample Archived Urine Sample MR-RBF Checklist		Initial Visit + 24 months
Interim Phone Visit	FV-08.6	Follow-Up Study & Events		Initial Visit + 30 months
Alternate Year Lab	FV-09	Alternate Year Labs Follow-Up Study & Events		Initial Visit + 36 months
Interim Phone Visit	FV-09.6	Follow-Up Study & Events		Initial Visit + 42 months
Special Events	When Needed	Shipping Manifest-Blood Shipping Manifest-Urine Shipping Manifest-SC Missed Visit Study Withdrawal Transfer Death Notification		

7.2.1. Development Phase (April 2006-March 2007)

- Protocol refinement, consent form development for CRISP II, local IRB approval
- Forms and MOP development
- Center expansion to include University of Kansas and University of Alabama in Birmingham for measurement of renal blood flow
- Submission of all renal blood flow measures done in CRISP I to Washington University for central review
- Quality Assurance protocol for renal blood flow acquisition at all PCC's
- Review and concept approval of CRISP II protocol by the EAC of CRISP I.
- Continue analyses of longitudinal data initiated in CRISP I
- Complete transfer of data and biologic samples to NIDDK repositories

7.2.2. Baseline or YR1 visit (April 2007-March 2008)

- First PCC visit for CRISP II participants
- Semi-Annual contact with participants via telephone for detailed review of medications, medical visits, hospitalizations
- Annual acquisition of plasma creatinine (duplicate determination)

7.2.3. YR2 visit (April 2008-March 2009)

- Annual acquisition of plasma creatinine (duplicate determination)
- Semi-Annual contact with CRISP extension participants for detailed review of medications, medical visits and hospitalizations
- Initiate analyses of combined CRISP I and CRISP II longitudinal data

7.2.4. YR3 visit (April 2009-March 2010)

- Second full PCC visit of CRISP II participants
- Semi-Annual contact with participants via telephone for detailed review of medications, medical visits and hospitalizations
- Continue analyses

7.2.5. YR4 visit (April 2010-March 2011)

- Annual acquisition of plasma creatinine (duplicate determination)
- Semi-Annual contact with CRISP extension participants for detailed review of medications, medical visits and hospitalizations.
- Data analysis, close out visits, transfer of CRISP II data and samples to NIDDK repositories, completion of ancillary studies.

7.3. Eligibility and patient recruitment for CRISP II

CRISP I participants will be invited to participate in CRISP II. At entry into CRISP I participants met a number of inclusion and exclusion criteria. Exclusion criteria for participation in CRISP II are as follows:

1. Current psychiatric or addiction or non-compliance disorder that in the discretion of the principal investigator indicates that the subject will not successfully complete the study;
2. Current medical problem that in the discretion of the principal investigator would make unsafe the participation in the study;
3. Inability to provide written informed consent

PCC visits and annual blood samplings for participants who are pregnant will be postponed until six months following the delivery of a child and termination of lactation.

CRISP I participants with new MRI incompatible clips or pacemakers or who have developed severe claustrophobia can be recruited into CRISP II, but will not undergo MR studies.
To enroll in CRISP II, individuals must provide written informed consent meeting the requirements of the local IRBs. A typical consent process will include at least two consent forms, one that covers the basic elements of the CRISP II study and a separate consent form requesting permission to contact family members. Consenting to the latter will not be required to participate in the study. Separate consent forms will be developed to obtain historical and clinical information and a blood sample from known affected family members and for site-specific studies not covered in the main study consent form.

The CRISP II protocol does not exclude participants that enroll in other interventional trials. If CRISP II participants are recruited into an interventional trial (e.g. HALT clinical trial) that also requires imaging studies, the visits for CRISP II and for the interventional trial will be coordinated to avoid duplication of tests and undue burden on the participant. Only data from baseline visits in interventional trials will be initially used for CRISP II analysis. Analysis of the data obtained on subsequent visits will be held until the interventional trial is completed. The CRISP II coordinating center and the intervention trial coordinating centers will share tracking and data collection schedules so that data on images completed can be stored. We anticipate that most of the CRISP II biochemical, imaging and urinary data will be collected as part of the other trials. These include serum creatinine, urine albumin, BP measurements, weight and kidney volume. Medical information related to CRISP II will in part be collected in other trials, but there will be some CRISP II specific information that may need to be acquired by the CRISP II coordinators. For example, measurements of the GFR by the iothalamate clearance may not be performed in the intervention trials but will be performed in CRISP II participants.

7.4. Study Visits

Study visits will include PCC visits on years 1 and 3; annual visits on years 2 and 4 to either the PCC or a local physician's office/laboratory; semi-annual telephone interviews; recruitment of family members, sample collection and DNA isolation.

7.4.1. PCC Visits (years 1 and 3)

These visits will be conducted at each PCC following the same standardized protocol. Participants will be admitted to the in-patient GCRC in the late afternoon or evening or in the morning prior to eating or taking medication.

7.4.1.1. Clinical and Laboratory Tests

On admission, participants will meet with one of the investigators, sign the consent form and undergo a formalized medical history interview. Information regarding medications (prescribed and over the counter), quality of life, and level and quality of pain will be obtained using procedures identical to those used in CRISP I. A family history questionnaire will also be obtained. Quality of life (SF-36v2), pain, and family history questionnaires can be completed at any time during the PCC visits. Subjects will undergo a complete physical examination with standardized blood pressure determinations. If indicated, a B-HCG qualitative urine pregnancy test will be performed.

Blood and urine samples will be collected in the morning, prior to morning hydration or taking medications or food. Blood will be collected for:

1. Serum Creatinine – Serum samples will be obtained in duplicate, one processed at the local lab and the other frozen and batch shipped to the Cleveland Clinic Laboratory.
2. Total Electrolyte Panel – Sodium, potassium, chloride, total CO2 (at PCC).
3. Lipid Panel – Total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol (at PCC).
4. Twenty mL will be collected in two SST tubes (tiger-top, 10 mL each) and 16 mL in two PST tubes (green/grey-top, 8 mL each). Samples are to be centrifuged (without decanting) and shipped refrigerated (on frozen cold packs) to the NIDDK Biosample Repository at Fisher Bioservices on the day of collection, where they will be aliquotted into 1 mL tubes and archived.

Urine will be collected for:

1. Urine albumin and creatinine (at PCC).
2. Freshly voided urine specimens will be centrifuged in 50 mL PP tubes at 500 g for 5 minutes as soon as possible, with volume, processing times, and voiding times noted (processing times should be no longer than 20-30 minutes from the time of acquisition). Tubes will be kept in ice throughout this process. The bottom 250 µL pellet (sometimes barely- or non-visible) will be transferred with a 1.0 mL pipette to a 1.5 mL eppendorf tube previously prepared with 750 µL of TriReagent (Molecular Research Center, Inc. Cincinnati, OH), and inverted several times and put on ice prior to freezing at -80˚C for future RNA/DNA retrieval. The remaining urine sample will then be transferred to 10 mL polypropylene (not polystyrene) Falcon culture tubes, stored in six 5 mL aliquots, and sent to the NIDDK Repository at Fisher Bioservices. The NIDDK Repository will supply all tubes, labels and shipping materials.
3. Urine samples for MCP-1 analysis will be sent annually from the NIDDK Repository at Fisher Bioservices to KUMC.

Whether in-patients or out-patients, the participants will have been instructed to drink three 8 oz glasses of water between 9:00 p.m. and 10:00 p.m. on the evening before the testing and to remain fasting but free to drink water ad lib. They will be asked to go to bed at 10:00 p.m. In the morning between 6:00 a.m. and 8:00 a.m. they will be asked to drink six 8 oz glasses of water in preparation for the iothalamate clearance determination which will start at 8:00 a.m., according to the protocol outlined in Section 3.12.2. GFR determinations will be performed using the short non-radiolabeled iothalamate clearance with standardized conditions and monitoring of bladder emptying using a bladder scan to maximize accuracy. The concentrations of iothalamate in plasma and urine will be measured by capillary electrophoresis. The duration of the test for the iothalamate clearance is approximately 2 hours. The plasma and urine samples will be packaged in a "refrigeration specimen" transport box and mailed to Mayo Medical Laboratories. The measurements will be performed at Mayo Medical Laboratories.

After completion of the GFR determination, the participants will undergo an MR examination of the kidneys and liver and determination of renal blood flow. This should take approximately 30 minutes.

Prior to the visit to the PCC, participants will be mailed a family history questionnaire. During the PCC visit, the study coordinator will review the completed questionnaire and the information regarding the family history of ADPKD will be updated. The study coordinator will ask the participants permission to contact their relatives and to sign a separate informed consent for this purpose.

7.4.1.2. Blood Pressure Measurements

The standardized HALT method for obtaining blood pressure will be used. These measurements will be obtained at the time of the PCC visits, annually for local patients or only at the 2007 and 2009 visits for the rest. Blood pressures will be determined in the morning prior to antihypertensive medication intake using automated or non-automated oscillometric techniques (Dinemap, Critikon) and devices maintained and calibrated at the GCRCs or PCCs. The non-dominant arm (in terms of handedness) will be used to obtain BP readings unless there is a reproducible (on at least three consecutive measurements) difference in systolic BP of 20 mm Hg or more between arms. If there is a reproducible difference in systolic blood pressure of 20 mm Hg or more between both arms, the arm with the higher blood pressure will be used. In all other cases, the non-dominant arm will be used. Participants will also be instructed to abstain from smoking and consuming caffeine for 30 minutes prior to taking their BP measurements. After sitting quietly for at least 5 minutes with the arm resting at heart level, three readings will be obtained at least 30 seconds apart. If there is a difference of more than 10 mm Hg (systolic or diastolic) between the second and third readings in one sitting, a fourth and fifth reading will be recorded for that sitting.

7.4.1.3. Serum Creatinine Measurements

Serum creatinine will be determined annually for all participants. Blood will be drawn at the PCC and serum samples will be obtained in duplicate. One sample will be for serum creatinine determinations at the PCC. The other will be batch shipped every three months to the Cleveland Clinic for validation. HALT participants will have the serum creatinine done at the annual HALT visit. For non-local participants who are unable to return to the PCC on years 2 and 4, a blood sample will be obtained in duplicate at a local facility. Duplicate serum samples will be shipped to the PCC, one for processing and creatinine measurement at the PCC and the other will be batch shipped annually to the Cleveland Clinic. For standardization purposes the local labs will be contacted directly with the procedure to be followed.

7.4.1.4. MR Imaging

The imaging protocol for CRISP II has been revised from the MR imaging protocol used in CRISP I. The rationale of this revision is as follows. In December 22, 2006, the FDA issued a Public Health Advisory notifying healthcare professionals of 90 reports of Nephrogenic Systemic Fibrosis or Nephrogenic Fibrosing Dermopathy (NSF/NFD) in patients who have moderate to end-stage kidney disease and received gadolinium-based contrast agents for MRI and MRA. Further information may be found at the following websites:

http://www.fda.gov/medwatch/safety/2006/safety06.htm#Gadolinium
http://radiology.rsnajnls.org/cgi/content/full/2423061640v1

Although a causative relationship between gadolinium contrast medium and NSF/NFD has not been definitely established, published data raised the suspicion that there may be an association between NSF/NFD and gadolinium contrast medium in patients with compromised renal function. In view of these concerns, we will stop using gadolinium contrast medium in our revised MR imaging. Gadolinium-enhanced MR imaging facilitates the process of measuring the kidney volume and identifying the renal arteries, however, is not absolutely required. Instead, an additional fast imaging sequence, 2D true-FISP (FIESTA) without fat sat, will be obtained to image the kidneys just as T2 imaging. This will provide an additional cue to help delineate the kidney border on T1 images. We will acquire 2D true-FISP (FIESTA) with fat sat to depict the renal arteries prior to the phase-contrast RBF measurement sequence.

MR images will be obtained at each PCC using the procedures described below. After the acquisition, MR images will be reviewed locally at each PCC site and securely transferred via secure internet connection to the Image Analysis Center (IAC). The procedures for MR scanning of the heart (HALT study only), kidneys and liver are as follows:

BEFORE EACH STUDY, THE MR SCANNER WILL BE ADJUSTED FOR PROPER SHIMMING.

1. Breath-holding instruction will be provided, and the subject will be coached prior to MR scanning. Administration of oxygen via nasal cannula may help improve the breath-hold capacity, particularly for subjects with limited breath-hold capacity.
2. EKG pads will be placed over the chest. If EKG gating is not available or functioning, it may be replaced with a peripheral pulse gating.
3. Subject will be placed supine on the MR table with his or her arms to the side.
4. A phased-array surface coil will be positioned with its center over the inferior costal margin, i.e. over the expected location of the kidneys.
5. Scout scan to locate the scan range of the entire kidneys. A stack of axial images to cover the most anterocaudal and posterocranial aspects of the kidneys is highly recommended.
6. The field-of-view (FOV) should be kept as small as possible (30-35 cm) without producing wrap-around artifacts.
7. Breath-hold, coronal T2 scan (SSFSE/HASTE with fat sat) with 9mm fixed slice thickness, usually achievable in a single breath-hold. Please make sure both kidneys are imaged completely without missing any anterior or posterior portions. This coverage assurance is critical for the following T1 imaging.
8. Coronal T1 scan (3D VIBE/FMPSPGR/LAVA without fat sat) with 3mm fixed slice thickness (acquisition will be performed at 6mm thickness and then the slice will be interpolated at 3mm, i.e., in GE, ZIP =2 in the slice direction). Keep the flip angle $\leq 15^{o}$. To improve SNR, keep the Bandwidth low (62 kHz or 42 kHz) and/or increase the number of phase-encoding steps (be aware, the acquisition time will increase). In GE LAVA sequence, turning off “optimize flip for CNR” will allow to

change the flip angle or bandwidth. Do NOT use parallel imaging (no SENSE, ASSET, iPAT or GRAPPA).

9. Breath-hold coronal T2 scan (SSFSE/HASTE with fat sat) with 3mm fixed slice thickness, which would require 1-4 breath-holds depending on the kidney size. Use as few breath-holds as possible. The first scan should cover the posterior aspect of the kidney. Neighboring image groups should be overlapped by a single 3mm slice. To determine correct table position choose the "shift-mean (starting point in GE)" of the second scan for example: the first shift-mean = -60mm, the number of slices in the first set =23, (23-1) x3=66mm, new shift mean =-60+66=6mm.
10. Breath-hold coronal T2 scan (SSFSE/HASTE without fat sat) of the kidneys with adjusted slice thickness, 3-6 mm, i.e. the slice thickness best attainable with a single breath-hold (The adjusted slice thickness may not remain the same in a follow-up MR scan if there is a change in the subject's breath-hold capacity or kidney size.) Repeat the scan over the liver with the same slice thickness. This scan and the scan for the kidney should share one overlapping liver slice (i.e., the most posterior slice of the liver scan should be identical to the most anterior slice imaging the liver in the kidney scan. If more than two scans are required to cover the anterior liver, again the neighboring scans should be overlapped by one slice.
11. Breath-hold coronal 2D true-FISP (FIESTA) without fat sat with 3mm fixed slice thickness, which would require 1-2 breath-holds depending on the kidney size. Use as few breath-holds as possible. The first scan should cover the posterior aspect of the kidney. Neighboring image groups should be overlapped by a single 3mm slice. To determine correct table position choose the "shift-mean (starting point in GE)" of the second scan for example: the first shift-mean = -60mm, the number of slices in the first set =23, (23-1) x3=66mm, new shift mean =-60+66=6mm.
12. (For renal blood flow measurement) Breath-hold, oblique-coronal 2D true-FISP (FIESTA) with fat sat with 4mm fixed slice thickness at 2mm spacing (i.e., overlap 50%) over the aorta and renal arteries. In Siemens MR Scanner, overlapping scan requires two separate breath-hold scans unlike GE. Thus, FIESTA with fat sat with 3mm fixed slice thickness with no gap will be sufficient. Typical parameters: 192x 256 matrixes, 75^{o} flip angle, 125 kHz BW, 15-sec scan.
13. (For renal blood flow measurement) Breath-hold, phase-contrast technique of renal blood flow measurement. From the FIESTA images, the renal arteries will be identified. To accurately measure velocity, it is important to choose the imaging slice perpendicular to a vessel. Velocity encoding (VENC) value of 100 or 50 cm/sec will be used. Small FOV (14-16 cm) and large matrix (256x192 or 512x512) are important for an accurate measurement of the vessel size. Segmented, prospectively cardiac-triggered phase contrast flow measurements will be obtained to compute the mean and peak velocities, as well as the total mean flow, during the cardiac cycle.

For image transfers, images will be pushed from the local PCC MR scanner to the PC workstation. For participant confidentiality, participant names and identifiers will be removed and replaced with CRISP-ID numbers and accession numbers prior to image transmission to the IAC. A virtual private network (VPN) client has been installed on the PC workstation to encrypt the data for secure transmission via the Internet. The IAC will review the images and generate quality control reports for PCCs. Images determined to be inadequate for measurement must be reacquired.

The stereology method, a quantitative morphology by statistical analysis of the structures of random sections, is widely used in cytopathology and medical imaging analysis. A point-counting stereologic technique involves a simple, fast method of segmenting an object by counting the number of intersections of a randomly oriented and positioned grid over the object. This method does not require border tracing or threshold determination, but relies on the operator's decision of selecting each point that intersects the object. The areas of the whole kidney in each image can be calculated from the collection of points, and volume measurements can be made from a set of contiguous images. Analysis

software, written by the Mayo Foundation, will be utilized for making stereology measurements. Each volumetric measurement will be made by a trained analyst at the DCC, and will be reviewed by a radiologist for quality control. Agreement between the radiologist and technician in the CRISP Study was very high (97%). The result from the radiologist's review of stereology measurements will be used to calculate the whole kidney volume.

7.4.2. Annual Fasting Sample Collections

On off years, participants will have blood samples collected either at the PCC or at their respective clinics for the determination of creatinine concentrations (see above).

7.4.3. Semi-annual Telephone Interviews

During the interviews information regarding medication changes, hospitalizations, doctor visits and outpatient procedures will be recorded. A follow-up study form will be completed after each telephone interview. Any physician who has examined/treated the participant since the last visit or telephone interview will be contacted to obtain information about the participant's health.

7.4.4. Recruitment of Family Members, Sample Collection and DNA Isolation

A major component of CRISP II (Aim 3) is to collect more exhaustive family histories of all CRISP I patients and draw an electronic pedigree for each family (Progeny). Identified affected family members who agree to participate will be consented into the study and clinical and imaging data from the patient retrieved from clinical records. A blood sample will be collected for a determination of serum creatinine at the Cleveland Clinic laboratory (unless the participant is on dialysis or has received a transplant) and for DNA extraction and the establishment of EBV transferred lymphoblast cell-lines, employing the NIDDK Center for Genetic Studies, Rutgers University Cell and DNA Repository. Samples will be sought from all traceable individuals from each of the families with proven ADPKD by established imaging criteria. We estimate from preliminary analysis of the CRISP families that approximately four further affected individuals over 18 years of age will be traceable in each family making a total of 800 family members. Analysis of known family data predicts that they will have an average age of ~53 years, that 53% will have ESRD and a further 11% renal insufficiency measured by a serum creatinine ≥1.4mg/dl, females and ≥1.6mg/dl males.

Participants will also be asked to complete a lifestyle questionnaire (to assess smoking history, caffeine exposure, estrogen exposure and levels of physical activity) and a family history questionnaire to further extend the traceable family. When possible, the most recent CT or MR examination of the abdomen, or if not available, the most recent ultrasound images will be reviewed and renal volume estimated using established formulae. Kidney volume will be calculated by the ellipsoid formula: Volume = length x width x thickness x pi/6, using maximum length in longitudinal plane and for width and thickness in the transverse plane perpendicular to the longitudinal axis of the kidney at the level of the hilum. If only coronal plane films are available, the kidney depth may be assumed to be equal to the width of the hilum so that the formula becomes: Volume = length x (width) squared x pi/6. Although not as accurate as the MR data available from CRISP I patients, it will be a relatively reliable means to assess renal disease severity in all patients. In approximately 200 of these family members we plan to obtain MR analysis to determine kidney volume as part of an ancillary study to CRISP II conducted by the CRISP investigators (an R01 grant that will be resubmitted) which will try to map modifier loci in this population. The severity of the cystic liver disease will also be estimated (grades 0-4: 0, no cysts; 1, <5%; 2, 2-20%; 3, 20-50%; 4, >50% of liver volume made up of cysts). All of this clinical and lifestyle information, plus the available genetic information on the family, will be stored in the CRISP database that is maintained by the DCIAC.

7.5. Analytical methods

All data are entered into a database maintained by the DCIAC and undergo a variety of quality control procedures to insure its validity. Prior to analysis, simple descriptive statistics and graphic displays will be examined to insure the integrity of the data. In all analyses issues of scaling and distributional assumptions will be carefully monitored.

7.5.1. Specific AIM 1

Extend the preliminary observations of CRISP-I to ascertain the extent to which quantitative (kidney volume and hepatic and kidney cyst volume) or qualitative (cyst distribution and character) structural parameters predict renal insufficiency and develop and test new metrics to quantify and monitor disease progression.

7.5.1.1. Hypothesis 1a

Increased renal volume in general and all renal volumes > 750 mL adjusted for age and other significant covariates in CRISP I predict rate of loss of renal function as well as progression to specific endpoints, e.g. KDOQI Stage IV, ESRD, and/or death.

We will use the following variables:

Dependent Variable: GFR as measured by a 2 hour iothalamate clearance and death. GFR will be analyzed as a continuous measure and will be used to define KDOQI Stage IV and ESRD.
Independent Variable: Total kidney volume (TKV) as a continuous measure and using the >750 mL cut point.

Planned covariates will include: gender, age, race, baseline GFR, hypertension status, urine albumin (UAE) excretion, baseline and follow-up average systolic, diastolic and mean arterial blood pressures and site. Potential modifiers to be investigated will include body mass index (BMI), serum uric acid, HDL and LDL cholesterol, 24 hour urine volume, dietary sodium and protein intake, estimated use of tobacco and class of antihypertensive medication use. We will also explore the addition of parenchyma volume as a modifier (however, it is calculated from total volume so we will need to assess multicolinearity first). Due to the documented co linearity and dependence between total kidney volume and total cyst volume (37),we cannot use this variable as a covariate or modifier but may explore additional analyses using total cyst volume as our primary independent variable. There is a hypothetical possibility that the non cystic volumes (parenchyma volume) may play an important role in disease progression. It will not be possible to determine this effect in this study due to the increased variability of measurement of cyst volume. The hypothesis would be either that parenchyma volume remains constant and cyst and renal volume are totally dependent or that at some point parenchyma volume goes down and the co linearity between cyst and renal volume disappears. It is important to note that parenchyma volume can vary greatly from individual to individual although it represents only a small fraction of TKV. In fact, clinicians make a semi quantitative assessment of parenchyma tissue in imaging studies when they discuss prognosis with individual patients.

Measures: For both our independent and dependent variables we will have one baseline measure, three follow-up measures from CRISP I and two from CRISP II.

GFR and TKV as a continuous measure:

STEP 1: We will use scatter plots and Pearson and Spearman correlation coefficients to assess the relationship between GFR and TKV at each time period. We expect to see a curvilinear relationship (27). This relationship appears to be curvilinear based on iothalamate/MR data as well as other ultrasound and creatinine data (38), and we will assess this with the use of log transformations, amongst others, as has been done in prior publications (27).

STEP 2: We will use repeated measures ANOVA to test the relationship between GFR and time specifically focusing on tests for linear and quadratic trends.

STEP 3: We will use GEE based regression models with GFR as our dependent measure. Recent advances in GEE research and updates to statistical packages such as STATA allow use of GEE for Gaussian based continuous dependent variables as well as dichotomous or count data. However, GEE is sensitive to missing data and we may use a generalized mixed models approach instead. We will have five follow-up measures per person. Baseline TKV will be included in the model at every time period to adjust for possible regression to the mean (39). The model will contain a time variable (for which we will explore alternative correlation structures) and TKV. From this model we can evaluate how much GFR changes with a one unit change in TKV, whether or not the TKV at follow-up significantly predicts the GFR at follow-up above and beyond the baseline TKV value, and how much the addition of time influences that change. We can also test whether time behaves linearly and whether the slope changes over time by including the time x TKV interactions.

Because we are developing the model based on the premise that TKV predicts GFR we will explore whether or not use of TKV at the same time point GFR is measured or use of TKV lagged one follow-up time period is appropriate. Given that there is a one year difference it is possible that TKV at the same time period could act as a predictor but it is more likely that the lag effect is most appropriate. What we expect is that the baseline values primarily predict GFR and that subsequent time point measurements only marginally add to the predictive power of the model. Use of time-lagged GEE models will be tested in all subsequent analyses where appropriate.

The model will be refined by assessing whether the addition of baseline covariates and modifiers improve the model, and whether the addition of other time varying covariates and modifiers improve the model. Since GEE is preferred for prediction models it is our first choice. We will explore use of mixed models instead if the GEE model does not converge appropriately (e.g. due to missing data). While GEE is the typical approach when the dependent measure is dichotomous or count data we prefer to utilize GEE in the context of continuous dependent measures as well. We will also explore random coefficient mixed models as needed. Our guiding reference for this analysis will be a book by Twisk (40).

Power: Starting with the simplest case where we run separate regression analysis at each time point to assess how TKV predicts GFR, a sample size of 220 achieves 80% power to detect an R-Squared of 0.03 assuming no covariates. Using an alpha of 0.01 (Bonferroni correction for doing five models (one for each time point) increases the detectable R-squared to 0.05. The addition of baseline TKV, covariates and moderators will decrease the amount of R-squared we can detect. Using all time points will reduce this even further. The baseline correlation between TKV and RBF was r=-0.344 which corresponds to an R-squared of 0.11.

GFR and TKV as a dichotomous cut point:

STEP 4: At each time point we will compare whether the mean GFR is different for our two TKV groups using independent group t-tests.

STEP 5: GEE will be used with GFR as our dependent measure. Our between subjects factor will be TKV Group status, our within subject factor will be follow-up number and baseline TKV will be a covariate to adjust for regression to the mean. From this model we can evaluate how much GFR changes with TKV Group status and how much the addition of time influences that change. We can also test whether time behaves linearly with the inclusion of TKV in the model. The model will be refined by considering whether there is a time x TKV interaction, whether the addition of baseline covariates improves the model, and whether the addition of other time varying covariates improves the model. Because our covariates and modifiers are not necessarily equal for the two TKV groups we will explore use of propensity scores instead of the traditional approaches to covariate adjustments. As an alternative to GEE we may explore use of repeated measures mixed models as needed.

Power: A repeated measures design with TKV cut point (<= or > 750) as the between factor and day as the within factor has 2 groups. We assume 64% in the > 750 group with the remaining 36% in the ≤ 750 group based on an extrapolation of baseline CRISP I data. Each subject is measured five times. This design achieves 80% power to detect a decrease of 2.7 in GFR assuming the GFR in the low volume group is 98.2 mL/mm/1.73 m^2 with a SD of 24.9 using a Geisser-Greenhouse Corrected F Test with a 5% significance level. This analysis also assumed an autoregressive correlation structure across the 6 time periods with an initial correlation of 0.3. Using log transformed GFR would result in an even smaller detectable change.

While there are no standard approaches to power assessment for GEE, in a simulation study, Jung and Ahn (41) showed they would need 167 subjects to detect a time x group interaction beta coefficient of 0.1 with a 30% / 70% distribution for the group variable, 80% power, alpha=0.05 and an autocorrelation structure with initial correlation of 0.6. Like us, the simulation assumed one baseline and 5 follow-up measures.

Time to Event:

STEP 6: Cox proportional hazards regression will be used to determine whether total kidney volume predicts time to development of KDOQI Stage IV, ESRD, and/or death. We expect 18% of individuals will have CKD Stage 4 and 8% to have ESRD by study end. Actual time of event (day) may not be available. Rather we will know the event most often within ± 3 weeks. Consequently the time of event for our subjects will be measured in overlapping intervals. In this case the model will need to incorporate interval censoring. We will build the model first with only baseline TKV and second with the TKV values at each time point prior to the event by including the TKV by time interaction. We will build separate models with TKV as a continuous measure and as a dichotomous grouping variable. Finally, other covariates will be added as appropriate.

Event status at end of study:

STEP 7: Since each individual will be followed for eight years we will assess whether or not increasing TKV is related to whether or not the individual was at KDOQI Stage IV, ESRD or dead by year eight. We will follow the same modeling stages as STEP 6 but use logistic regression instead of Cox. We will assess whether increasing TKV increases the probability of the event occurring when TKV is continuous and, separately assess whether or not TKV values above 750 mL increase the probability of having the event. We may also incorporate the time period where the event occurred. In this case GEE where our independent variable is dichotomous and there are clustered (fixed time points) observations within each subject indicating trends up to the point the subject was classified as having the adverse outcome. Although, the number or time points may vary (i.e. subjects experiencing an event at varying times relative to baseline), so it we may use a generalized linear mixed model approach instead.

Power: Table 3 shows a range of detectable hazards ratios of TKV on CKD Stage 4 and ESRD in a Cox regression model at alpha=0.05 and 80% power for different levels of r-squared where r-squared denotes the estimate of explained variability of outcomes based on the model with all covariates but TKV status. It also shows the corresponding odds ratios for the logistic regression model to assess the events at the end of the study. The Model assumptions were that 18% of the 220 subjects will have CKD Stage 4 by study end and 8% will have ESRD. The continuous measure of TKV is in log10 units and the TKV group variable is based on the 750 cut point.

Table 3

	CKD Stage 4				ESRD			
	TKV Continuous		TKV Two Groups		TKV Continuous		TKV Two Groups	
R^2	HR	OR	HR	OR	HR	OR	HR	OR
0.0	1.17	1.63	2.53	2.51	1.27	2.01	4.02	3.30
0.1	1.18	1.68	2.66	2.63	1.28	2.08	4.33	3.49
0.2	1.19	1.73	2.82	2.78	1.30	2.18	4.74	3.72
0.3	1.21	1.80	3.03	2.95	1.33	2.30	5.27	4.00
0.4	1.23	1.89	3.31	3.20	1.36	2.46	6.03	4.41

7.5.1.2. Hypothesis 1b

Baseline medullary vs. non-medullary cyst volume and cyst number in CRISP I predict loss of renal function over time.

With the focus narrowing to assess medullary cyst volume we will use the following variables:

Dependent Variable: GFR as measured by a 2 hour iothalamate clearance and death. GFR will be analyzed as a continuous measure.

Independent Variables:

1) The degree of cortical cyst distribution (CCD) on a scale from 1 to 5 (1: mostly medullary, 3: diffuse, 5: mostly cortical) at baseline
2) The ratio of medullary to cortical cyst area percentages (MPCP). A ratio of 1 implies a diffuse distribution; values above 1 imply that the percentage of cysts occupying the medullary area is greater at baseline.
3) The ratio of number of cysts in the medullary region to the number of cysts in the cortical area (MNCN) at baseline.

Potential covariates and modifiers: same as hypothesis 1a

GFR and MPCP or MNCN as a continuous measure:

STEP 8: We will use GEE based regression models with GFR as our dependent measure. Baseline MPCP (MNCN) will be included in the model at every time period to adjust for possible regression to the mean (39). The model will also contain a time variable (for which we will explore alternative correlation structures) and MPCP (MNCN). From this model we can evaluate how much GFR changes with a one unit change in baseline MPCP (MNCN) and how much the addition of time and subsequent MPCP (MNCN) values impacts that change. We can also test whether baseline MPCP (MNCN) values affect GFR differently over time by including the time by MPCP (MNCN) interaction.

The model will be refined by considering whether inclusion of total cyst volume or total kidney volume improves the model (the extent of multicolinearity will be evaluated first), whether the addition

of baseline covariates and modifiers improves the model, and whether the addition of other time varying covariates improves the model.

GFR continuous and CCD:

STEP 9: GEE modeling will be used with GFR as our dependent measure. Our between subjects variable will be CCD (5 levels or 2 levels if we dichotomize as primarily medullary vs. not) and our within subjects variable will be time. From this model we can evaluate how much GFR changes as a function of baseline cyst distribution and how much the addition of time influences that change. We can also test whether there is a change in the effect of baseline CCD on GFR over time by including the time by CCD interaction.

The model will be refined by considering whether inclusion of total cyst volume or total kidney volume improves the model (the extent of multicolinearity will be evaluated first), whether the addition of baseline covariates and modifiers improves the model, and whether the addition of other time varying covariates improves the model.

Power: Since there is no baseline or prior study reporting of any of our independent measures we were unable to do specific power calculations. However, with 220 subjects we can detect a Pearson correlation coefficient between cyst volume and renal function of 0.16 at alpha=0.05 and 80% power.

7.5.1.3. Hypothesis 1c

Prediction models (formulas) utilizing age and renal volume at baseline in CRISP I will effectively predict loss of renal function over time. While we have established with CRISP I data that TKV is a predictor of adverse outcomes and have established that its predictive power remains after statistical adjustment for age, gender, race and other clinical and laboratory measurements, it needs to be translated into guidelines that can be applied by the clinician to provide quantitative prognostic information.

To explore this hypothesis we have developed an age and gender-adjusted indicator of volume severity. The polycystic kidney severity index (PSI) is the ratio of the measured TKV (subject)/ Maximal TKV in the CRISP I cohort (estimated from the equation for the line defining Age vs. Maximum TKV) determined for each subject's age at enrollment. When multiplied by 100, the PSI is the percentage of maximal kidney volume for the stated age of the subject.

GFR and PSI continuous

Step 10: From a statistical perspective developing a linear formula to predict GFR from PSI would be an obvious first step. We will explore this approach but experience shows that doctors tend not to use formulas in the clinical setting. Consequently, we expect that the most clinician-friendly use of the PSI will be to develop ranges of the PSI which will define individuals into groups with relatively homogenous prognosis. For example, if a patient has a PSI of 0.5 and an initial GFR of 98 it is projected to increase by 20% in two years. We will use PSI percentiles and GEE to determine how granular to make our groupings in order to maximize the predictive ability of PSI. We will first divide PSI into two groups based on the median, then three groups based on the tertiles (using two dummy coded variables), then four groups based on the quartiles etc. and continue the process until we have non-significant pair wise differences. GFR will be our dependent measure, PSI groupings our between-subjects factor and time our within subjects variable. We will add the PSI group and time interaction to see if baseline PSI predicts GFR also as a function of time. We will then incorporate age and gender into the model and see if they are significant (our hypothesis being that they will not be as these variables were incorporated into the PSI calculations). Finally, we will assess whether the incorporation of information about the baseline cyst volumes or distribution, genotype, or other covariates substantially improve the clinical utility of using the PSI.

ESRD and PSI
Step 11: Chi-Squared Automated Detection (CHAID) will be used to determine the PSI cut point that best distinguishes who will achieve ESRD by the end of the study. CHAID will look at all possible splits of PSI and determine the split that best predicts ESRD. The same staged modeling approach used in Step 10 (first adding time then age and gender then other covariates) will be done to assess how baseline knowledge of these variables improves the predictability of our PSI cut point.

NOTE 1: We will attempt to determine the appropriate groups of PSI in steps 10 and 11 with half of our sample (or 2/3) and use the remaining subjects to validate the chosen groupings.

NOTE 2: Should PSI not prove a successful predictor we will explore use of Classification and Regression tree algorithms with TKV, age and gender to develop a decision tree algorithm to predict ESRD at study end. For example, the tree may predict that if you are a female African American you are most likely to develop ESRD when your baseline TKV is xx.

7.5.1.4. Hypothesis 1d

Baseline liver cyst volume adjusted for the appropriate variables predicts rate of increase in liver cyst volume in CRISP I participants.

We will use the following variables:

Dependent Variable: Liver cyst volume (LCV).
Independent Variables: Liver cyst volume at baseline

Potential covariates will include gender, age, race, hypertension, blood pressure and site. Potential modifiers to be investigated will include total cyst volume (TCV), total kidney volume, age of menarche if possible, progesterone use (if data are reliable), alkaline phosphatase, GFR, number of pregnancies, and years of estrogen use. We will also explore the possible inclusion of caffeine use and LDL and HDL cholesterol depending on the reliability of the data.

STEP 11: We will use GEE regression models with LCV as our dependent measure. Our independent variables will be LCV at baseline, and time (baseline as the reference group). From this model we can evaluate how much LCV changes over time and the influence of our value at baseline. We can also test whether time behaves linearly with the inclusion of baseline LCV in the model by assessing the interactions. The model will be refined by considering whether the addition of baseline covariates and modifiers improve the model. We are particularly interested in whether the slope of the line changes for age and gender.

Power: Starting with the simplest case where we run separate regression analysis at each time point to assess how baseline LCV predicts LCV, a sample size of 220 achieves 80% power to detect an R-Squared of 0.03 assuming no covariates. Using an alpha of 0.01 (Bonferroni correction for doing five models (one for each time point) increases the detectable R-squared to 0.05. The addition of covariates and moderators will decrease the amount of R-squared we can detect. Using all time points will reduce this even further.
A repeated measures design with follow-up time period as the within factor has 1 group with 220 subjects and data on LCV collected 5 times. This design achieves 82% power to detect an increase in log10 LCV of 0.2 from baseline to the final follow-up measure assuming an overall SD of log10 LCV of 2 (based on CRISP I data) using a Geisser-Greenhouse Corrected F Test with a 5% significance level. This analysis assumed a correlation of 0.3 between the baseline and final follow-up value.

7.5.2. Specific AIM 2

Extend the preliminary observations of CRISP I to ascertain the extent to which age and sex-adjusted measurements of renal blood flow by MR technology predict the rate of renal growth; and renal blood flow and kidney volume predict the rate of renal function decline in ADPKD.

7.5.2.1. Hypothesis 2a

Baseline renal blood flow predicts the rate of increase in renal volume in CRISP I participants

We will use the following variables:

Dependent Variable: TKV Total Renal Volume (continuous)
Independent Variables: RBF Renal Blood Flow at baseline (continuous)

Planned covariates will include gender, age, and race. Potential modifiers include total kidney volume, body mass index (BMI), hypertension status, specific class of antihypertensive medication use, statin use, serum uric acid, HDL and LDL cholesterol, urine sodium (UNaE) and albumin (UAE) excretions, and estimated use of tobacco. Another potential modifier will be the average mean arterial blood pressure during the study to reflect blood pressure control.

TKV and RBF as continuous measures:

STEP 12: We will use GEE regression models with TKV as our dependent measure. Our independent variables will be baseline RBF (and functions of RBF if the relationship is not linear), and time (baseline as the reference group). From this model we can evaluate how much TKV changes with a one unit change in baseline RBF and how much the addition of time influences that change. We can also test whether baseline RBF values affect TKV differently over time by including the time by RBF interaction.

The model will be refined by considering whether inclusion of total cyst volume improves the model (the extent of multicolinearity will be evaluated first), whether the addition of baseline covariates and modifiers improves the model.

Power: Starting with the simplest case where we run separate regression analysis at each time point to assess how baseline RBF predicts TKV, a sample size of 220 achieves 80% power to detect an R-Squared of 0.03 assuming no covariates. Using an alpha of 0.01 (Bonferroni correction for doing five models (one for each time point) increases the detectable R-squared to 0.05. The addition of covariates and moderators will decrease the amount of R-squared we can detect. Using all time points will reduce this even further.
A repeated measures design with follow-up time period as the within factor has 1 group with 220 subjects and data on TKV collected 5 times. This design achieves 82% power to detect an increase in 67 from baseline to the final TKV follow-up measure assuming an overall SD of 670 (based on CRISP I data) using a Geisser-Greenhouse Corrected F Test with a 5% significance level. This analysis assumed a correlation of 0.3 between the baseline and final follow-up value.

7.5.2.2. Hypothesis 2b

Baseline renal blood flow, independent and in addition to baseline renal volume, predicts loss of renal function in CRISP I participants

The analytical approach will basically be to add RBF to the existing **baseline** analyses and models developed in Aim 1 and assess whether adding RBF improves the ability to predict loss of renal function. Potential RBF and TKV or TCV interaction will also be considered.

7.5.2.3. Hypothesis 2c

Combining longitudinal measures of renal blood flow and renal volume may enhance the capacity to predict loss of renal function in CRISP I participants.

The analytical approach will basically be to add RBF to the longitudinal analyses and models developed in Aim 1 and assess whether adding RBF improves the ability to predict loss of renal function. Potential RBF and TKV or TCV interactions will also be considered.

7.5.3. Specific AIM 3

Collect DNA samples and clinical information from CRISP family members known to have ADPKD for use to examine genotype-phenotype relationships and by an independently funded study to identify genetic modifiers.

7.5.3.1. Hypothesis 3a

Genetic heterogeneity and mutation type and/or location affect disease severity in the CRISP population.

This analysis will be similar to previous studies of ADPKD populations (30). The questions to be asked concern the extent to which genic and allelic effects are associated with the phenotype, defined by the imaging and biochemical measures of renal function available in this population. For gene type (PKD1 and PKD2) comparisons will be made with the renal volume data and GFR (and last GFR prior to ESRD) using mixed-model ANOVA and t-test analysis, adjusting for age and gender (30). Within family correlations will be taken into account using generalized estimating equations (GEEs). Data analysis concerning mutation type and position will initially be limited to the PKD1 gene, as there will be far less PKD2 data. As many different mutations to PKD1 cause disease and none is common, to maximize the likely significance of the results, PKD1 mutations will grouped according to type. As we have not found mutation type significant in previous studies (30) we will restrict the analysis to two groups, truncating, compared to in-frame, that mechanistically are most likely to be relevant.

Using all identified individuals with PKD1 from the CRISP families' population (n~800 individuals) we will test for an association of mutation type with renal disease severity. Renal volume, calculated GFR and age at onset of ESRD will be used as the measurements of disease severity. As renal severity differs significantly within families, and use of family averages limits the power of the analysis, this variable will be analyzed per individual. Multiple hierarchical linear regression will be used to model current individual GFR levels as a function of mutation type, age, and gender; taking into account potential within-family correlations using GEEs.

Other endpoints include age at onset of RI or ESRD, age at onset of ESRD alone, and at onset of Stage 3 or Stage 4 RI. Life table methods (Kaplan-Meier, log rank test) will be used to analyze age at onset of the

combined endpoint of Stage 3 or 4 RI or ESRD by mutation type. Individuals without the event of interest will be censored at age of their last renal evaluation. The Cox proportional hazards model will be used to assess and test the effects of type of PKD1 mutation on survival while controlling for gender. Data will be presented using median survival estimates, and Cox model hazard ratios and 95% confidence intervals. As survival times for individuals within a family may not be entirely independent, the robust variance (with family as the cluster variable) will be used when testing for effects with the Cox model. We will also explore use of unordered multi-event survival methods to handle the clustering affect of family members.

Power: We estimate that 65% of 800 patients from typical families will have the combined endpoint of ESRD or RI; renal volume measurements will be available in all cases, and mutation data in 90%. With 650 events, the survival analysis will have 80% power to detect hazard ratios as small as 1.4 when comparing mutation groups (truncating [~65% of patients] vs. in-frame [~35%]). With renal events beginning at about age 30 and median renal survival occurring at about age 50, a hazard ratio of 1.4 translates to being able to detect a difference in median survival as small as 5.7 years between mutation groups. When comparing GFR levels between mutation groups, a difference of 5.6 mL/min can be detected with 80% power, assuming a standard deviation of 30 mL/min. While these power calculations do not consider the effect of within family correlations in disease severity, our experience has been that these correlations are quite small, and as such have little impact on the power estimates. Overall this analysis will show whether there is a correlation between mutation type and the severity of renal disease, with small hazard ratios detectable. The other reason for collecting this information, and especially the DNA samples, is to allow analysis for modifier genes that will be undertaken in the CRISP II ancillary studies R01 grant application to be resubmitted in November 2007 by the CRISP investigators.

7.5.3.2. Hypothesis 3b

Genetic factors that modify the renal and hepatic phenotypes will be detected by a genome-wide association study employing a high resolution SNP array. (Note: This hypothesis will be examined using the CRISP population by an ancillary study to be resubmitted as a separate R01 application in November 2007).

In the modifier study a genome-wide association study (GWAS) employing a high resolution SNP array (Illumina, 317,000 SNPs) will be employed to look for genetic factors that modify the renal and hepatic phenotypes in the CRISP cohort and their families. This ancillary study will first screen the CRISP cohort, using the baseline and longitudinal imaging data as the primary end-points. A second phase of the study will complete a GWAS of the CRISP families' samples employing renal volume and GFR as the primary endpoints. Loci positive in both populations at a level of P=<0.001 or in either group independently at $P=<10^{-6}$ will be screening specifically in an additional ADPKD population. ANOVA will be the primary analysis tool for this study using appropriate transformation to identify a data scale under which ANOVA assumptions are met. Important co-variants for this study are age, genotype, gender and some lifestyle factors such as smoking history and BMI. Identification of one or more modifying locus that significantly influences the clinical phenotype outcome in ADPKD will be of prognostic importance.

7.5.4. Specific AIM 4

Maintain and expand a database of uniformly and accurately collected information including renal structural and functional parameters and a repository of biological samples which can be used by ancillary or independently funded studies initiated by CRISP or non-CRISP investigators.

An ancillary study started during CRISP I began to examine whether urine MCP1 concentrations, a product of cyst formation and growth excreted in increased amounts in baseline urine collections, predict clinical renal imaging patterns and disease course. This study will continue during CRISP II with the specific aims to determine whether the pattern of urinary excretion of MCP1 in individual patients remains stable from year to year and whether baseline urinary excretion of MCP-1 predicts total kidney

volume and total cyst volume and number, loss of renal function, and progression to specific endpoints, e.g. KDOQI Stage IV, ESRD, and/or death. Urinary excretion levels of periostin and other potential markers identified by micro-array screening of human ADPKD tissues will also be studied. Much of the development work for this ancillary study has been done under the auspices of another NIH project by Dr. D.P. Wallace at the NIH funded Polycystic Kidney Disease Center at the University of Kansas Medical Center. Affymetrix gene chip screening has identified several candidate products that are especially well-suited for exploration in CRISP patients as biomarkers of disease progression. Among them, periostin was markedly over expressed in ADPKD cyst epithelial cells compared to tubule cells from normal human kidneys. The goal of this ancillary study is to apply those new findings to the CRISP cohort in which the disease has been fully characterized. For the most part, the statistical analysis will follow the plans for Specific AIMS 1 and 2.

Chapter 8. CRISP Imaging

8.1. Participants

8.1.1. Frequency of Imaging Exams

Imaging studies will be obtained at FV06 and FV08, for all participants. For subjects who are enrolled in the HALT Study A, imaging study obtained during the HALT study will be used for the CRISP study.

8.1.2. Dietary Restrictions

NPO or light diet several hours prior to the scan to minimize intestinal motility.

8.1.3. Contraindications

Each site study coordinator should work with dedicated CRISP II MR technologists and be familiar with MR contraindications, including the size and weight restrictions of the designated study scanner (it may be useful to produce a "hula hoop" in the size of the scanner diameter, or to merely use a tape measure), aneurysm clips, cardiac pacemakers and other implanted electronic devices, metallic foreign objects in the eye or other sensitive locations, cochlear implants, etc. Common contraindications to MR imaging acquisition are:

- Cardiac Pacemaker.
- Presence of MR incompatible metallic clips (e.g. clipped cerebral aneurysm). If there is any question or concern, please consult with site MR technologists and radiologists.
- Body weight >159 kg (350 lbs)
- Untreatable claustrophobia

8.2. Imaging Protocol and Quality Control at PCC

8.2.1. Imaging Protocol and Measurement

Detailed MR imaging protocol is described in Section **7.4.1.4.** In brief, it includes:

- Kidney morphology imaging (for kidney volume and renal cyst volume measurements)
    - 3DSPGR T1 (VIBE/LAVA) **no** fat sat with 6mm thickness and 3mm interpolated spacing
    - 2D T2 (SSFSE/HASTE) fat sat at 3mm thickness and 9mm thickness
    - 2D T2/T1 (FISP/FIESTA/BFFE) **no** fat sat at 3mm thickness
- Liver morphology imaging (for liver volume and liver cyst volume measurements)
    - 2D T2 (SSFSE/HASTE) no fat sat at 3-6mm thickness
- Renal artery blood flow imaging (for renal artery blood flow measurement)
    - 2D T2/T1 (FISP/FIESTA/BFFE) fat sat at 4mm thickness with 50% overlap or at 3mm thickness with no gap
    - Localized oblique axial plane where the renal artery runs in-plane
    - Cardiac-gated, breath-hold phase-contrast with small FOV (VEC=100 or 50cm/s)

8.2.2. Image Quality Control at PCC

Imaging study should be performed on the designated study scanner by the appropriate technologist. It is expected that the PCC site radiologist will directly monitor the quality of images immediately after the acquisition of each sequence while the participant is on the scanner. He/she should monitor and make

modifications as needed. If the quality of images is in question while the participant is still on the scanner, a repeat scan should be conducted and sent to the DCIAC along with proper documentation.

The adequacy of images will be determined by evaluating the scan coverage and recognizing the presence of artifacts and respiratory motion. Field of view may be increased from initial study parameters to allow complete coverage of the kidneys and to avoid aliasing artifact. If in an individual the kidneys are too large to cover in a single breath hold with standard study parameters, the radiologist may: increase slice thickness on T1 weighted images to 3 or 4-5 mm maximum. If this is not sufficient, 2 acquisitions may be made. If a patient cannot complete the entire examination for some reason, they shall be rescheduled to return for completion as soon as possible. If it is not possible in certain circumstances for the PCC site radiologist to monitor directly, he/she may designate for this purpose another radiologist who is familiar with the objectives and protocol of the study.

The PCC radiologist shall examine the images from each procedure to assure quality. He/she also will identify presence or absence of any significant findings in addition to cystic disease. A local report should be generated at no charge to the patient or third party payer to document performance of the examination and presence or absence of any significant findings for the medical record. If there are significant findings, they shall be transmitted to the principle investigator and the patient's primary care physician, or other physician designated by the patient. If the patient has no primary care physician, they may be referred to the PCC primary care clinic. If there are significant imaging related findings, those should be sent to the DCIAC (using the patient's study code only). If further evaluation is needed, that can be recommended to the patient's physician, but costs of that workup will not be borne by the CRISP study. Serious illnesses that would have significant likelihood of preventing the patient from completing participation in the full course of the study, such as incidental malignancy, may be considered as an indication to drop the patient from the study.

It is the responsibility of the technologist and radiologist at each PCC to monitor the patient for adverse events during the MR procedure. Each PCC shall have established procedures for such monitoring, which may be delegated by the study radiologist to another appropriate physician if necessary. If necessary, an adverse event should be treated appropriately, and reported by the PCC site radiologist to the local study coordinator, the PCC principle investigator, the local Institutional Review Board and to the DCIAC. If of a serious enough nature to warrant it, the adverse event should be reported to the IRB's at the other PCC sites.

8.2.3. Rescanning After the Participant Has Left the PCC

Once images have been transferred, the DCIAC will contact the PCC to request a rescan if the quality of images received is unacceptable. In such cases, participants should be rescanned as soon as possible and within the following timeframe: At baseline, local participants should be rescanned within four weeks and participants traveling greater distances to the PCC should be rescanned within four months.

Although PCCs are free to rescan, per the clinical judgment of the PI and in accordance with budgetary constraints, the study analysis must include only authorized images (i.e., rescans requested by the DCIAC).

8.3. Image Transfer Procedures

8.3.1. Overview

After the initial PCC visit has been scheduled, the participant will be registered to the study (entered into the database) and randomly assigned a CRISP participant ID code. Prior to imaging, an image study identifier (accession number) will be assigned for each imaging study. These image study identifiers are printed on the imaging forms when the forms are generated at the local PCC.

Following the acquisition of MR images, at the direction of the radiologist, the images will be sent from the imaging modality (MR scanner) to the PCC Workstation. Software on the PCC workstation allows study personnel to de-identify or "scrub" images by removing the participant's confidential information from image headers and replacing it with the CRISP participant ID code and image study identifier. The de-identified image study is then queued and ready for transmission to the DCIAC. Initiation of the Cisco client software enables the establishment of a secure virtual private network (VPN) channel over the Internet. The digitally encrypted transfer is initiated by study personnel at the PCC.

Complete details for de-identification and image transfer are outlined in the subsections below.

Process Summary: Quick Guide to Image Transfer

1. DICOM files are sent from the scanner to the PCC Workstation.
2. Establish the VPN connection via Cisco client in order to transfer.
3. Open CSW program in order to de-identify and send images.
4. *Scrub Headers*: Select imaging study; replace name and local patient ID with CRISP ID and imaging accession number.
5. *Queue De-identified Images*: Click Export, Destination IAC, and Export again.
6. *Transfer*: Images will be transferred via VPN, check status of transmission.
7. *Archive*: Burn a backup CD of the imaging study if necessary. Exit VPN and CSW after all images have been transmitted.

8.3.2. PCC Workstation

A standardized computer has been purchased and configured by the DCIAC for each PCC. This system is to be used primarily for transferring images to the DCIAC and could be used for printing forms and data entry via the CRISP website. Each system is equipped with Clinical Studies Workstation (CSW) and Cisco client software. CSW is a software product developed by Washington University to facilitate research studies involving image data from clinical or research instruments. The software allows the user to store images and modify header attributes, such as patient name and local patient ID, before the data is sent to a research system. This allows the user to protect study participant confidentiality and substitute appropriate research identifiers which cannot be entered at the clinical device. The Cisco client software allows for the secure transmission of de-identified images to the DCIAC.

8.3.3. Header Scrubbing and Image Transmission

8.3.3.1. Establish VPN Connection

After the entire imaging study has been sent from the imaging modality (MR scanner) to the PCC Workstation, start the Cisco client and enter the assigned password. This step connects your computer to the virtual private network (VPN) used by the DCIAC and allows you to send de-identified data to the DCIAC storage system.

Establishing the VPN connection removes your computer from your campus network until the VPN software is disconnected. Therefore, it is important that this step take place after the MR scanner has completed its transmission to the PCC Workstation.

8.3.3.2. De-identify Headers and Transmit Images via CSW Software

The Clinical Studies Workstation (CSW) program is launched from the shortcut icon on the PCC Workstation.

The program allows the user to modify certain header attributes and queue images for transmission to the DCIAC. The goal of scrubbing headers is to replace personal identifying information (participant's name and local patient ID) with CRISP participant ID and imaging accession number in order to protect the privacy of study participants. Changes made for de-identification are not retained by the CSW application. When the application is exited and started again later, the system will show the original patient name and local patient ID which came from the scanner.

The CWS application provides several different views of the data received from the MR scanners and stored by the DICOM Storage Service on the PCC Workstation. Figure 8.1 is an example of the Study View from the CSW application. The red Device Studies banner denotes that these are imaging studies which have been received from a scanner. Although a Series View is also available you will usually send an entire study to the DCIAC.

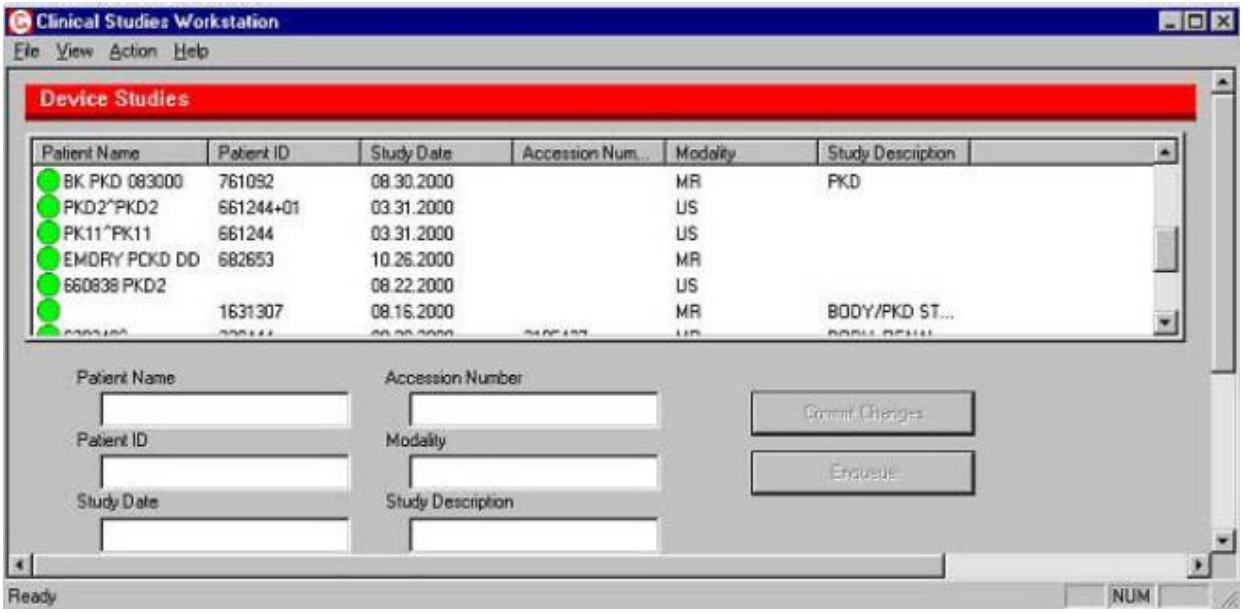


Figure 8.1. Screenshot – Study View from CSW Application

To de-identify and send an imaging study to the DCIAC**, follow these steps in Study View:**

1. Select the study to be transmitted (single click).
2. De-identify images: Remove the Patient Name. Replace the local Patient ID with the CRISP participant ID. Add the imaging study identifier (accession number).
3. Select the ***Commit Changes*** button. The circle icon next to the study will change color from *green* to *yellow* to indicate the study has changed. As noted above, this stores the changes in local memory (desktop) and does not change files on disk.
4. Select the study to be transmitted again (single click). You should see your new values for Patient Name, Patient ID, and Accession Number appear in the text boxes. Make sure the participant's name and local patient number do not appear.
5. Select the ***Export*** button.
6. Queue images: Select the destination "IAC" and click the ***Export*** button.
7. Repeat the steps above for each study or series in the study protocol.

8.3.3.3. Transmissions Pending

Selecting the Export button the second time (step 6 above) writes a text file in the queue area and instructs the DICOM Export Service to send images to the DCIAC. Transmission will begin after about one minute and may take upward of 15 minutes to complete. The CSW application can be used to view the queue entries for images to be transferred to the DCIAC.

You can monitor the progress of the transmission by following these steps:

1. On the menu bar of the CSW application, select View and Queue Pending. A screen similar to Figure 8.2 below will appear and provide the current status of the studies being transmitted.
2. Click the Refresh button to update the status. A "failed" status usually indicates the VPN connection is not active. When the queue is empty, the Cisco client software can be disconnected to allow the PCC Workstation to return to its normal network connection.
3. To confirm that images have been sent, refer to Figure 8.3 in the next section.

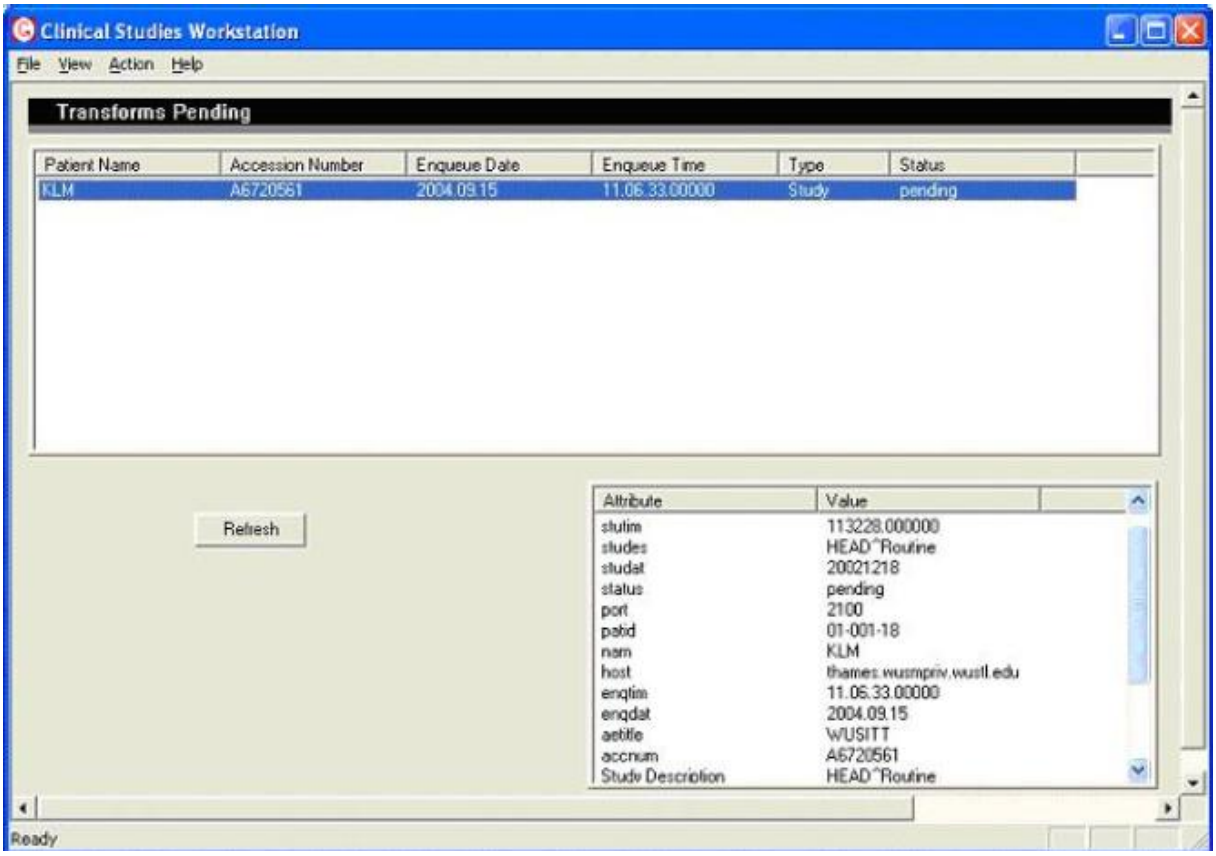


Figure 8.2. Screenshot – Current Status of Studies being Transmitted

8.3.3.4. Transmission Confirmation

Following header scrubbing, study personnel enable a software client that creates a virtual private network (VPN) connection between the PCC Workstation and the firewall device at the DCIAC. Point-to-point Tunneling Protocol (PPTP), Layer 2 Tunneling Protocol (L2TP), and IPSec are used to establish a secure channel over the Internet. Encryption (Data Encryption Standard – 128 bits) is then applied to the image data sent via VPN. Images are decrypted by the firewall device at the IAC and forwarded over a private local area network to a DICOM storage application on the UNIX computer system dedicated to CRISP II.

To see if a study has been transmitted, select View and Queue Complete. A screen similar to Figure 8.3 will appear providing a list of all studies transmitted. Clicking on individual studies provides details on the study in the lower right hand corner of the window. Scroll down to the "total images sent" attribute to confirm the number of images that were transmitted.

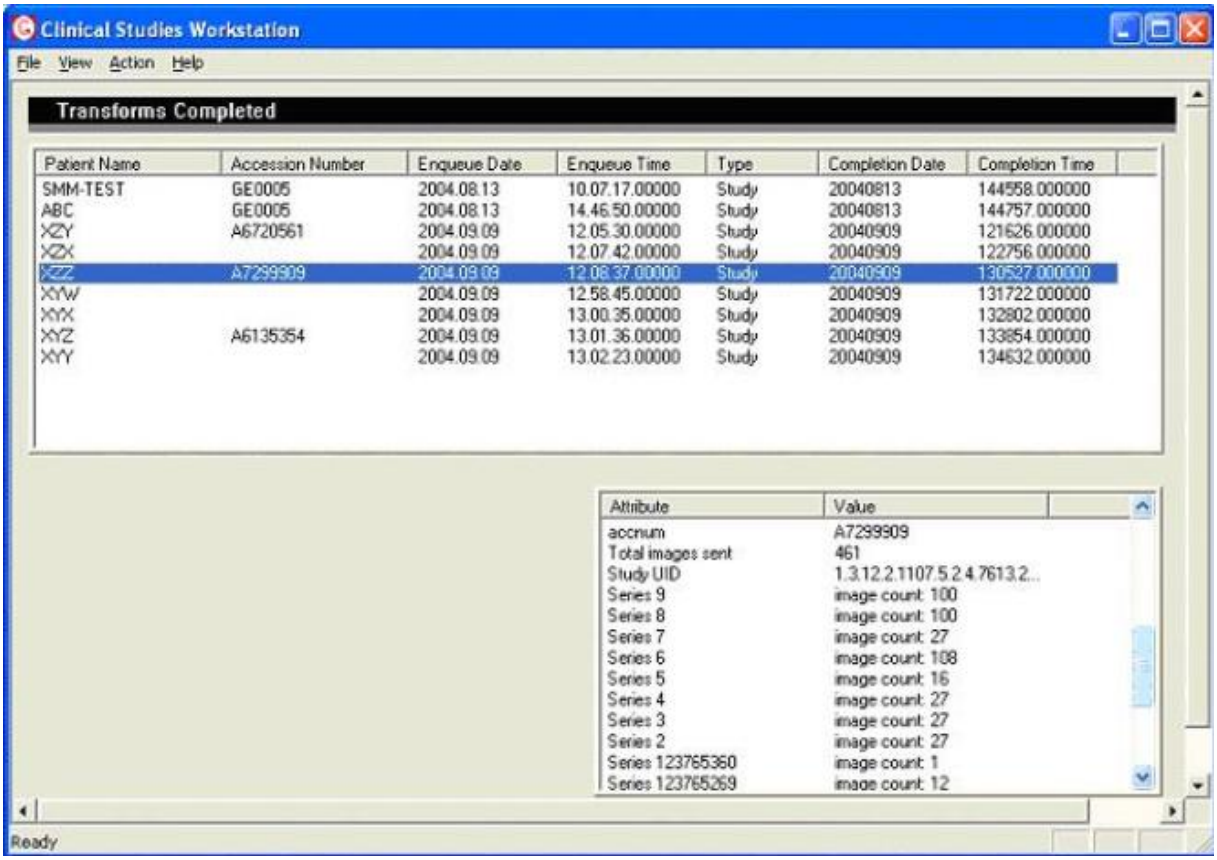


Figure 8.3. Screenshot – List of all Transmitted Studies

8.4. Image Archive

Each PCC is to archive all CRISP imaging studies received from the MR scanner. Some PCCs may wish to create backup copies on CD−ROM at the time of transfer, and a CD−ROM drive is provided with the PCC Workstation for this purpose. To create an archive copy of a study, repeat the steps in section 8.3.3.2 but change the destination in Step #6 to "Local Disk for Backup/Media Export". The studies are saved in the C:/CSW/Export/Images folder on the PCC Workstation. Use the available CD burning software to copy the study to a CD−ROM (multiple images will fit on a single CD). Studies that have been successfully transmitted to the DCIAC, once archived, may be deleted from the PCC Workstation. To delete a study from the PCC Workstation, simply highlight the study in the Device Studies View, click **A**ction in the menu bar, and click Delete from the drop down list. Click **Y**es to delete the study. Be careful that you don't accidentally delete studies that have not yet been archived or transmitted to the DCIAC.

8.5. Central Processing and Analysis

The CRISP study will include acquisition, storage and analysis of data from a variety of different sources. First, the PCCs will enter a variety of types of data directly into the web-based data-entry system. This data-entry system includes all features of a data-management system, including data-editing, data-entry and data-deletion. Second, the image data will be transmitted to the imaging section at the DCIAC. After data analysis has been performed by the imaging group, relevant data will be transferred to the data-management system. Third, a variety of data will be analyzed at each PCC and will also be entered into the web-based data-entry system.

8.6. MR Scanner

8.6.1. Breakdown

It is likely that at some point during the HALT PKD study, an MR scanner will undergo technical failure such that the imaging protocol cannot be performed or completed as scheduled. At those sites with more than one scanner, a backup scanner should be designated. If an identical scanner is available, it should be validated as the backup scanner. If a scanner is available but not identical, as long as it can perform the study sequences, it may be validated as a backup. The validation may be done using a kidney phantom or human subject. The study protocol then needs to be saved in the memory of the designated backup scanner. At sites where there is no available backup scanner, the participant will need to be rescheduled for the earliest available date for rescanning, preferably within 2 weeks. If only MR imaging must be performed, the participant may be rescheduled as an outpatient.

8.6.2. Replacement

At present it is expected that the MR sequences, developed and finalized for the CRISP protocol, will be in use for the duration of the study. There may be some modification in MR sequences and scanning techniques, but no dramatic change requiring new hardware. Over the course of the study, however, upgrade or replacement of the designated MR scanner(s) may occur. This change must be communicated to the IAC, and it is the responsibility of the PCC radiologist to validate a new scanner. If only a software upgrade is performed, as long as the study protocol can be followed, there is no concern. If a new device is installed, it must be validated for equivalent magnetic field strength and homogeneity, as well as for its ability to perform the study sequences (or equivalents), preferably by use of a kidney phantom. Alternatively, comparison of a scan on a study subject that has had a previous MR may be used. If new technologists are added to a site, they must be trained in the objectives and procedures for CRISP study imaging at the direction of the PCC radiologist, with the assistance of the study technologist(s).

8.6.3. Quality Control

It is the responsibility of the PCC radiologist to assure continued image quality. It is expected that a regular Quality Control Program of the MR facility (as is routine for clinical purposes) has been established at each site. The radiologist is to monitor study procedures as they are performed and document proper performance. The radiologist is also to document any and all reasons for variations from standard protocol or variations in quality. Overall quality should be reviewed weekly or monthly, depending on volume, over the course of the study. Periodic review with the technologist to address any decline in quality should be done as needed.

8.7. Certification

It is required that CRISP study/imaging personnel undergo training and be certified prior to performing CRISP imaging procedure. Imaging equipment must also be identified and certified prior to performing CRISP imaging procedure.

8.7.1. Personnel

For best image quality, MR examinations should be performed by experienced MR technologists who are ARRT-registered radiology technologists, preferably with MR Registry. At the discretion of the PCC radiologist, a specific technologist may be designated as CRISP study technologist. A backup study technologist should also be designated. Depending on local operations, the radiologist may choose to designate a pool of technologists to perform MR scans on CRISP study participants. It is the responsibility of the PCC radiologist to thoroughly train all participating technologists in proper study procedures, as well as to make certain they understand the objectives and proper imaging protocol for the CRISP study.

8.7.2. Equipment

It is the responsibility of each PCC, under direct supervision from the study radiologist, to identify the MR scanner to be used for MR data collection for the CRISP study. This should be the most up-to-date 1.5 T scanner. The scanner will be identified and validated by means of scanning a series of normal or PKD subjects, such that the capability of the scanner to perform the imaging sequences required by the study protocol will be documented. The validated study scanner is then to be used for collection of MR imaging data on CRISP participants. An institution with multiple, similar scanners may elect to validate more than one scanner for study use. The preferred approach would be to have a single, designated scanner that has been validated by repeated scanning of normal or PKD subjects with CRISP protocol and the evaluation of the quality of acquired images. Imaging sequences should be saved as a clearly identified CRISP protocol so that each participant is scanned with the proper set of sequences.

8.8. Image Check-in and Image Quality and Protocol Evaluation

8.8.1. Image Check-in

MR images that are transmitted to the DCIAC will be reviewed and placed into appropriate DCIAC image database by means of 'check-in' procedures. Patient ID and the accession number of the images will be compared with those in the transmitted PCC image acquisition form. Image series and image header information will be compared with those recorded in the image acquisition form. The transmitted images are in a DICOM format. They will be converted to the AVW format which is the standard format for ANALYZE software that we use for image evaluation and analysis. Image check-in procedure is conducted by the following steps:

A.1.1:

A.1.2: Print out the MR Session Information Form

1. Go to the website http://www.crisp2.pitt.edu
2. Log into the website.
3. Print the MR Session Information form out.

A.1.3: Convert DICOM images to Analyze Format

1. Window 1:

cd /space/pcc-images/staging/CRISP2/MAYO_CRISP2

NOTE: Record the last 4 or 5 digits of the DICOM study UID name for later use such as *42512.

2. Window 2

cd /crisp2a/pcc-images / MAYO_CRISP2

ls (make sure there is no duplicated case)

mkdir xxxxxxx

3. Window 1

cp –rp *42512 /crisp2a/pcc-images/CRISP2-MAYO/xxxxxxx

du –sk *42512

4. Window 2

du –sk xxxxxxx (make sure got the same or similar size in both windows)

chmod –R 775 /crisp2a/pcc-images/CRISP2-MAYO/xxxxxxx

cd xxxxxxx/*42512

5. pwd, make sure the directory is: cd /crisp2a/pcc-images/CRISP2-MAYO/xxxxxxx/*1.3.46.670589.11.0.0.11….. 42512*

crisp2_report_1 .

Copy the listing from the computer screen and paste it into a Excel spreadsheet. Compare this report with the series report printed from the Biostatistics Web Data Entry System (WDES). Make sure that the Patient ID, Accession Number, series numbers and the slice account match on both reports. Also put the site name and the receive date on the spreadsheet. Print the spreadsheet and attach it to the MR Session Information form.

6. Window 3

cd /crisp2a/pkd/conversions/scripts/production

mkdir xxxxxxx

cd xxxxxxx

7. pwd (then copy the results of the pwd into Step 8)

8. Window 2.

Pwd, make sure it is the correct directory

/crisp2a/pcc-images/CRISP2-MAYO/xxxxxxx/1.3.46.670589.11.0.0.11…..42512

crisp2_gen_mr_conv.pl institution >/crisp2a/pkd/conversions/scripts/production/xxxxxxx/xxxxxxx.csh

The highlighted text is copied and pasted from Step 7 above.

9. * Review the conversion script.

❶ window 3, Start the Cygwin program, type “startx” in the terminal window.

nedit xxxxxxx.csh

❷ Make sure the TARGET = /crisp2b/pkd/pat/bv01/$ACCESSION.

❸ Delete scout series/Renal Blood Flow/MRA/Timing Bolus/gad bolus renals series. Save the change.

10. From /crisp2a/pkd/conversions/scripts/production/xxxxxxx directory:

chmod 775 *.csh

xxxxxxx.csh > xxxxxxx.log

more xxxxxxx.log NOTE: You only need to do this if errors are produced during the above run.

If any errors appear in the log file, you need to correct the script and run it again. Running the script several times until everything works is not a problem.

11. Window 4

```
cd  /crisp2b/pkd/pat/bv01
chmod  –R  775   xxxxxxx
cd  xxxxxxx
ls  –al
```

To make sure all of the files can be written to by the group.

Create Entries in CRISP2 Database

1. Go to website http://pkd2:8080/CRISP2/
2. Click “check in”.
3. Click “No. Studies in Queue” to open up each site studies.
4. Find the right case, click on the UID.
5. Make sure the “Patient ID”, “Accession Number”, “Visit Number”, “Directory name where the DICOM Study is stored” and “Directory Name where the Analyze Files are stored” are correct.
6. Select correct description for each series form the scroll down window. Fill out “Scan Duration” and “FOVxFOV”.
7. Click “Submit Update”.

Enter Check-in information into the Database

Open up the Access crisp2 database.
“Tables” → “dbo_checkin”, fill out “received_date” and “checkin_date”.

8.8.2. Image Quality and Protocol Evaluation

1. Load all the series under the same Accession No. to Analyze 8.0 dialog on the second day of check-in.

2. Look at all the series carefully, choose the slices and give the scores for the image quality and protocol followed.
    - Regular FatSat T2 9mm images. To evaluate an overall expression of the patient’s situation.
    - Regular FatSat T2 3mm images. Choose the slices covered the whole kidneys (sometimes you need to combine multiple series together). The image quality and protocol are graded 1 to 5 with consideration of image and protocol factors such as table position, thickness, FOV, sequence, coil location, artifact, etc.

- Score 1: Poor – unacceptable (need to be rescanned)
- Score 2: Not adequate, coverage incomplete
- Score 3: Adequate, acceptable
- Score 4: Very good, coverage complete
- Score 5: Excellent
    - Non FatSat T1 3mm images. Choose the slices you will use to create the file that can be used to measure the kidney volume.

- Non FatSat Fiesta 3mm images. To define the whole kidney coverage that will be used as reference series to help defining the kidney boundary as to measure the kidney volume and kidney cyst volume.
- Regular Non FatSat T2 6mm adjustable thickness images for liver. To ensure the slices you will use to create the file that can be used to measure the liver volume and the liver cyst volume. Use the same score system as the kidney series.
- Renal blood flow images. First convert DICOM format to AVW format by using 'import/export' function. To see whether the renal artery is clear enough to measure. Use the same score system as the kidney series.

3. Enter all the scores and comments in the Scan Evaluation Form on the CRISP2 website.

4. Enter QC information to the database
   Open up the Access crisp2 database.
   "Forms" → "dbo_Study_from_MR_Query4" → type the accession number into "Find Accession #" → fill QC score into "image quality" and "protocol quality" columns and the rescan required sequences in the "study_comment".
   Tapy "y" in the "measure_needed" if the sequence acceptable for measurement; the slice range in "slices_to_meaure" column; the comments in "orientation" column; QC information in "mri_param_comment" column. If rescan is required, select "y" in the "repeat_MR_scan" column corresponding to the sequence.

8.9. Image Analysis and Measurement

8.9.1. Personnel and Training

Image analysts, who are professionally trained radiologists, are selected to perform image analysis during the course of the CRISP study, will have to be trained in order to process and measure the image data. A detailed set of training procedures are created and used to instruct the Image Analyst how to process the images using Analyze software, and how to measure the images once processed. After the training period is complete, a set of test images are used to test the Image Analyst's ability to process the data and/or measure the data. The results obtained from the test images will be compared to standardized results. If the Image Analyst's results are not within an acceptable range as determined by the DCIAC principal investigator, then the Image Analyst's will need additional training. For each task, there will be a primary and a secondary Image Analysts to ensure a back-up personnel is available.

8.9.2. Image Analysis and Measurements at DCIAC

8.9.2.1. Kidney Volume Measurement

The volume of each kidney is measured on a set of 3DSPGR T1 (VIBE/LAVA) no fat sat images using stereology method. Stereology is a simple, fast method of measuring the area or volume of an object by counting the number of intersections of a randomly oriented and positioned grid over the object to be measured. This technique has been widely used in cytopathology and medical imaging analysis. The advantage of the stereology technique is it allows the operator to utilize the complex interaction of the human eye and shape recognition to segment complex images, but its weakness is that it is operator-dependent and somewhat subject to display window settings. Thus, accurate and reliable measurement requires training an operator and consistent initial adjustment of display window settings.

After the T1 series which contains multiple adjacent images is loaded, the operator will view an image (slice) located in the approximate middle of the kidney(s) and set the maximum threshold to a value that does not saturate the kidney or cysts, but yet enhances the contrast between the kidney and surrounding tissue. Setting the threshold is necessary to improve the visual recognition of the kidney parenchyma and cysts. Grid points over the renal parenchyma and cysts will be mouse-clicked and marked over one kidney at each slice throughout the series. The analyst will also load the FIESTA and/or T2 images at the same time as an additional cue to help determine the kidney boundaries on the T1 images. On each processed slice, the cross-sectional renal area will be calculated by counting the number of marked grid points and using a conversion factor determined in the DICOM image header, while the volume will be computed from the cumulative number of marked grid points for each kidney.

The images that are marked with stereology grids and segmented by the initial Image Analyst will be saved and double-checked by a second Image Analyst who is more experienced in quantifying kidney volume. If necessary, further adjustment and revision of stereology grids will be performed, and the final processed images with marked grids will be archived.

8.9.2.2. Kidney Cyst Volume Measurement

The kidney cyst volume is measured on a set of 2D T2 (SSFSE/HASTE) fat sat images using region-based thresholding method.

Step 1: Kidney Boundary Segmentation

After the T2 series which contains multiple adjacent images is loaded, the operator will view an image located in the approximate middle of the kidney(s) and set the maximum threshold to a value that does not saturate the kidney or cysts, but yet enhances the contrast between the kidney and surrounding tissue. The advantage of this region-growing by seed placement method allows the operator to place a seed within the kidney and adjust the upper and lower threshold of the seed until the perimeter of the kidney is visually delineated by the operator on an image-by-image basis. First, a histogram for the signal intensities of the voxels covering the abdomen is obtained. An intensity value corresponding to 90% maximum value of the histogram is selected. With this value as the maximum threshold, after a seed point is placed over the kidney, threshold range is adjusted until the growth or shrinkage of the boundary outlining the kidney optimally fits visualized kidney region. After the kidney perimeter is determined, the exterior region is set to a value not found in the kidney (normally set to zero). Therefore, the result is a segmented kidney after all the images have been segmented in this manner. The disadvantages of this method are (1) the subjectivity of determining the initial window setting to improve kidney and surrounding tissue contrast, (2) the subjectivity of determining the best threshold for each individual slice to delineate the perimeter of the whole kidney, and (3) the subjectivity of drawing limits when the region-growing includes the kidney or spleen in the perimeter. The Image Analyst is required to manually draw a limit along the edge of the kidney perimeter in order to exclude the unwanted tissue(s).

After a kidney has been segmented, it may be saved and the volume measured using Analyze Region-of-Interest (ROI) software. The voxels are automatically counted in ROI by choosing a threshold set above the base value that eliminates the background surrounding the kidney and only includes the perimeter and interior of the kidney. Since the ROI software only counts voxels, the voxel count has to be converted to a volume using a conversion factor (number of voxels times the volume of a voxel) determined by knowing the voxel dimensions as found in the DICOM image header.

Step 2: Renal Cyst Segmentation

Within the segmented kidney boundary, renal cysts are detected because of their bright signal (water has a long T2 value compared to other tissue or fat) against the renal parenchyma which is gray in signal intensity. The segmentation of renal cysts is performed by using the following steps: (1) A histogram is generated from the pixel values within the segmented kidney boundary; (2) A threshold value, which provides a maximum separation of the cysts from the background parenchyma, is determined in the histogram; (3) The image is reviewed and the analyst adjusts and determine a threshold that renders the pixels within the image into binary values, i.e., cysts are white and the background is black; (4) The volume of cysts within the image is calculated by summing the number of voxels in the cysts. The region-based thresholding method is reproducible and less operator-dependent, but choosing the correct threshold value may be subjective. If the regions (cysts and background) to be separated in the series have well-segregated pixel values in the histogram, a consistent threshold value throughout the entire volume is likely attainable. Otherwise, the binary threshold should be determined in each slice.

Step 3: Complex Renal Cyst Segmentation

While most cysts contain simple fluid and present with dark signal on T1 and bright signal on T2 images, some cysts may contain various substances (e.g., blood, protein) in addition to simple fluid and present with complex MR signal intensity, often gray or dark signal intensity on T2 images. These T2 'dark' cysts are usually bright on T1 images, while simple cysts are invariably dark on T1 images. Consequently, after simple cysts are segmented and volumetrically measured on T2 images, complex cysts that are not measured can be segmented separately on T1 images. T2 and T1 images at the same slice level will be compared side-by-side. All simple and some complex cysts that have been segmented and measured on T2 images will be ignored. Only the complex cysts that have not been segmented on T2 images will be additionally measured on T1 images using Stereology and included into the total sum of kidney cyst volumes.

8.9.2.3. Liver Volume and Liver Cyst Volume Measurements

The liver volume will be measured on a set of 2D T2 (SSFSE/HASTE) non fat sat images. The Image Analyst will review each slice and manually delineate the boundary of the liver including the liver parenchyma and cysts against the peritoneal fat and lung. After each liver region is segmented, it will be converted into a binary image and the liver area will be measured using Analyze Region-of-Interest (ROI) software.

Within the segmented liver boundary, liver cysts are detected because of their bright signal against the liver parenchyma which is dark in signal intensity. Liver cysts are much more homogenous in signal than renal cysts. This allows the Analyst to readily adjust and determine a threshold that renders the pixels within the image into binary values, i.e., cysts are white and the background is black. The volume of cysts within the image will be calculated by summing the number of voxels of the cysts.

8.9.2.4. Renal Artery Blood Flow Measurement

Renal artery blood flow is measured on cardiac-gated, breath-hold phase-contrast MR images using QFlow software (Medis medical imaging systems). Measurement procedures we follow are described in detail in the QFlow User Manual that is available at the DCIAC. Some of the key steps involved in the flow measurements are as follows:

Creating Contours

QFlow offers tools for quickly and accurately detecting and drawing contours that mark vessel areas.

To detect a contour

1. Click in the toolbar.
2. In the Phase or Modulus View, click in the center of the vessel.
   This adds a center point and a vessel contour to the image.
3. If the contour does not exactly fit, click to place a new center point. This removes the old contour and creates a new one.

You can also draw a contour manually, in line mode or (even more accurately) in pixel mode.

To draw a contour using the trace tool

1. In the Object section of the toolbar, click.
2. In the Mode section of the toolbar, click.
3. When you move the cursor over the Phase or Modulus View, it becomes cross-shaped.
4. Click in the image, hold down the left mouse button and trace the vessel contour.
5. When you reach the end of the contour, release the mouse button.
   This automatically closes the contour.
   Saving and Loading Contour Files

Save contours in a contour file

Select File > Save contours as… from the menu bar or press CTRL+SHIFT+S.
This opens the Save Contours As dialog box.

Perform a flow analysis

1. Select the image with the highest contrast between the vessel and the background.
2. Click in the toolbar.
4. In the Phase or Modulus View, select the center point of the vessel in the image.
   If the vessel has a shape that is hard to detect or if the image quality of the study is poor, make sure to draw the first contour. Refer to Chapter 4 for detailed instructions on drawing and editing contours.
5. Press CTRL+D to automatically detect contours in the other images, or select Contour detection > Full automatic contour detection.
6. Check if all contours have been detected correctly. Make sure to edit or delete incorrect contours. Press CTRL+D again to automatically redetect the contours. Repeat this procedure until all contours have been detected correctly.
7. If you want to analyze a second, third, or fourth vessel in the same study, click , or in the toolbar and repeat steps 3 through 5 for each next vessel.

To view flow analysis results

When you have performed the flow analysis, you can view diagrams that display the mean velocity of blood flow in one or more vessels, the maximum velocity of blood flow in one or more vessels, the flow volume in one or more vessels, the area of one or more vessels, velocity distribution in a vessel, and cumulative velocity distribution in a vessel.

Select View > Graph, press F7, or click .

This displays the results of your analysis in the Mean Velocity diagram, which looks similar to the following. Click the button of the contour number or numbers that you want to view in the diagram.

Chapter 9. Data Management

9.1. CRISP II Study Forms

Forms development and updating will be done during the initial phase of the CRISP II study. The Forms Committee closely supervises this process, using email and other electronic communications tools, and indicates final approval of all forms. The Steering Committee met in January of 2007 to review the CRISP I forms for CRISP II modification and to discuss potential new forms. Between January and July of 2007 several iterations of forms were developed. A freeze on form changes has been implemented in August 2007 so that the web data entry and tracking systems can be finalized. The DCIAC will store information on required form changes and implement them in batch every 6 months or so.

All forms are available on the web site in a generic and unlabeled manner (pdf documents), and can be examined by CRISP personnel at any time.

9.2. CRISP II Paper Data Entry System

- accessing the website
- reviewing the forms
- printing forms for a participant
- accessing the study calendar
- Special Instructions: How to get an accession number
- Special Instructions: the Family History Form

9.2.1. Accessing the Website

The website is https://www.crisp2.pitt.edu. Your logins were sent to you via email. If you cannot find the information, you may click on the lost password link on the login screen. Once signed in you can change your password by clicking on the password link in the top menu.
Once you are logged in you will see this screen:

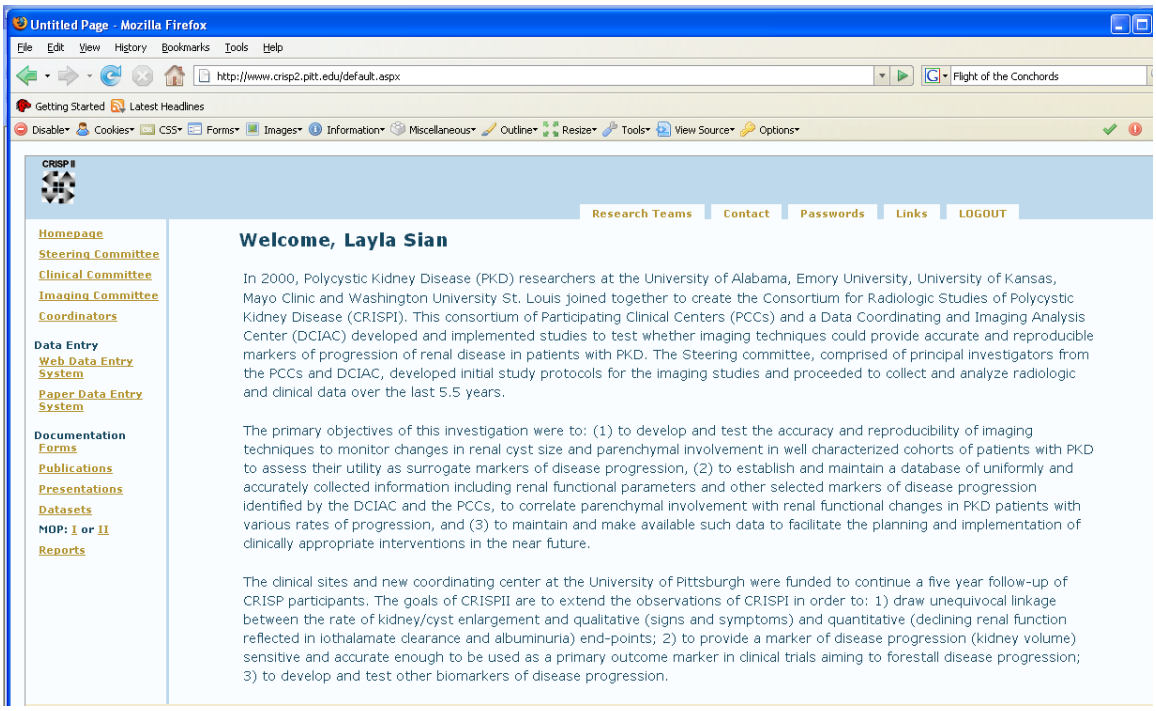


Figure 9.1. Screenshot – Welcome Screen

9.2.2. Reviewing the Forms

If you just want to review the paper forms, you can open them separately from generating forms for a specific visit. Here are the steps:

1. From the left-hand menu, locate “Documentation.”
2. Click on “Forms,” which is the first link under “Documentation.”
3. You will see this screen.

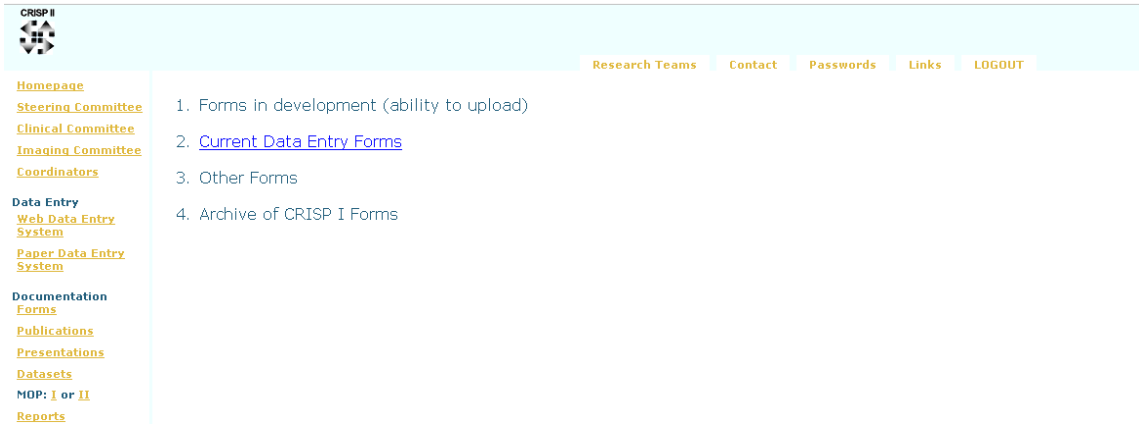
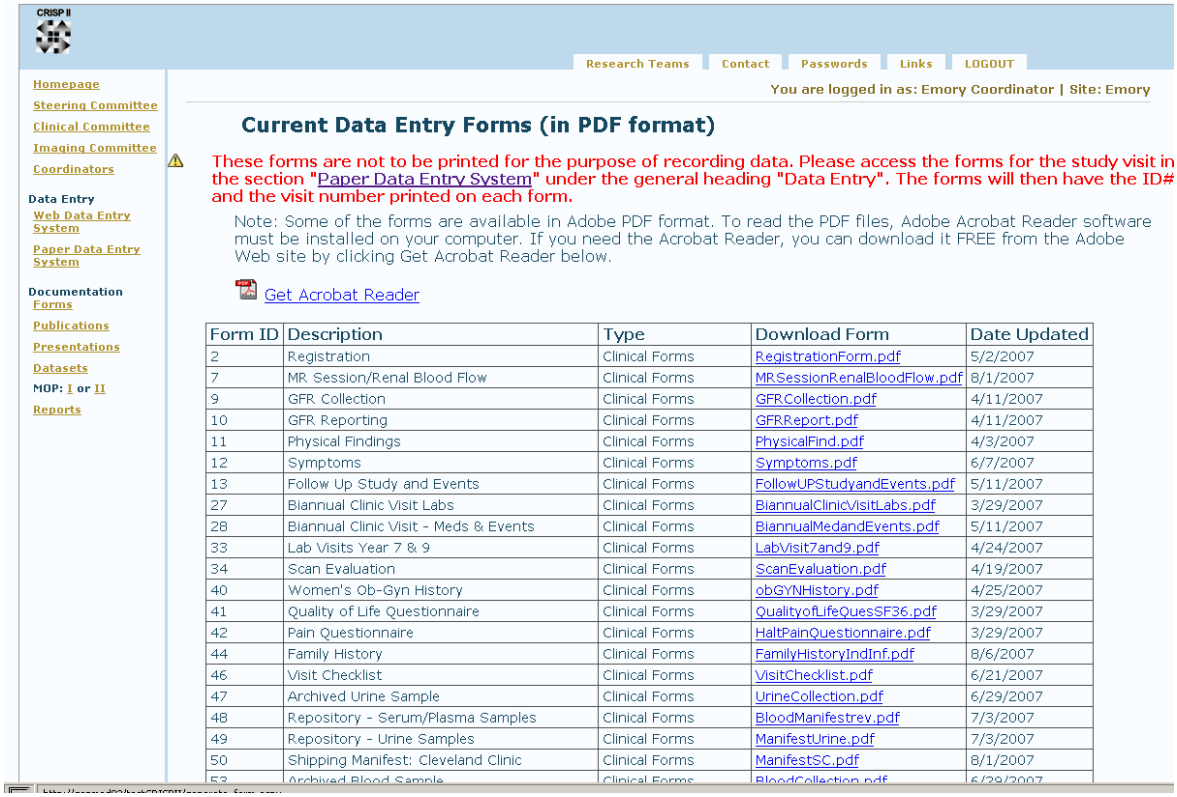


Figure 9.2. Screenshot –Forms for Reviewing

4. Click on “Current Data Entry Forms.” You will see this screen:



Form ID	Description	Type	Download Form	Date Updated
2	Registration	Clinical Forms	RegistrationForm.pdf	5/2/2007
7	MR Session/Renal Blood Flow	Clinical Forms	MRSessionRenalBloodFlow.pdf	8/1/2007
9	GFR Collection	Clinical Forms	GFRCollection.pdf	4/11/2007
10	GFR Reporting	Clinical Forms	GFRReport.pdf	4/11/2007
11	Physical Findings	Clinical Forms	PhysicalFind.pdf	4/3/2007
12	Symptoms	Clinical Forms	Symptoms.pdf	6/7/2007
13	Follow Up Study and Events	Clinical Forms	FollowUPStudyandEvents.pdf	5/11/2007
27	Biannual Clinic Visit Labs	Clinical Forms	BiannualClinicVisitLabs.pdf	3/29/2007
28	Biannual Clinic Visit - Meds & Events	Clinical Forms	BiannualMedandEvents.pdf	5/11/2007
33	Lab Visits Year 7 & 9	Clinical Forms	LabVisit7and9.pdf	4/24/2007
34	Scan Evaluation	Clinical Forms	ScanEvaluation.pdf	4/19/2007
40	Women's Ob-Gyn History	Clinical Forms	obGYNHistory.pdf	4/25/2007
41	Quality of Life Questionnaire	Clinical Forms	QualityofLifeQuesSF36.pdf	3/29/2007
42	Pain Questionnaire	Clinical Forms	HaltPainQuestionnaire.pdf	3/29/2007
44	Family History	Clinical Forms	FamilyHistoryIndInf.pdf	8/6/2007
46	Visit Checklist	Clinical Forms	VisitChecklist.pdf	6/21/2007
47	Archived Urine Sample	Clinical Forms	UrineCollection.pdf	6/29/2007
48	Repository - Serum/Plasma Samples	Clinical Forms	BloodManifestrev.pdf	7/3/2007
49	Repository - Urine Samples	Clinical Forms	ManifestUrine.pdf	7/3/2007
50	Shipping Manifest: Cleveland Clinic	Clinical Forms	ManifestSC.pdf	8/1/2007
53	Archived Blood Sample	Clinical Forms	BloodCollection.pdf	6/29/2007

Figure 9.3. Screenshot –Current Data Entry Forms

All of the forms are listed in order of form ID, clinical forms first, then administrative. You can open or download any form from this screen. Please note that they are in PDF format, and you will need a PDF viewer such as Acrobat Reader to open them.

5. IMPORTANT: Remember that these are NOT the forms to be used for a participant visit. However if you just need to look up a form for reference, or just want a copy of the latest form, this is where you should go. Then you don't have to worry about printing copies with participant IDS that you don't need.

9.1.3. Printing Forms for a Participant

Please follow these steps to prepare forms for a study visit.

1. From the left-hand menu, click on "Paper Data Entry System."
2. You will see this screen:

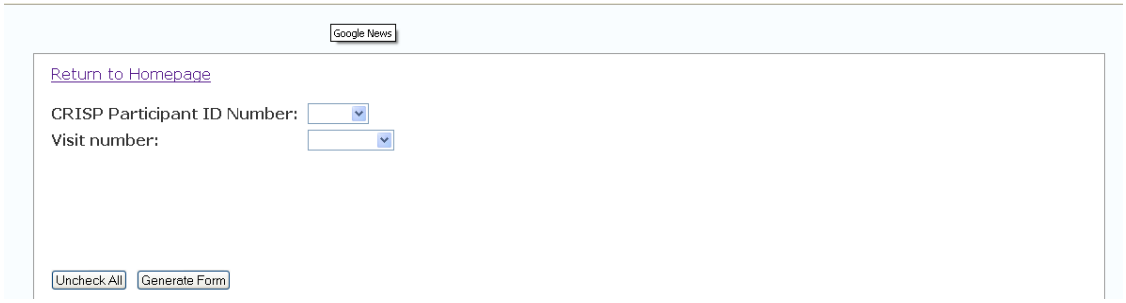


Figure 9.4. Screenshot – Generating Forms for Participants

3. Select the Participant ID from the first drop down box.
4. Select the visit number from the second drop down box.
5. Once you have done this, all of the appropriate forms for that visit will be displayed, and they will already be selected for you. You may uncheck any forms you may not need, or uncheck them all with the “Uncheck All” button on the bottom left. If the visit includes an MR scan, you are asked whether it is a repeat scan or not. You will not be able to proceed until this is answered.

Figure 9.5. Screenshot – List of Forms for Printing

6. Click on the “Generate Form” button on the bottom right. You will then be prompted to open or save the file. Save the file, so you can print or re-print it as needed. The file will be named with the participant ID and the current date, for easy reference. If you forget, and select open, you may save it to your computer at that point.

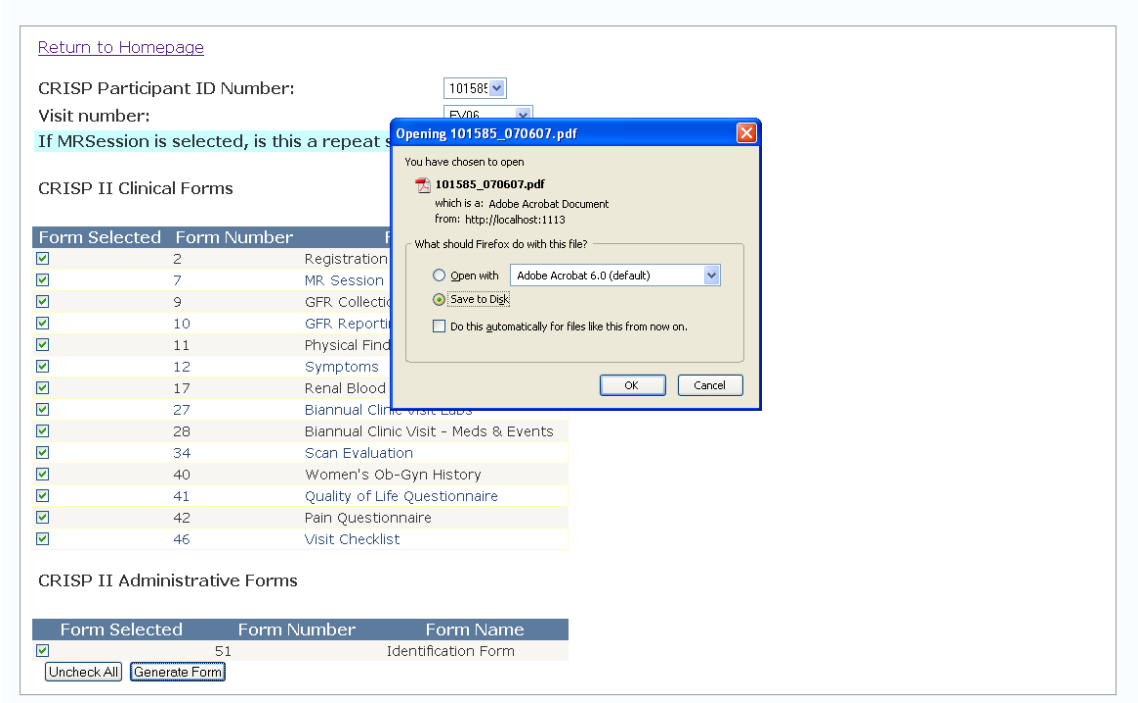


Figure 9.6. Screenshot – Save or Open the file window

7. NOTE: Under the Visit Number drop down box, there is an "As Needed" option. This is for you to access forms to be filled out as needed under a special circumstance. For instance, the Missed Visit form, Data Change form, Study Withdrawal Form, and even the Follow-Up Study and Events (if being used for an event outside of the "Initial Visit + 6 months" visit) are all forms that might be printed out as needed, and not for a specific study visit.

   You may consult the Study Calendar to refresh your memory about which forms are needed at which visit.

9.2.4. Accessing the Study Calendar

Follow these steps to access the Study Calendar:

1. From the left-hand menu, under "Documentation," select Forms.
2. Next, click on Other Forms, seen below:

Figure 9.7. Screenshot – Steps to Access the Study Calendar

3. Click on the "Study Calendar" link, to view the calendar. You can also save it to your machine.

9.2.5. Special Procedure: How to Get an Accession Number

1. Accession numbers are generated when the relevant form is selected for printing through the Paper Data Entry System. Recall that the Paper Data Entry System menu looks like the following:

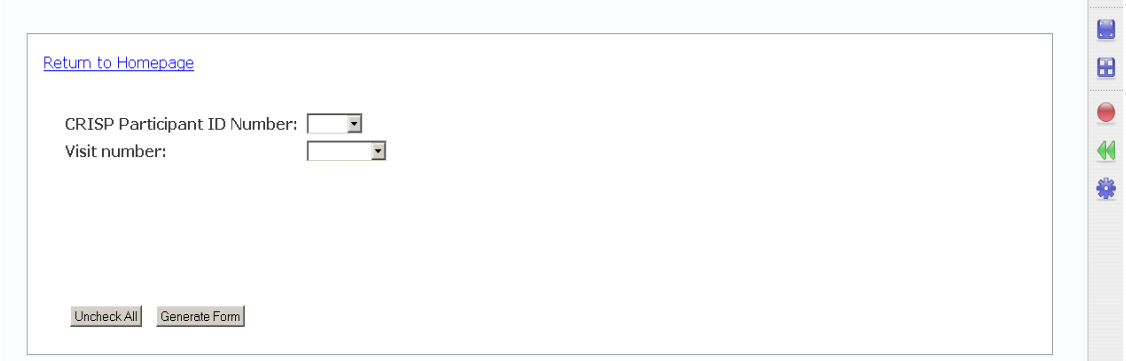


Figure 9.8. Screenshot – Paper Data Entry System Menu

2. Once you select the visit, the appropriate forms will be listed and pre-selected for you.

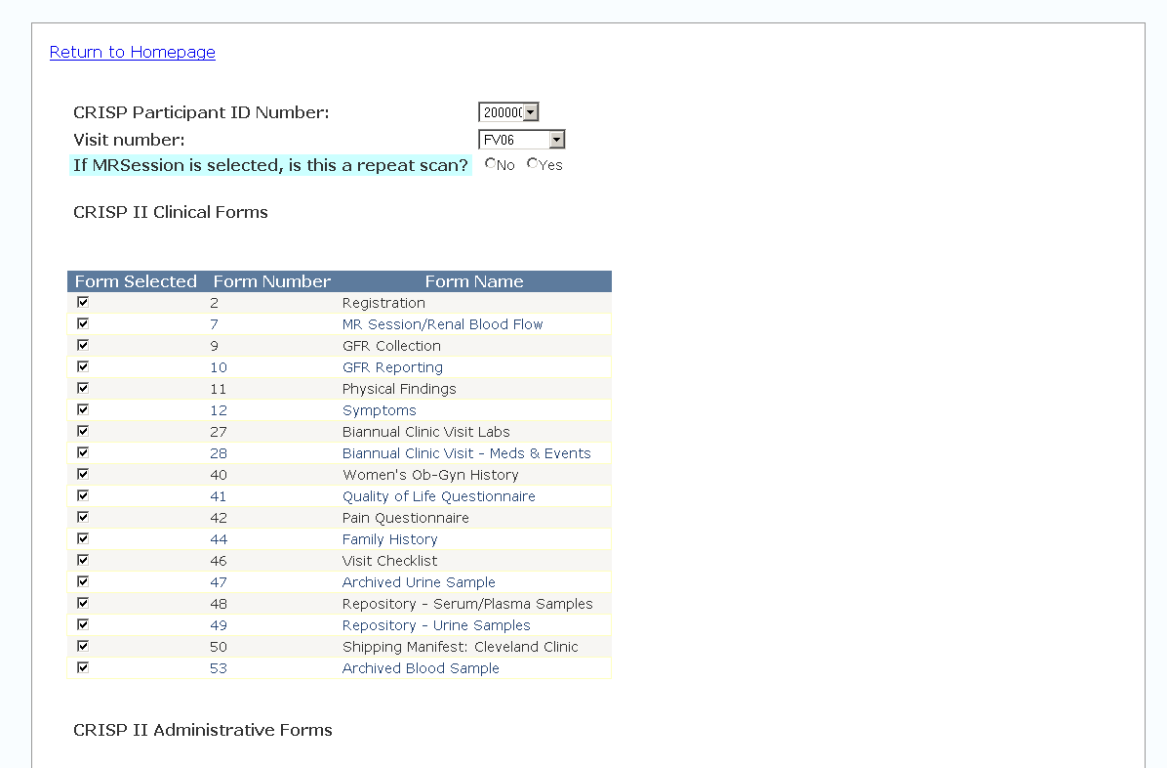


Figure 9.9. Screenshot – List of Pre-selected forms

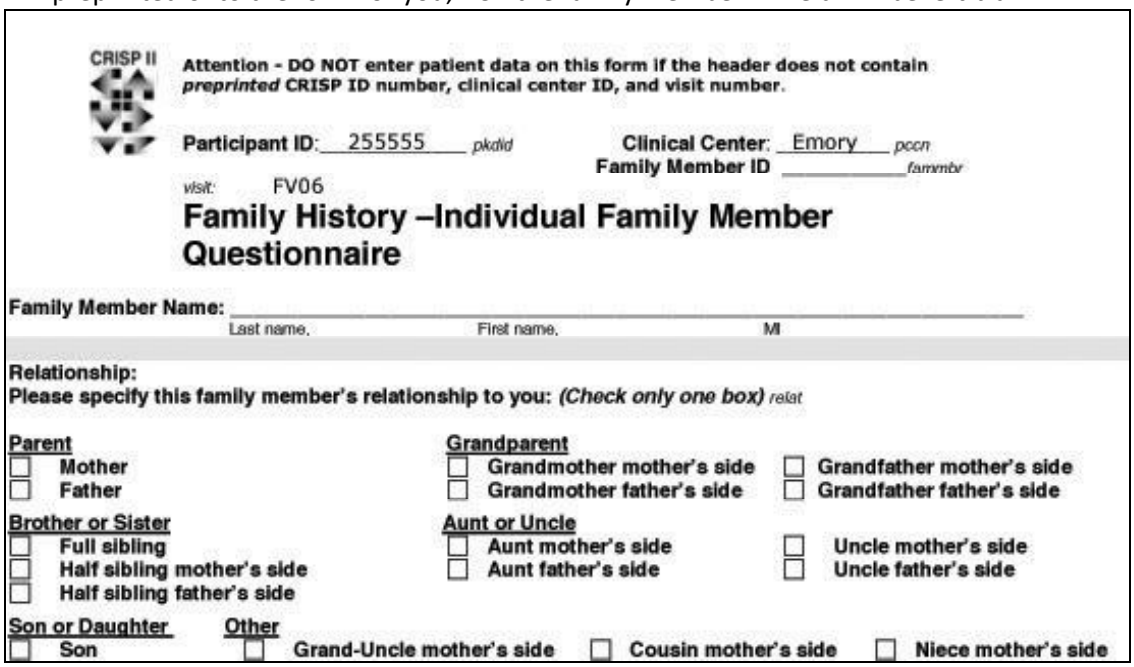
3. If you are printing out a form that requires an accession number (form 7) then a unique accession number will be automatically generated by the website and printed onto the form for you. Therefore PLEASE MAKE SURE to only print form 7 once. It is goof practice to save the pdf to your computer, in case you need to re-print it later.

4. A new unique number is generated every time you print a form that needs it, so again PLEASE MAKE SURE to print the form once!

9.2.6. Special Procedure: the Family History Form

Please keep the following in mind for the Family History Form:

1. When this form is generated for a patient visit, the participant ID, site, and visit number are preprinted onto the form for you, BUT the family member ID field will be left blank.



CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID: 255555 *pkdid* **Clinical Center:** Emory *pccn*

Family Member ID _____ *famnbr*

visit: FV06

Family History –Individual Family Member Questionnaire

Family Member Name: _____

Last name, First name, MI

Relationship:

Please specify this family member's relationship to you: ***(Check only one box)*** *relat*

Parent
- ☐ Mother
- ☐ Father

Grandparent
- ☐ Grandmother mother's side
- ☐ Grandmother father's side
- ☐ Grandfather mother's side
- ☐ Grandfather father's side

Brother or Sister
- ☐ Full sibling
- ☐ Half sibling mother's side
- ☐ Half sibling father's side

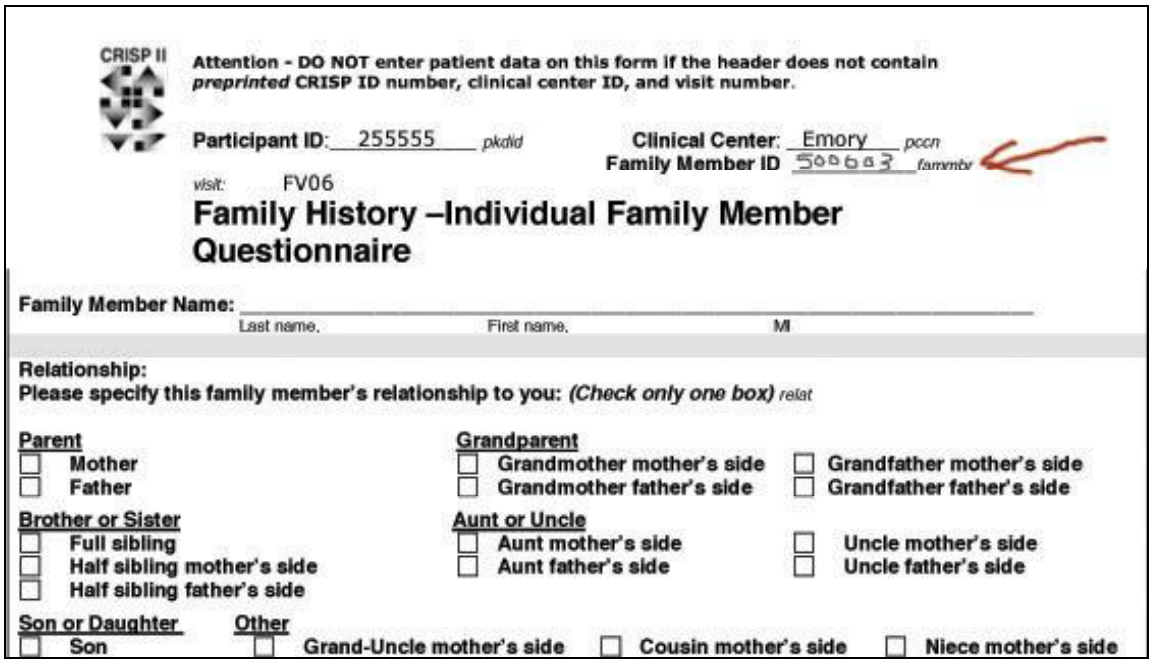
Aunt or Uncle
- ☐ Aunt mother's side
- ☐ Aunt father's side
- ☐ Uncle mother's side
- ☐ Uncle father's side

Son or Daughter
- ☐ Son

Other
- ☐ Grand-Uncle mother's side
- ☐ Cousin mother's side
- ☐ Niece mother's side

Figure 9.10. Family History Form

2. Please make 15 copies of this form for the patient to fill out. If they need more, you can generate another copy of the form by returning to the Paper Data Entry System menu. DO NOT give a patient a copy of the Family History form without the preprinted information on the header (participant ID, site, and visit number)
3. The Family Member ID will be generated by the system upon data entry.
4. Once the form is data entered and the family member ID is generated, you are to hand write it onto your paper form before submitting the form to the DCIAC:


CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID: 255555 *pkdid*

Clinical Center: Emory *pccn*

Family Member ID 500603 *fammbr*

visit: FV06

Family History –Individual Family Member Questionnaire

Family Member Name: _____
Last name. First name. MI

Relationship:
Please specify this family member's relationship to you: *(Check only one box)* *relat*

Parent
- ☐ Mother
- ☐ Father

Grandparent
- ☐ Grandmother mother's side
- ☐ Grandmother father's side
- ☐ Grandfather mother's side
- ☐ Grandfather father's side

Brother or Sister
- ☐ Full sibling
- ☐ Half sibling mother's side
- ☐ Half sibling father's side

Aunt or Uncle
- ☐ Aunt mother's side
- ☐ Aunt father's side
- ☐ Uncle mother's side
- ☐ Uncle father's side

Son or Daughter
- ☐ Son

Other
- ☐ Grand-Uncle mother's side
- ☐ Cousin mother's side
- ☐ Niece mother's side

Figure 9.11. The Family Member ID number needs to be hand written in the Family History Form

9.3. CRISP II Web Data Entry System

-accessing the website
-entering the forms
-filing a missing data report
-filing a data change request
-reviewing forms (Site Coordinators only)
-SPECIAL INSTRUCTIONS: the Family History Form/generating a family member ID

9.3.1. Accessing the Website

The website is https://www.crisp2.pitt.edu. Your logins were sent to you via email. If you cannot find the information, you may click on the lost password link on the login screen. Once signed in you can change your password by clicking on the password link in the top menu.

Once you are logged in you will see this screen:

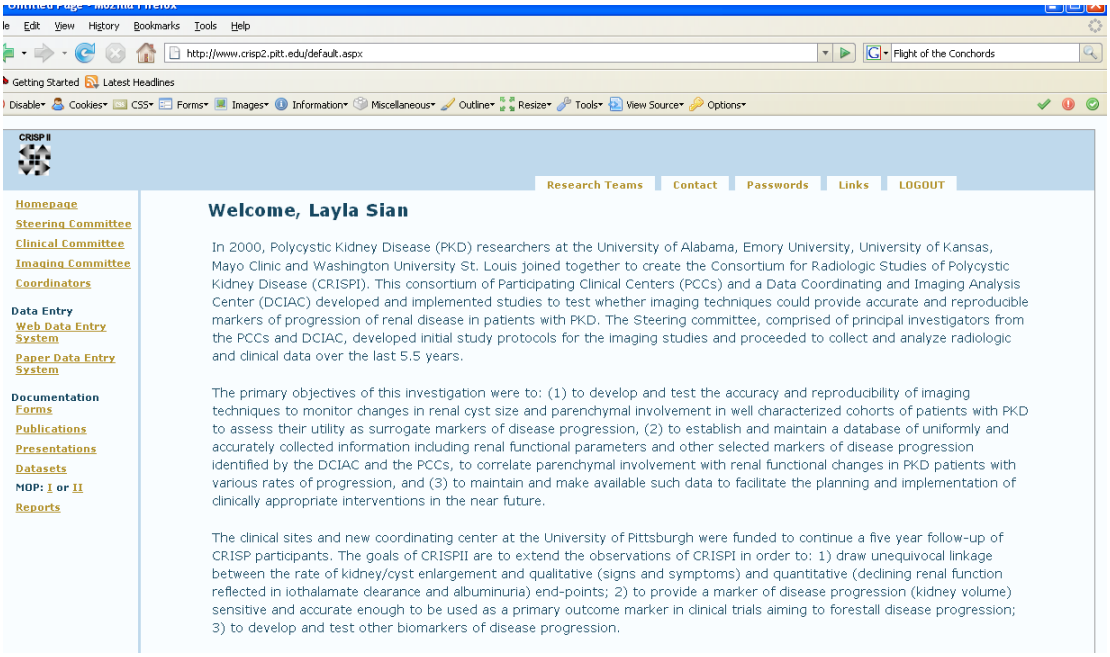


Figure 9.12. Screenshot – Welcome Screen

9.3.2. Entering the Forms

To data enter already completed paper forms, please follow these steps:

(***NOTE: Please check over the paper form carefully before you begin data entry. It is much better for you if you find the missing data problem, and file this missing data report BEFORE you try to fill out your CRISP II form online, and find that you cannot complete it.***)

6. From the left-hand menu, locate and click "Web Data Entry System."
7. You will see this screen.

Figure 9.13. Screenshot –Current WDES Entry Forms

8. Click on "Enter New Form" and it will scroll you down to the list of forms. You can also just scroll down to click on a form for data entry. For an example, I will click on the first one, Form 2: Registration. NOTE: after you select the participant and visit number (in most cases – but for certain forms, different fields may determine a unique record), the system checks to make sure that the form has not already been data entered. If it finds a matching form you will be alerted:

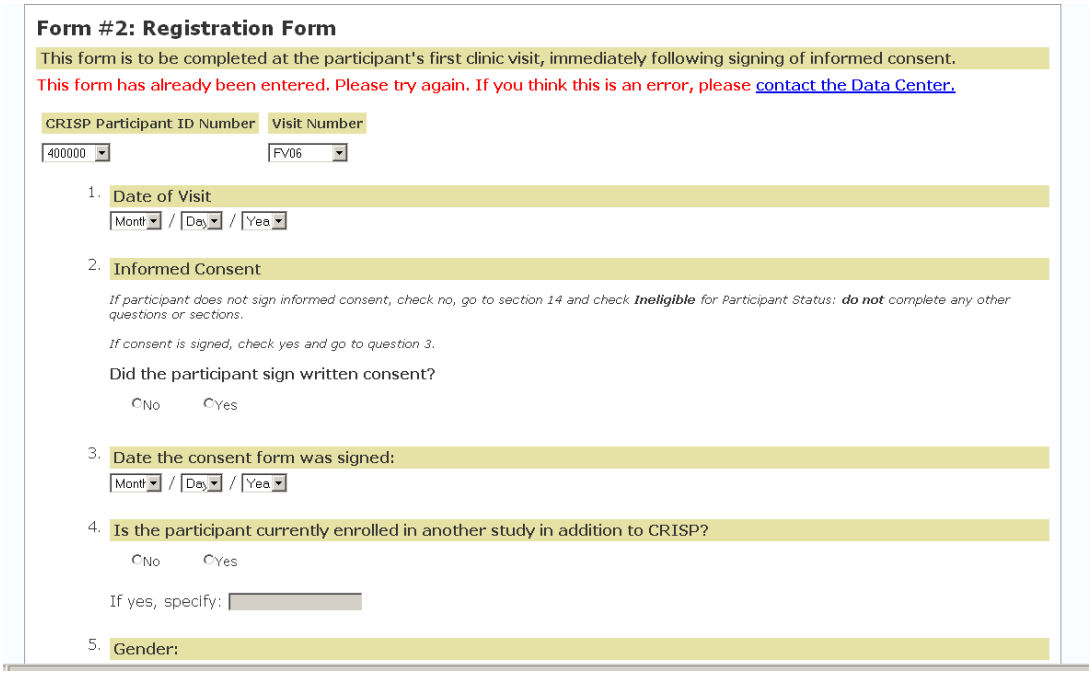


Figure 9.14. Screenshot – Enter New Form: Alert Message

Of course, in most cases you will not see this message. Continue filling out the form. At the bottom of every form you will end by filling in the name of the CRISP staff member who completed the paper form, and the date that they did so. There is no need to fill in your (data entry/primary) name or date you are data entering, as the system knows this information and automatically stores it for you.

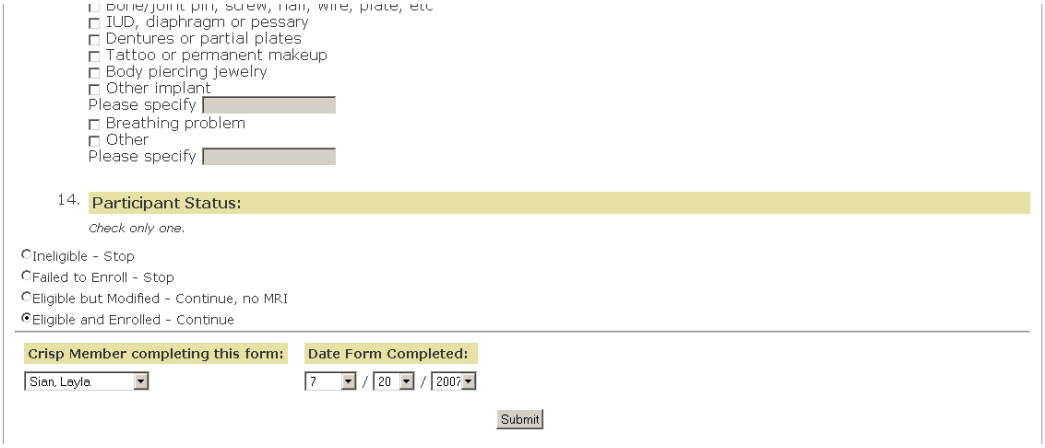


Figure 9.15. Screenshot – New Form: CRISP staff member completing the paper form

9. Once you have double-checked your work and completed the form, click the SUBMIT button at the bottom of the web form. You will now see a success message:

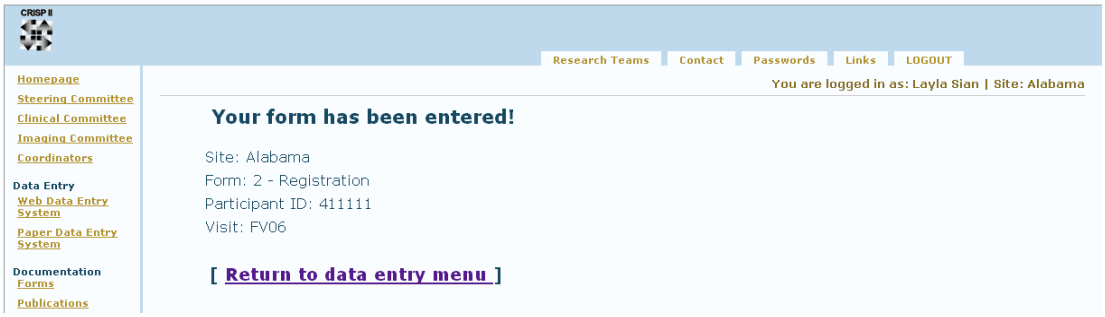


Figure 9.16. Screenshot – Complete Entry Form Message

You may now click on "Return to data entry menu" to enter another form, or click the LOGOUT tab at the top right to sign out of the site.

9.3.3. Filing a Missing Data Report

(***NOTE: Please check over the paper form carefully before you begin data entry. It is much better for you if you find the missing data problem, and file this missing data report BEFORE you try to fill out your CRISP II form online, and find that you cannot complete it.***)

You will need to file this report in the event that you are unable to submit a form on the website due to missing data for a required field. Hopefully this will happen rarely, if ever, but sometimes there may be a reason that the paper form is blank where data is expected, and you are unable to obtain the required information. In this case you need to fill out the missing data form on our website, and we will respond by giving you a "fake" value to enter in place of the missing data.
Please follow these steps to file a missing data report:

1. Once logged in to the website, click on "Web Data Entry System."
2. The missing data form is form 54.
3. Fill out all of the fields and hit submit. One of the fields we ask for is something we call variable. We assign something we call a variable to every distinct piece of data to be entered. PLEASE NOTE: On the paper forms, by every piece of data to be entered is a variable name in italics. Let's take form 7 for example. Looking at question 6 we see that the variable name for series # 1 is sid1, and the variable name for series # 1 sequence is descr1. It is very important that variables be reported this way, to have complete clarity about what you are reporting as missing.
4. Upon successful submission of this form, the Pittsburgh DCIAC and you will receive an email confirming the details of the entered form.
5. The Pittsburgh DCIAC will then respond by email to give you a missing data value to be entered for the required field in question.

9.3.4. Filing a Data Change Report

You will need to file a data change form when you find an incorrect value has been data entered for a form. Follow these steps to file a data change report:

1. Once logged in to the website, click on "Web Data Entry System."
2. The Data Change form is form 52.

3. A form should be submitted PER PARTICIPANT. You are able to request changes to multiple forms per participant in this data change report. Fill out all of the fields and hit submit. Please remember to select AS NEEDED for the visit if it was not at a scheduled visit.
4. Upon successful submission of this form, the Pittsburgh DCIAC and you will receive an email confirming the details of the entered form.
5. The Pittsburgh DCIAC will then respond by email to confirm that the data has been updated in the system.

9.3.5. Reviewing Entered Forms (Site Coordinators only)

Please follow these steps to review already data entered forms:

1. Once you are logged in, click on "Web Data Entry System" on the left-hand menu. You will then see these options:

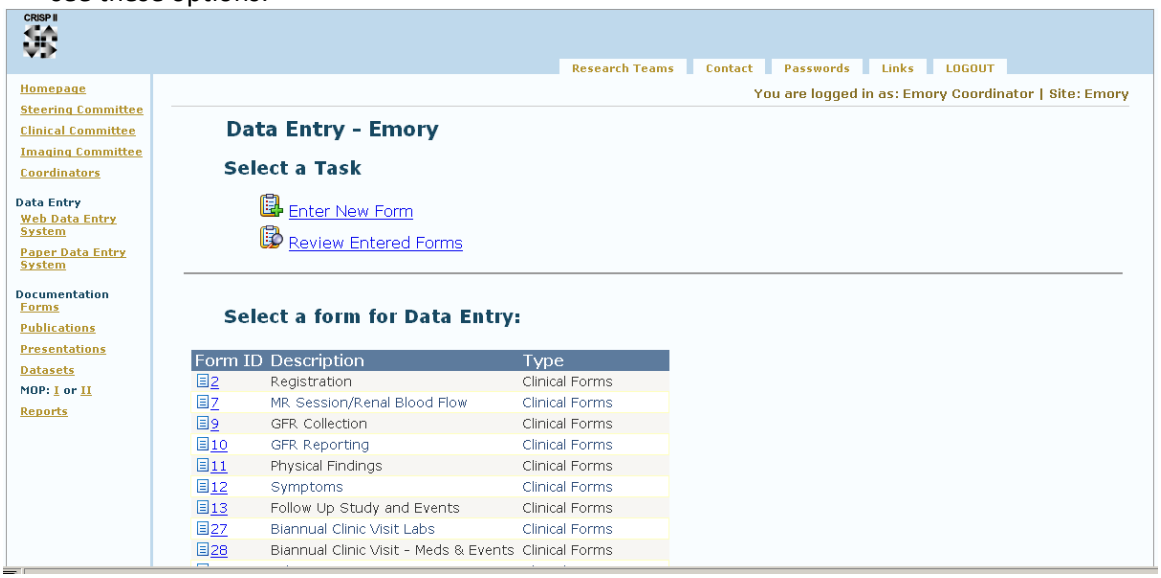


Figure 9.17. Screenshot – Reviewing Entered Forms

2. Click on Review Entered Forms and you will be sent to this page:

Figure 9.18. Screenshot – Review a Form

3. If NO match is found you will see an error message. If a match is found you will be taken to the form, already filled out with the recorded values. You can view the page, but there are no buttons to submit the form; you are not to use this screen to make changes, but instead to confirm entered data, should you choose to, or also to see if a form has been entered into the system. To leave the screen, click on the "Return To Web Data Entry System Menu" link at the top of the screen:

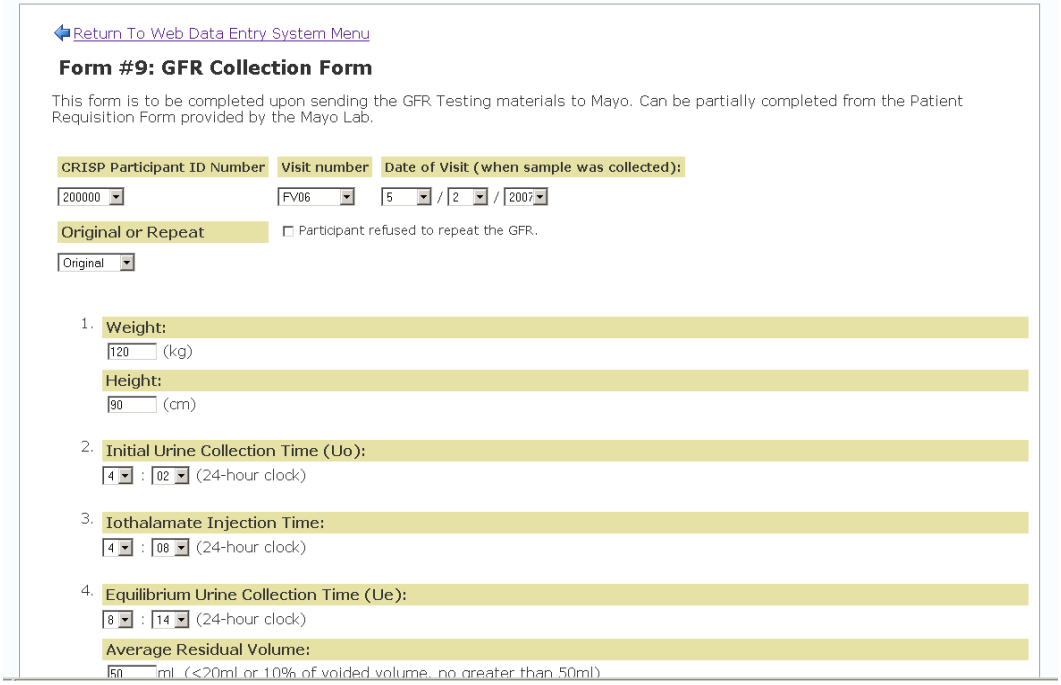


Figure 9.19. Screenshot – Return to the WDESM link

9.3.6. Special Instructions for the Family History Form (#44)

Please follow these steps carefully to make sure individual family member IDs are properly recorded:

1. The paper form generated by our Paper Data Entry System will have the participant ID, site and visit number preprinted on them. The space for Family Member ID will be left blank.
2. At the bottom of the form the submit button reads "Submit and Generate Unique ID":

Figure 9.20. Screenshot –Family History Form (#44)

3. On the following screen you will see the usual success message indicating the form has been saved to the database message. In large red letters you will also find the unique ID created for that family member.

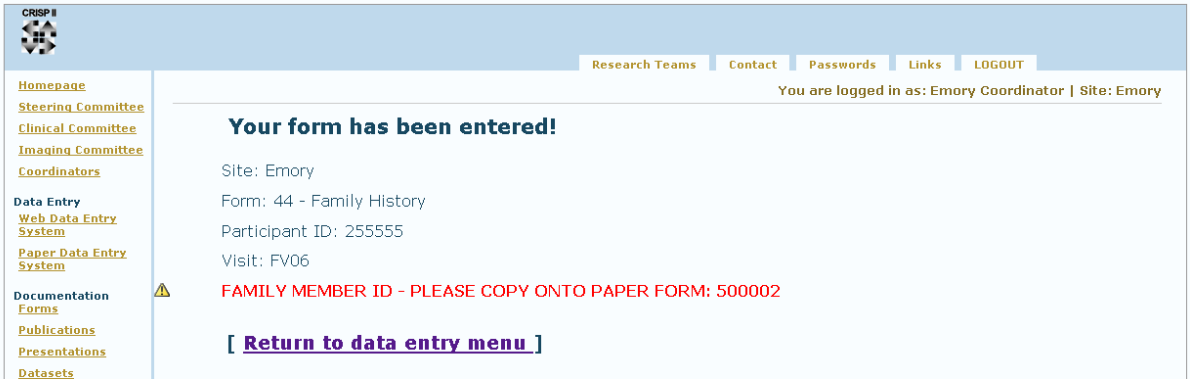
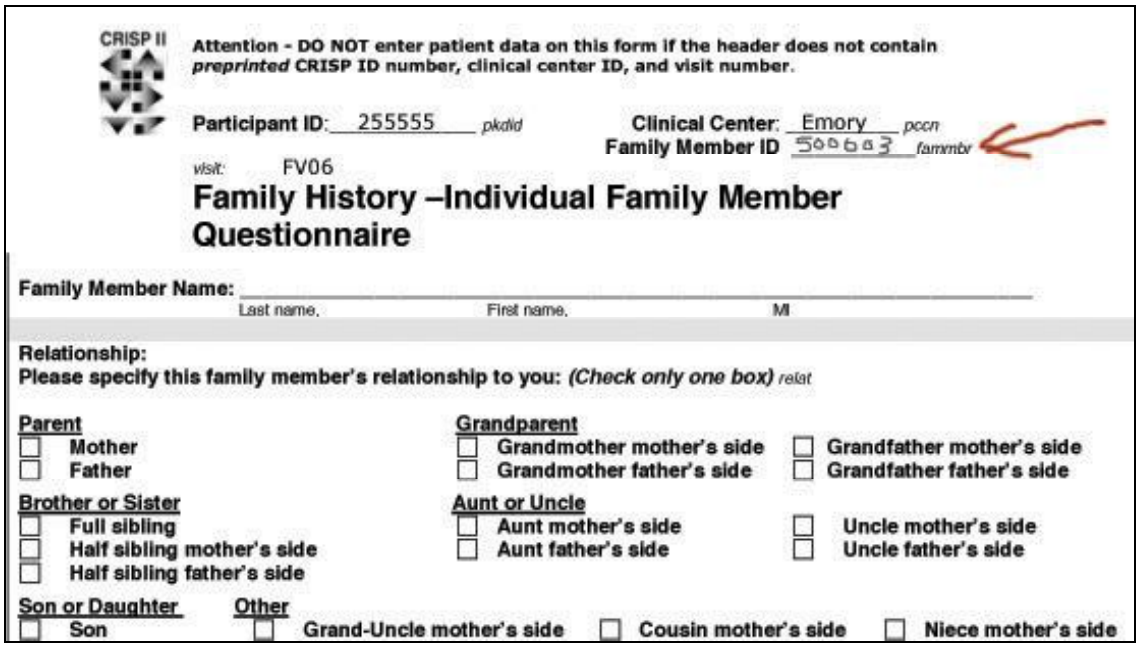


Figure 9.21. Screenshot – Family History Form completion message

4. Copy this number into the blank Family Member ID field on the top of the paper form. This must be done before the form is then submitted to the DCIAC.


CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID: 255555 *pkdid*

Clinical Center: Emory *pccn*

Family Member ID 500603 *fammbr*

visit: FV06

Family History –Individual Family Member Questionnaire

Family Member Name: _____
Last name. First name. MI

Relationship:
Please specify this family member's relationship to you: *(Check only one box)* *relat*

Parent
- ☐ Mother
- ☐ Father

Grandparent
- ☐ Grandmother mother's side
- ☐ Grandmother father's side
- ☐ Grandfather mother's side
- ☐ Grandfather father's side

Brother or Sister
- ☐ Full sibling
- ☐ Half sibling mother's side
- ☐ Half sibling father's side

Aunt or Uncle
- ☐ Aunt mother's side
- ☐ Aunt father's side
- ☐ Uncle mother's side
- ☐ Uncle father's side

Son or Daughter
- ☐ Son

Other
- ☐ Grand-Uncle mother's side
- ☐ Cousin mother's side
- ☐ Niece mother's side

Figure 9.22. Screenshot – Family Member ID field

5. Please make sure the paper form has the Family Member ID written in before sending the forms to the DCIAC.

9.4. Data Entry/Verification

CRISP II employs a double data entry system whereby each data form is entered twice, each time by different individuals. The initial data entry is done by the nurse interviewers after they have completed data collection on paper forms. Once the initial data entry is done, copies of the paper forms will be sent to the DCIAC, where the secondary entry will be performed.

Paper Form Shipping Policy

Once data collection forms have been entered into the Web Data Entry System (WDES) and signed off, *readable copies (no originals)* of the forms should be sent via Federal Express to the DCIAC every 2 weeks.

If possible, copies of all data collection forms required for a patient visit should be sent in one packet, with the exception of those shipping manifests which are completed quarterly (Form #49: Shipping Manifest - Urine, and Form #50: Shipping Manifest - Cleveland Clinic). Copies of forms 49 and 50 may be sent later once they are completed. If not possible to complete all forms for the entire visit before the 2 week time period has expired, it is permissible to send copies of forms completed to date. Please send copies to:

University of Pittsburgh
Center for Research on Health Care Data Center
200 Meyran Ave.
Suite 200 Room 206
Pittsburgh, PA 15213
Attention Del Gannon

Data will be verified at regular intervals using software which compares matching records and generates a report which details discrepancies between the two entries. These discrepancies are reviewed by the DCIAC data manager, and resolved either by reviewing the original paper form or following up with the nurse interviewer to determine the correct value. Once all discrepancies have been resolved, the records are flagged as verified, and do not need to be compared again. This is an ongoing process, and provides a means of verifying data as it is being collected. This method provides continuous feedback to site coordinators regarding common errors and misinterpretations that may be occurring, and enables these problems to be corrected as they happen.

9.5. Form Storage and Processing

9.5.1. Latest CRISP II Forms

There are two sets of data entry forms maintained by the CRISP II Study. The first is a set of documents created with the word processing software Microsoft Word (MS Word). These are considered the standard forms. When modifications need to be made to any standard form, the MS Word form is modified by the DCIAC staff and then sent to the CRISP II steering committee for approval. Once approved, the form is converted to a PDF form for use in the CRISP II web data entry system. Both the word forms and the web PDFs and are stored on a shared, secure access DCIAC research server, and are backed up on a regular basis (see Data Archiving section).

9.5.2. CRISP II Forms for Data Entry

The copied forms sent to the DCIAC from the sites for double data entry will also be securely stored at the DCIAC for the duration of the study.

9.5.3. CRISP II Additional Data

The CRISP II study will include the acquisition, storage and analysis of data from a variety of different sources. First, the PCC's will enter a variety of types of data directly into the Web Data Entry System. Next, the DCIAC will double data enter all forms and correct inconsistencies working with the PCCs. Second, the image data will be transmitted to the imaging section at the DCIAC. After data preparation is done by the imaging group, the relevant data will be transferred to the data management system. Third, a variety of data will be analyzed by either the central laboratory at Mayo Clinic, or by each of the PCC's. These data will also be entered into the WDES.

9.5.4. Data Archiving and Quality Control

The database will include routine data edit checks for consistency both within and between forms. Once edited, temporary files will be merged to generate files for data analysis. All files will be backed-up daily and archived weekly. Database development and maintenance will occur with SQL Server and .Net programming available through the CRHC network. Analysis will be performed using SAS, SPSS, or Stata.

All study subjects will be assigned unique study identifiers that will appear on all data collection instruments, tapes, documents, and files used in the statistical analysis and manuscript preparation. In order to be HIPAA compliant, no personal information concerning study participants will retained in the database.

Several steps will be taken to ensure data quality and data integrity: 1) use of standard methods of data collection and recording specified in a manual of operations, 2) a formal staff workshop on research integrity at the beginning of the study and when new personnel are hired, and 3) data accuracy through the programming of the data management system. Other data quality assurance measures will include detailed documentation of computer operations and data editing procedures and regular meetings with

project staff to review any changes in procedure. The DCIAC also has specific data quality measures that will be implemented. These include verifying the data, out of range data checks, and repeated evaluation of the data process.

9.5.5. Image Registration, Editing and Transmission Preparation

Once the patient has been registered in the DCIAC database, a unique patient identifier is assigned. An image study identifier (accession number) is made available for the current imaging study). These identifiers are printed on the patient forms at the local PCC site. The PCC workstation provides software which allows the operator to remove the patient confidential information from the image headers and inserts the DCIAC assigned patient study identifier and accession numbers.

9.6. CRISP II STUDY Visit Tracking System

The CRISP II tracking system enables the research team to monitor the progress and completion of various aspects of a research study. By providing a variety of reports, reminders, and other feedback, the tracking system assists the study group in determining if the study is fulfilling its intended goals and reaching expected milestones. It ensures that subjects are being contacted at the appropriate times for follow up, and provides a means of gathering summary data for statistical analysis and the generation of regular reports relating to screening, enrollment and demographics.

Follow Up Tracking Report. The CRISP II follow up tracking report can be run on an as needed basis by any authorized user. Once the user enters the date range of interest (Figure 9.23.), a screen listing all participants who have a visit due within the specified date range will be displayed (Figure 9.24.).The due date for the next expected visit or phone call will also be displayed for each participant. A participant and any relevant due date(s) will continue to be displayed on the report until the visit or call has been completed, or until the interview has been flagged as unable to complete (Figure 9.25.).

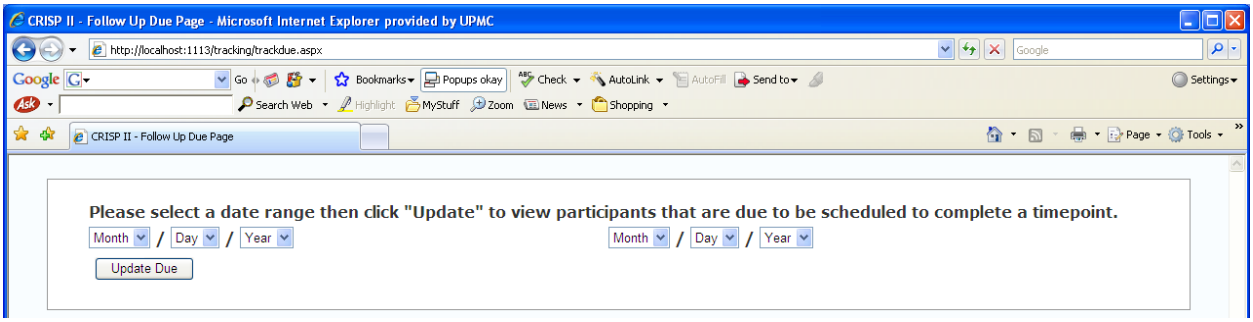


Figure 9.23. Screenshot – CRISP II Tracking Report

Figure 9.24. Screenshot – CRISP II Tracking Report List of Participants

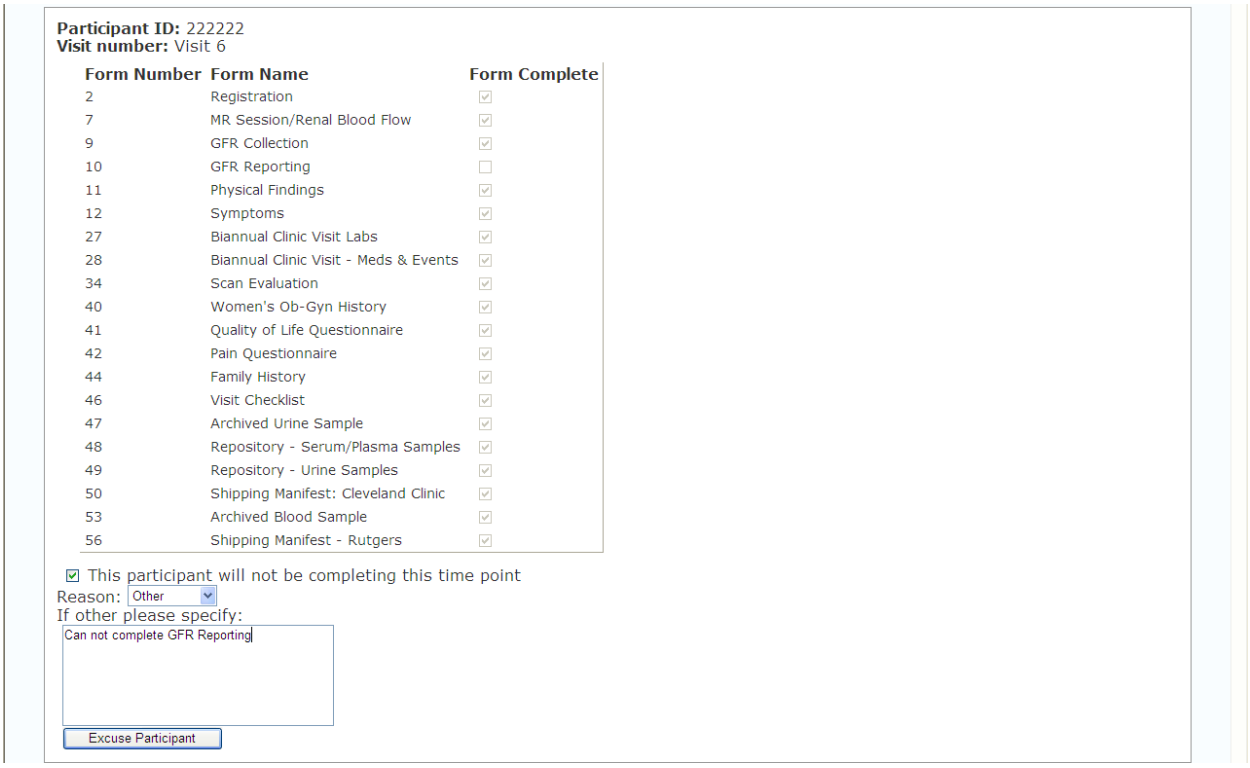


Figure 9.25. Screenshot – Follow up Tracking Report

The only identifier listed for each participant is the CRISP II ID. The user can look up the contact information stored in the participant chart and take appropriate action. This may include checking to see if the participant is scheduled for a visit on an appropriate date, calling the participant for a follow up phone call, or calling the participant to schedule a visit.

The follow up tracking report should be run on a regular basis; at least once a week is suggested. The start date of the date range requested should always be the start date of the study, and the end date should be a date that ends the period of desired follow up, usually one week from the current date, so that all participants due since the beginning of the study are included.

9.7. CRISP II Study Tracking System Instructions

To enter the tracking system, you must first be logged in as a site coordinator (1).

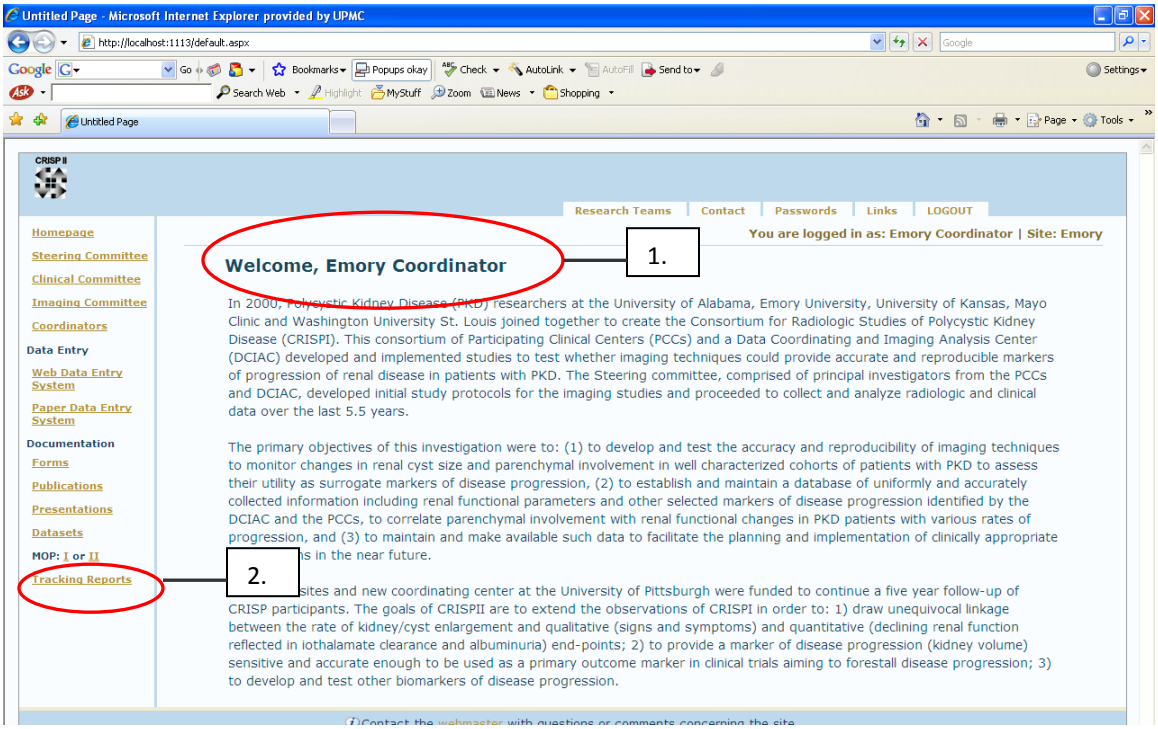


Figure 9.26. Screenshot – Tracking Reports Link

Then click the tracking reports link at the bottom left of the main menu (2). You will then be taken to the CRISP II tracking system's main page, where you can select a range of dates to view participants (3).

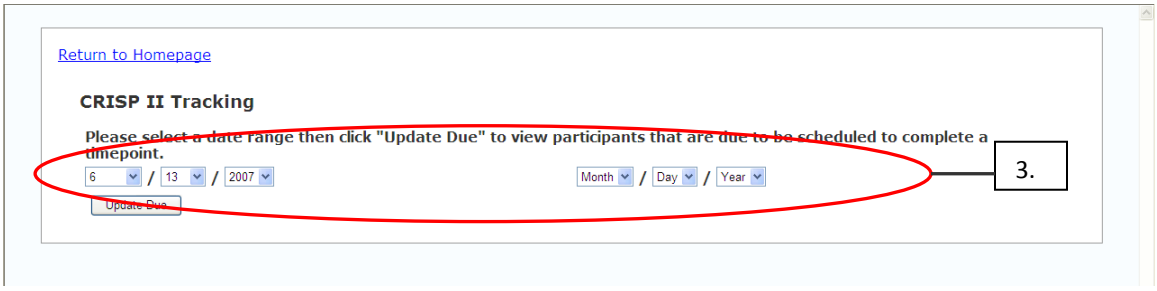


Figure 9.27. Screenshot – Tracking System Main Page

Once you select the date range, click the "Update Due" button (4) and a list of participants that have visits due within the selected date range will appear in a list. This list shows each Participant ID, the date that they registered, and the visit that is due within the given date range. By clicking on a specific participant ID (5), you will be able to view the specific forms that the selected participant still needs to complete to finish the visit.

The 'Status Page' shows what forms still need to be completed to finish the visit in the upper left hand corner of the screen (6). If visits are complete, the check boxes are checked, if they are not complete, they are not checked (7).

In the event that a participant cannot complete the visit in (6), just click the checkbox in the upper right hand corner (8) that says “This participant will not be completing this time point”. Next, select a reason from the drop down box. If the reason is not there, just select “other” from the drop down box and specify the reason in the box below. When this is complete, click “Excuse Participant” and the Participant as well as the visit that they were excused from will be removed from the list on the main page of the tracking system.

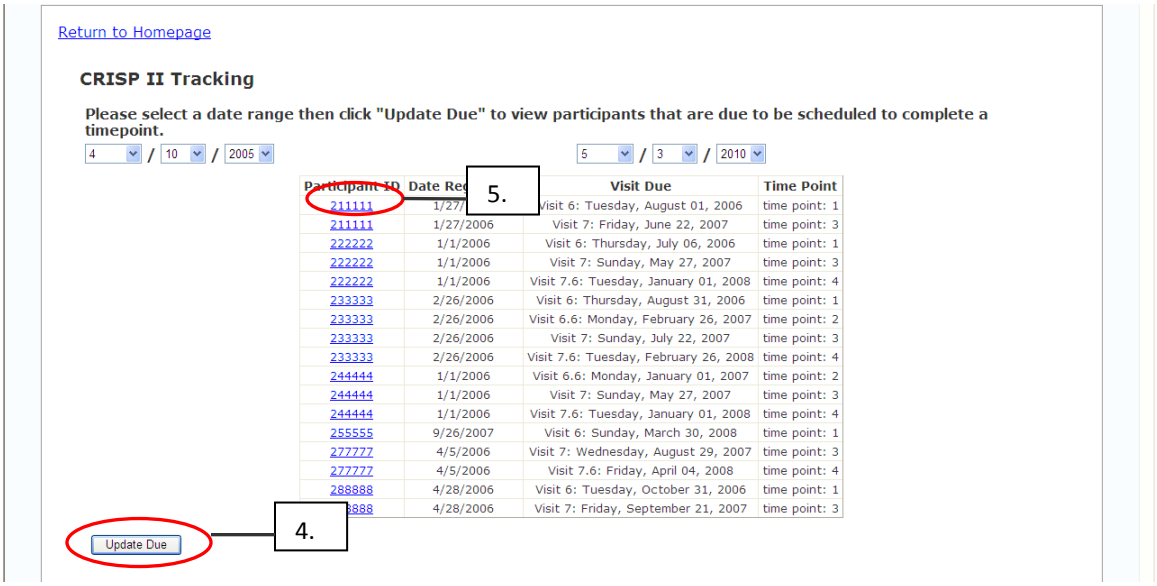


Figure 9.28. Screenshot – Tracking System Status Page

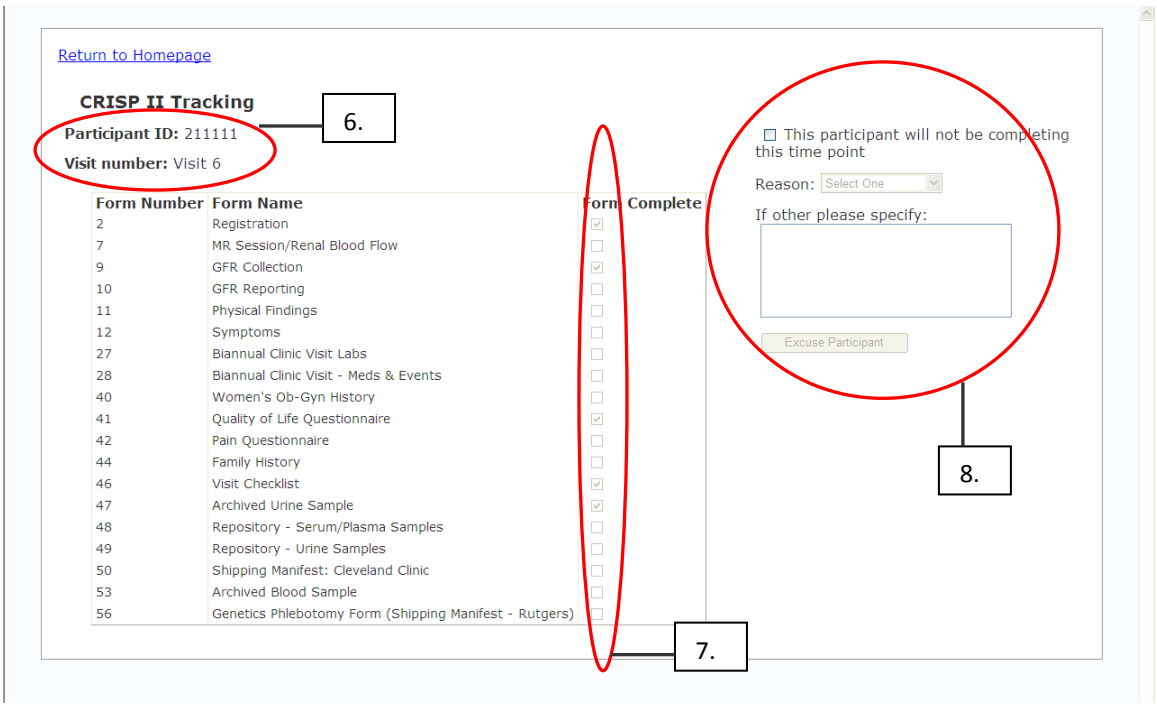


Figure 9.29. Screenshot – Tracking System

Bibliography

1. Gabow P. Definition and natural history of autosomal dominant polycystic kidney disease. In: Watson M, Torres V (eds). *Polycystic Kidney Disease*, vol. 1. Oxford University Press: Oxford, 1996, pp 333-355.
2. Sutters M, Germino GG. Autosomal dominant polycystic kidney disease: molecular genetics and pathophysiology. *J Lab Clin Med* 2003; **141:** 91-101.
3. Chapman A, Johnson A, Gabow P, Schrier R. Overt proteinuria and microalbuminuria in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol* 1994; **5:** 1349-1354.
4. Grantham JJ. The etiology, pathogenesis and treatment of autosomal dominant polycystic kidney disease: recent advances. *Am J Kidney Dis* 1996; **28:** 788-803.
5. Watson ML. Hypertension in polycystic disease. In: Watson ML, Torres VE (eds). *Polycystic Kidney Disease*. Oxford University Press: Oxford, 1996, pp 407-429.
6. Gabow P, Duley I, Johnson A. Clinical profiles of gross hematuria in autosomal dominant polycystic kidney disease. *Am J Kidney Dis* 1992; **20:** 140-143.
7. Torres VE. Vasopressin antagonists in polycystic kidney disease. *Kidney Int* 2005; **68:** 2405-2418.
8. Torres VE, Wilson DM, Hattery RR, Segura JW. Renal stone disease in autosomal dominant polycystic kidney disease. *Am J Kidney Dis* 1993; **22:** 513-519.
9. Elzinga LW, Bennett WM. Miscellaneous renal and systemic complications of autosomal dominant polycystic kidney disease including infection. In: Watson ML, Torres VE (eds). *Polycystic Kidney Disease*, vol. I. Oxford Medical Publications: Oxford, 1996, pp 483-499.
10. Segura JW, King BF, Jowsey SG, Martin P*, et al.* Chronic pain and its medical and surgical management in renal cystic diseases. In: Watson ML, Torres VE (eds). *Polycystic Kidney Disease*, vol. I. Oxford Medical Publications: Oxford, 1996, pp 462-480.
11. Bajwa ZH, Gupta S, Warfield CA, Steinman TI. Pain management in polycystic kidney disease. *Kidney Int* 2001; **60:** 1631-1644.
12. Dalgaard OZ. Bilateral polycystic disease of the kidneys: A follow-up of two hundred and eighty-four patients and their families. *Acta Med Scand* 1957; **328:** 1-255.
13. Churchill DN, Bear JC, Morgan J, Payne RH*, et al.* Prognosis of adult onset polycystic kidney disease re-evaluated. *Kidney Int* 1984; **26:** 190-193.
14. Gabow P, Johnson A, Kaehny W, Kimberling W*, et al.* Factors affecting the progression of renal disease in autosomal-dominant polycystic kidney disease. *Kidney Int* 1992; **41:** 1311-1319.
15. Johnson A, Gabow P. Identification of patients with autosomal dominant polycystic kidney disease at highest risk for end-stage renal disease. *J Am Soc Nephrol* 1997; **8:** 1560-1567.
16. Parfrey P, Bear J, Morgan J, Cramer B*, et al.* The diagnosis and prognosis of autosomal dominant polycystic kidney disease. *N Engl J Med* 1990; **323:** 1085-1090.
17. Roscoe JM, Brissenden JE, Williams EA, Chery AL*, et al.* Autosomal dominant polycystic kidney disease in Toronto. *Kidney International* 1993; **44:** 1101-1108.
18. Klahr S, Breyer J, Beck G, Dennis V*, et al.* Dietary protein restriction, blood pressure control, and the progression of polycystic kidney disease modification of diet in renal disease study group. *J Am Soc Nephrol* 1995; **5:** 2037-2047.
19. Franz KA, Reubi FC. Rate of functional deterioration in polycystic kidney disease. *Kidney Int* 1983; **23:** 526-529.
20. Welling LW, Grantham JJ. Cystic Diseases of the Kidney. In: Tisher CC, Brenner BM (eds). *Renal Pathology with Clinical and Functional Correlations*, 2nd edn. JP Lippincott Co: Philadelphia, 1994, pp 1312-1354.
21. Norman J, Gatti L, Wilson P, Lewis M. Matrix metalloproteinases and tissue inhibitor of matrix metalloproteinases expression by tubular epithelia and interstitial fibroblasts in the normal kidney and in fibrosis. *Exp Nephrol* 1995; **3:** 88-89.
22. Gardner K, Jr., Burnside J, Elzinga L, Locksley R. Cytokines in fluids from polycystic kidneys. *Kidney International* 1991; **39:** 718-724.
23. Murray S, Grubman S, Perrone R, Rojkind M*, et al.* Matrix metalloproteinase activity in human intrahepatic biliary epithelial cell lines from patients with autosomal dominant polycystic kidney disease. *Connect Tissue Res* 1996; **33:** 249-256.

24. Qian Q, Harris PC, Torres VE. Treatment prospects for autosomal dominant polycystic kidney disease. *Kidney Int* 2001; **59:** 2005-2022.
25. Bae KT, Commean PK, Lee J. Volumetric measurement of renal cysts and parenchyma using MRI: phantoms and patients with polycystic kidney disease. *J Comput Assist Tomogr* 2000; **24:** 614-619.
26. Chapman A, Guay-Woodford L, J.J. G, Torres V*, et al.* Renal structure in early autosomal dominant polycystic kidney disease (ADPKD); the Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) Cohort. *Kidney Int* 2003; **64:** 1035-1045.
27. Grantham JJ, Torres VE, Chapman AB, Guay-Woodford LM*, et al.* Volume progression in polycystic kidney disease. *N Engl J Med* 2006; **354:** 2122-2130.
28. King BF, Reed JE, Bergstralh EJ, Sheedy PF, II*, et al.* Quantification and longitudinal trends of kidney, renal cyst, and renal parenchyma volumes in autosomal dominant polycystic kidney disease. *J Am Soc Neph* 2000; **11:** 1505-1511.
29. Sise C, Kusaka M, Wetzel LH, Winklhofer F*, et al.* Volumetric determination of progression in autosomal dominant polycystic kidney disease by computed tomography. *Kidney Int* 2000; **58:** 2492-2501.
30. Harris PC, Bae KT, Rossetti S, Torres VE*, et al.* Cyst number but not the rate of cystic growth is associated with the mutated gene in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol* 2006; **17:** 3013-3019.
31. King B, Torres VE, Glockner J, Chapman A*, et al.* Magnetic resonance measurements of renal blood flow as a marker of disease progression in autosomal dominant polycystic kidney disease (ADPKD). *JASN* 2001; **12:** 538A.
32. Chapman A, Gabow P, Schrier R. Reversible renal failure associated with angiotensin-converting enzyme inhibitors in polycystic kidney disease. *Ann Intern Med* 1991; **115:** 769-773.
33. Torres VE, Harris PC. Mechanisms of disease: autosomal dominant and recessive polycystic kidney diseases. *Nature Clin Prac Nephro* 2006; **2:** 40-54.
34. Zheng D, Wolfe M, Cowley BD, Jr., Wallace DP*, et al.* Urinary excretion of monocyte chemoattractant protein-1 in autosomal dominant polycystic kidney disease. *J Am Soc Nephrol* 2003; **14:** 2588-2595.
35. Bae KT, Zhu F, Guay-Woodford LM, Chapman AB*, et al.* Magnetic resonance imaging evaluation of hepatic cysts in early autosomal dominant polycystic kidney disease. *Clin J Am Soc Nephrol* 2006; **1:** 64-69.
36. Rule AD, Torres VE, Chapman AB, J. GJ*, et al.* Comparison of methods for determining renal function decline in early autosomal dominant polycystic kidney disease: The Consortium of Radiologic Imaging studies of Polycystic Kidney Disease Cohort. *J Am Soc Nephrol* 2006**:** published on February 1, 2006 as doi:2010.1681/ASN.2005070697.
37. Grantham JJ, Chapman AB, Torres VE. Volume progression in autosomal dominant polycystic kidney disease: The major factor determining clinical outcomes. *Clin J Am Soc Nephrol* 2006; **1:** 148-157.
38. Fick-Brosnahan GM, Tran ZV, Johnson AM, Strain JD*, et al.* Progression of autosomal-dominant polycystic kidney disease in children. *Kidney Int* 2001; **59:** 1654-1662.
39. Barnett AG, van der Pols JC, Dobson AJ. Regression to the mean: what it is and how to deal with it. *Int J Epidemiol* 2005; **34:** 215-220.
40. Twisk JWR. *Applied Longitudinal Data Analysis for Epidemiology: A Practical Guide.* Cambridge University Press, 2003.
41. Jung SH, Ahn C. Sample size estimation for GEE method for comparing slopes in repeated measurements data. *Statistics in medicine* 2003; **22:** 1305-1315.

Appendices

CRISP II Data Collection Forms

Table 4. List of CRISP II Data Collection Forms

Form ID	Data Collection Forms
2	Registration Clinical Form
7	MR Session/Renal Blood Flow Clinical Form
9	GFR Collection Clinical Form
10	GFR Reporting Clinical Form
11	Physical Findings Clinical Form
12	Symptoms Clinical Form
13	Follow Up Study and Events Clinical Form
27	Biannual Clinic Visit Labs Clinical Form
28	Biannual Clinic Visit - Meds & Events Clinical Form
33	Lab Visits Year 7 & 9 Clinical Form
34	Scan Evaluation Clinical Form
40	Women's Ob-Gyn History Clinical Forms
41	Quality of Life Questionnaire Clinical Forms
42	Pain Questionnaire Clinical Form
	Family Instructions
44	Family History Clinical Form
46	Visit Checklist Clinical Form
47	Archived Urine Sample Clinical Form
48	Repository - Serum/Plasma Samples Clinical Form
49	Repository - Urine Samples Clinical Form
50	Shipping Manifest: Cleveland Clinic Clinical Form
53	Archived Blood Sample Clinical Form
55	MRI Status Verification Clinical Form
56	Genetics Phlebotomy Form (Shipping Manifest - Rutgers) Clinical Form
15	Death Notification Administrative Form
18	Transfer Form Administrative Form
19	Study Withdrawal Administrative Form
24	Missed Visit Administrative Form
51	Identification Form Administrative Form
52	Data Change Administrative Form
	Web Access Administrative Form
54	Missing Data Administrative Form
56	HALT ID Form
58	Lifestyle Form Family Member

CRISP II

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Registration Form

This form is to be completed at the participant's first clinic visit, immediately following signing of informed consent.

1. Date of visit: *dvdate* ☐☐/☐☐/☐☐☐☐

2. Informed Consent

If participant does not sign informed consent, check no, go to section 14 and check ***Ineligible*** *for Participant Status:* ***do not*** *complete any other questions or sections.*

If consent is signed, check yes and go to question 3.

Did the participant sign written consent? *sigcon* 0 ☐ No 1 ☐ Yes

3. Date the consent form was signed: *condate* ☐☐/☐☐/☐☐☐☐

4. Is the participant currently enrolled in another study in addition to CRISP? *parten* 0 ☐ No 1 ☐ Yes

If yes, which study? *enrol*

1 ☐ Halt
2 ☐ Tempo
3 ☐ Other, Specify: _____ *enrolsp* **Duration:** ____ months *duramt* _____ years *durayr*

5. Gender *gender* 1 ☐ Male 2 ☐ Female

6. Birth Weight *brwgt* _____ pounds *broz* _____ ounces ☐ check if birth weight is unknown

7. Was birth weight verified by the participant's birth certificate? *brcert* 0 ☐ No 1 ☐ Yes

8. Treating physician affiliation: *phys* 1 ☐ CRISP physician 2 ☐ Other nephrologist 3 ☐ Other physician

9. Education (in total number of years) *educ* _____ years

9a. Are you adopted? *adopt* 1 ☐ No 1 ☐ Yes

CRISP II

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Registration Form

10. Exclusion Criteria

*If yes is checked for **any** of the criteria listed in section 10, go to section 14 and check **Ineligible** for Participant Status; **do not** complete sections 11, 12, and 13.*

If all are no, go to section 11.

Does the participant have a current psychiatric or addiction non-compliance disorder that in the discretion of the principal investigator indicates that they will not successfully complete the study? *curpsyc*	0 ☐ No	1 ☐ Yes
Does the participant have a current medical problem that in the discretion of the principal investigator would make unsafe their participation in the study? *cur*	0 ☐ No	1 ☐ Yes
Does the participant have another condition that in the discretion of the principal investigator makes the participant ineligible? *ocrit*	0 ☐ No	1 ☐ Yes
If yes, please specify: _____ *otcritsp*		

11. Failed to Enroll Criteria

If the participant is unwilling to enroll in the study, indicate reason(s).

*If yes is checked for **any** of the criteria listed in section 11, go to section 14 and check **Failed to Enroll** for Participant Status; **do not** complete section 12 or 13.*

If all are no, go to section 12.

Is the participant unwilling to miss school/work? *schwork*	0 ☐ No	1 ☐ Yes
Is the participant unwilling to travel to clinics for visits? *travcl*	0 ☐ No	1 ☐ Yes
Is the participant unwilling to make a follow-up commitment? *fucom*	0 ☐ No	1 ☐ Yes
Is there any other circumstance that in the discretion of the principal investigator constitutes a valid reason for failing to enroll? *otenr*	0 ☐ No	1 ☐ Yes
If yes, please specify _____ *othensp*		

CRISP II

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Registration Form

12. Eligible but Modified Criteria – Part I

*Review **all** possible conditions listed in section 12 with the participant. Check any that apply. If **any** of the MR contraindications are checked, go to section 14 and check **Eligible but Modified** for Participant Status. **Do not** complete section 13.*

If none are checked, go to section 13.

- ☐ Weight > 158.6 kg (350 lbs) *weight*
- ☐ Pregnant *preg*
- ☐ Cardiac Pacemaker *cardpac*
- ☐ Implanted cardioverter defibrillator (ICD) *cardef*
- ☐ Neurostimulation system *neuron*
- ☐ Claustrophobia *claust*
- ☐ Spinal cord stimulator *spinal*

13. Eligible but Modified Criteria – Part II

*Review **all** possible conditions listed in section 13 (continued on the next 2 pages) with the participant. Check any that apply. If **any** are checked, please discuss with the radiologist to determine the Participant Status.*

*If none are checked, go to section 14 and check **Eligible and Enrolled.***

- ☐ Bone growth/bone fusion stimulator *bonfus*
- ☐ Cochlear, otologic, or other ear implant *earimp*
- ☐ Insulin or other infusion pump *insul*
- ☐ Implanted drug infusion device *druginf*
- ☐ Eyelid spring or wire *eyel*
- ☐ Tissue expander (e.g. breast) *tissex*
- ☐ Hx of working with metal *hxwkmet*
- ☐ Hx of metal in eyes *hxmeteye*
- ☐ Aneurysm Clip(s) *aneu*
- ☐ Hearing aid *hearaid*

CRISP II

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Registration Form

- ☐ Embolization coils *emcoil*
- ☐ Internal electrodes or wires *wires*
- ☐ Any type of prosthesis (eye, penile, etc.) *prost*
- ☐ Heart valve prosthesis *heart*
- ☐ Metallic stent, filter, or coil *metst*
- ☐ Artificial or or prosthetic limb *proslim*
- ☐ Shunt (spinal or intraventricular) *shunt*
- ☐ Vascular access port and/or catheter *vascath*
- ☐ Radiation seeds or implants *radseim*
- ☐ Swan-Ganz or thermodilution catheter *swan*
- ☐ Medication patch (Nicotine, Nitroglycerine) *patch*
- ☐ Any metallic fragment or foreign body *metfrag*
- ☐ Wire mesh implant *wimeim*
- ☐ Surgical staples, clips or metallic sutures *surstcl*
- ☐ Joint replacement (hip, knee, etc.) *jorep*
- ☐ Bone/joint pin, screw, nail, wire, plate, etc. *bojpin*
- ☐ IUD, diaphragm or pessary *iud*
- ☐ Dentures or partial plates *denppl*
- ☐ Tattoo or permanent makeup *tattoo*
- ☐ Body piercing jewelry *bopierc*
- ☐ Other implant *otimp*

Please specify: _____ *impsp*

- ☐ Breathing problem *breatpr*
- ☐ Other *other*

Please specify:_____ *othersp*

CRISP II

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Registration Form

14. **Participant Status:** *finenro* *(Check only one)*
1 ☐ Ineligible - **Stop**
2 ☐ Failed to Enroll - **Stop**
3 ☐ Eligible but Modified – **Continue, no MRI**
4 ☐ Eligible and Enrolled - **Continue**

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit: Accession ID: _____ *accn*

MR Session Information/Renal Blood Flow Form

This form is to be completed during scan at the participant's clinic visits.
This form is to be entered promptly and data transferred to the Imaging Analysis Center (Ac) right after the scan.

To be used ONLY with the Accession # status change:statch

1 ☐ This number is tied to a repeat scan
2 ☐ This accession number WILL NOT BE USED

1. Date of visit: *dvdate* | | | / | | | / | | | | |

2. Start Time: __ __:__ __ (24 hour) *tstime*

End Time: __ __:__ __ (24 hour) *tetime*

3. Machine name: _____ *mname*

Technologist name: _____ *tidnum*

Radiologist name: _____ *ridnum*

4. Series information *(see table on page 2)*
☐ N/A *(If N/A skip to question 7)*

5. Adverse events *(enter "None" for Event Description if no adverse events occurred)*

Series #	Event Description
_____ *ns1*	_____ *ed1*
_____ *ns2*	_____ *ed2*
_____ *ns3*	_____ *ed3*

Contents of form reviewed by:

☐ **Radiologist** (Signature Required) _____ *revnames* Date __ __/__ __/__ __ __ __ *reddate*

☐ **Technologist** (Signature Required) _____ *revnamet* Date __ __/__ __/__ __ __ __ *techdate*

6. Renal Scan Series information: **Accession Number:** _____*mraid*

*For T2 or FISP/FIESTA/BFFE, if the kidney is too large to cover in a single breath-hold, use multiple breath-holds, but as few as possible.
Have the first scan cover the posterior aspect of the kidney and then choose the 'shift-mean (starting point in GE)' of the second scan as follows:
For example, the **1st shift-mean** = -60 mm. **Number of slices in the 1st set** =23. (23-1) x 3 =66 mm. The **2nd shift mean** =-60 + 66 = 6mm.

Series #	Name MR Sequence (circle one)				Comments	#of Slices	Duration (seconds)	FOV
sid1	*descr1* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com1*	*sn1*	*sd1*	_____X_____ *fovw1* *fovh1*
sid2	*descr2* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com2*	*sn2*	*sd2*	_____X_____ *fovw2* *fovh2*
sid3	*descr3* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com3*	*sn3*	*sd3*	_____X_____ *fovw3* *fovh3*
sid4	*descr4* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com4*	*sn4*	*sd4*	_____X_____ *fovw4* *fovh4*
sid5	*descr5* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com5*	*sn5*	*sd5*	_____X_____ *fovw5* *fovh5*
sid6	*descr6* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com6*	*sn6*	*sd6*	_____X_____ *fovw6* *fovh6*
sid7	*descr7* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com7*	*sn7*	*sd7*	_____X_____ *fovw7* *fovh7*
sid8	*descr8* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com8*	*sn8*	*sd8*	_____X_____ *fovw8* *fovh8*
sid9	*descr9* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com9*	*sn9*	*sd9*	_____X_____ *fovw9* *fovh9*
sid10	*descr10* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com10*	*sn10*	*sd10*	_____X_____ *fovw10* *fovh10*
sid11	*descr11* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com11*	*sn11*	*sd11*	_____X_____ *fovw11* *fovh11*
sid12	*descr12* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com12*	*sn12*	*sd12*	_____X_____ *fovw12* *fovh1 2*
sid13	*descr13* T2 FatSat 9mm 3mm*	T1 Non-FatSat	FISP/FIESTA/BFFE* Non-FatSat	T2 Non-FatSat Adj-kidney Adj-liver*	*com13*	*sn13*	*sd13*	_____X_____ *fovw13* *fovh13*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit: Accession ID: _____ *accn*

MR Session Information/Renal Blood Flow Form

Omitted Series	Reason series was omitted/Unreadable *(If Missing Use Next Section)*
osn1	*osr1*
osn2	*osr2*
osn3	*osr3*
osn4	*osr4*
osn5	*osr5*
osn6	*osr6*
osn7	*osr7*
osn8	*osr8*
osn9	*osr9*
osn10	*osr10*
Missing Series	**Reason series was missing**
mser1	*reas1*
mser2	*reas2*
mser3	*reas3*
mser4	*reas4*
mser5	*reas5*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit: Accession ID: _____ *accn*

MR Session Information/Renal Blood Flow Form

7. Renal Blood Flow Information
☐ N/A

7a. Field of view: *fov*
1 ☐ 14 x 14 cm 2 ☐ 16 x 16 cm 3 ☐ 20 x 20 cm
4 ☐ Other Specify: R ____x____cm *fovrx* *fovry*
fovlx L ____x____cm *fovly*

7b. Matrix size: *mats*
1 ☐ 256 x 256 2 ☐ 256 x 224 3 ☐ Other Specify: R ____x ____ *marspx* *marspy*
L ____x____ *malspx* *malspy*

7c. Total number of cardiac phases measures per RR interval: _____ *tcprr*

gating 1 ☐ Prospective Gating 2 ☐ Retrospective Gating

7d. Recorded heart rate at the time of the exam: _____ *rhr*

7e.

Series#	Comments	# of Slices	VENC*	
			100	If other specify
series1	*comment1*	*slice1*	*venc1*☐	*oth1*
series2	*comment2*	*slice2*	*venc2*☐	*oth2*
series3	*comment3*	*slice3*	*venc3*☐	*oth3*
series4	*comment4*	*slice4*	*venc4*☐	*oth4*
series5	*comment5*	*slice5*	*venc5*☐	*oth5*
series6	*comment6*	*slice6*	*venc6*☐	*oth6*
series7	*comment7*	*slice7*	*venc7*☐	*oth7*
series8	*comment8*	*slice8*	*venc8*☐	*oth8*
series9	*comment9*	*slice9*	*venc9*☐	*oth9*

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II **Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.**

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

GFR Collection Form

This form is to be completed upon sending the GFR Testing materials to Mayo. Can be partially completed from the Patient Requisition Form provided by the Mayo Lab.

☐ Original ☐ Repeat 1 ☐ Repeat 2 *redo*

☐ **Participant refused to repeat the GFR.**

Date of visit (when sample was collected): *dvdate* ☐☐ / ☐☐ / ☐☐☐☐

Please enter appropriate units:

1. **Weight:**_____kg *weight* **Height:**_____cm *height*
2. **Initial Urine Collection Time (Uo):** *uotime* __ __:__ __ (24 hour)
3. **Iothalamate Injection Time:** *iitime* __ __:__ __ (24 hour)
4. **Equilibrium Urine Collection Time (Ue):** *uetime* __ __:__ __ (24 hour)

ureval **Average Residual volume** _____(<20ml or 10% of voided volume, no greater than 50 ml)

5. **Plasma Collection Time (P1):** *p1time* __ __:__ __ (24 hour)
6. **GFR Testing Urine Collection Time(U1):** *u1time* __ __:__ __ (24 hour)

uervol **Average Residual volume** _____(<20ml or 10% of voided volume, no greater than 50 ml)

7. **Plasma Collection Time (P2):** *p2time* __ __:__ __ (24 hour)
8. **U1 Collection Volume:** *u1cvol* _____ mls
9. **Date Sample sent to Mayo lab:** *ssdate* ☐☐ / ☐☐ / ☐☐☐☐

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate* *deidnum*

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

GFR Reporting Form

This form is to be completed upon receipt of the GFR Mayo lab report.

.

1. **Date of Visit** *(when sample was collected):* *dvdate*	__ __ / __ __ / __ __ __ __
2. **Date Sample was received at Mayo lab:** *srdate*	__ __ / __ __ / __ __ __ __
Test requested: Short Renal Clearance	
3. **Uncorrected Iothalamate Clearance:** *uic*	_____ml/min
4. **Corrected Iothalamate Clearance:** *cic*	_____ml/min/SA(1.73 m^2)

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Current Physical Findings Form

This form is to be completed by designated personnel (if medically trained) and/or PI at each Biannual visit.

dvdate
Date of Visit ☐☐ / ☐☐ / ☐☐☐☐

height
1. **Height:** __ __ __.__cm

Note**: If weight is greater than 158.6 kg (350 pounds), participant is not eligible to have a MRI. Change final participant status to **Eligible but Modified.

weight
2. **Weight:** __ __ __.__kg

3. **During the last 30 minutes, has the participant smoked or consumed caffeine?** *cigcaff* 0 ☐ No 1 ☐ Yes
(If yes, please wait 30 minutes since last cigarette or caffeine unit)

4. **Arm used:** *Use the arm determined at the initial visit, whenever possible.* *armused* 0 ☐ Right 1 ☐ Left

5. **Blood Pressure Monitors Used for Seated BP Readings:** *bpmonitor*

1 ☐ automated 2 ☐ PCC Monitor (non-automated): Brand_____ *bpbrand*

Note: The CRISP II Study Staff person signing this form is to complete the BP readings in items 6 and 7.

6. **SEATED Blood Pressure Readings (sequential):**
Participant is to rest 5 minutes with arm supported at heart level. Record at least three BP readings at least 30 seconds apart. If there is a difference of more than 10mm Hg (systolic or diastolic) between the second and third readings in one sitting, a fourth and fifth reading should be recorded for that sitting.

	Time (24 hour)	Systolic	Diastolic	Pulse Rate BPM
1	__ __:__ __ *r1time*	*sysl1*	*dial1*	*r1pr*
2	__ __:__ __ *r2time*	*sysl2*	*dial2*	*r2pr*
3	__ __:__ __ *r3time*	*sysl3*	*dial3*	*r3pr*
4	__ __:__ __ *r4time*	*sysl4*	*dial4*	*r4pr*
5	__ __:__ __ *r5time*	*sysl5*	*dial5*	*r5pr*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Current Physical Findings Form

Please Note: Average blood pressure will be automatically generated at data entry.

7. **STANDING BP Reading:** *Measure BP after 3 minutes standing with arm supported at heart level.*

	Time (24 hour)	Systolic	Diastolic	Pulse Rate BPM
1	__ __:__ __ *d1time*	*sysd1*	*diad1*	*d1pr*

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

SYMPTOMS FORM

This form is to be completed by designated personnel and/or PI at each Biannual Clinic Visit.

Date of visit: *dvdate* ☐☐ / ☐☐ / ☐☐☐☐

Please complete this form before your physical exam, then discuss your answers with designated personnel.

1. **Check "yes" or "no" for symptoms experienced since your last visit (or within the past month if this is your first visit). "**

Symptoms	Yes	No	Specify/Describe if applicable
CONSTITUTIONAL			
Malaise/Feeling sickly or ill *mal*			*malspy*
HEAD/NECK			
Headache *head*			*headspy*
Blurred Vision/Visual Changes *blur*			*blurspy*
Dry Eyes/Nasal Passages *dry*			*dryspy*
Nasal Congestion *nas*			*nasspy*
Sore Throat *sore*			*sorespy*
Dry Mouth/Excessive Thirst *drym*			*drymspy*
CARDIOVASCULAR			
Chest Pain *chest*			*chestspy*
Heart Palpitations *heart*			*heartspy*
Dizziness/Lightheadedness *diz*			*dizspy*
Fatigue/Weakness *fatig*			*fatigspy*
Leg Swelling/Edema *leg*			*legspy*
RESPIRATORY			
Shortness of Breath with Exertion *shbex*			*shbexspy*
Shortness of Breath at Rest *shre*			*shrespy*
Cough *cough*			*coughspy*
MUSCULOSKELETAL			
Joint Pain/Aches *joint*			*jointspy*
Muscle Pain/Cramping/Spasm *musc*			*muscspy*

Please continue on next page

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

SYMPTOMS FORM

Symptoms	Yes	No	Specify/Describe if applicable
GENITOURINARY			
Urinary Changes *urin*			*urinspy*
Visible Blood in Urine *vsbl*			*vsblspy*
Impotence/Decreased Libido *impot*			*impotspy*
Urinary Tract Infection *uti*			*utispy*
Kidney Stone *kidst*			*kidstspy*
DEMATOLOGIC			
Changes of the Skin or Hair *skin*			*skinspy*
GASTROINTESTINAL			
Nausea/Vomiting *naus*			*nausspy*
Diarrhea *diar*			*diarspy*
Constipation *const*			*constspy*
Stomach Discomfort/ Abdominal Pain *stom*			*stomspy*
Changes in Appetite *appe*			*appespy*
NEUROLOGICAL			
Mood Changes like Anxiety, Restlessness, Depression *mood*			*moodspy*
Tingling/Numbness *numb*			*numbspy*
Problems with Memory *mem*			*memspy*
Drowsiness *drow*			*drowspy*
Insomnia/Problems Sleeping *insom*			*insomspy*

Other Symptoms				
otsm1			*otsm1yn*	*otsm1spy*
otsm2			*otsm2yn*	*otsm2spy*
otsm3			*otsm3yn*	*otsm3spy*

Please complete History of Renal Pain on next page

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

SYMPTOMS FORM

2. History of Renal Pain in the last year.

2a. Was there pain in the right kidney in the last year? *locrp* 0 ☐ No 1 ☐ Yes

If no, go to 2d *Go to 2b*

2b. *If yes*, **how often?** *freqrp*

1 ☐ Rarely
2 ☐ Sometimes
3 ☐ Often
4 ☐ Usually
5 ☐ Always

2c. Severity: Indicate on a scale of 0 to 10, where 0=no pain and 10=pain as bad as you can imagine *severe*

☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
0	1	2	3	4	5	6	7	8	9	10

2d. Was there pain in the left kidney in the last year? *loclp* 0 ☐ No 1 ☐ Yes

If no, **Stop** *Go to 2e*

2e. *If yes*, **how often?** *freqlp*

1 ☐ Rarely
2 ☐ Sometimes
3 ☐ Often
4 ☐ Usually
5 ☐ Always

2F. Severity: Indicate on a scale of 0 to 10, where 0=no pain and 10=pain as bad as you can imagine *severel*

☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
0	1	2	3	4	5	6	7	8	9	10

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

SYMPTOMS FORM

3.	For Males Only.			
		If female, select N/A for Not Applicable		
3a.	Have you ever had seminal vesicle cysts? *semcysts*	☐ N/A	0 ☐ No	1 ☐ Yes
3b.	Have you ever had epididymal cysts? *epidcysts*	☐ N/A	0 ☐ No	1 ☐ Yes

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Follow-Up Study and Events Form

This form is to be completed for the scheduled Semi-Annual Phone Call and as needed for unscheduled phone calls and/or visits.

1. Date of visit *dvdate* | | | / | | | / | | | | |

Type of Event: *toe* 1 ☐ Scheduled Follow-up Visit 2 ☐ Serious Adverse Event

3 ☐ Other Specify_____ *evoth*

2. Since the last visit, has the participant had any illnesses ? *ilyn* 0 ☐ No **(*Go to #3*)** 1 ☐ Yes

If yes, **please specify briefly:** *ill*_____

_____

_____

3. Since the last visit, has the participant visited their primary care physician? *pvyn* 0 ☐ No **(*Go to #4*)** 1 ☐ Yes

If yes, complete Section 3

3a. Date of physician visit: __ __/__ __ /__ __ __ __ *pvyr*

pvmt *pvda* Month Day Year

3b. Were there multiple visits to this physician? *mvci* 0 ☐ No 1 ☐ Yes

3c. Name and address of physician treating participant:

Name: _____ *pvnme*

Address: _____ *pvadds*

City, State, Zip: _____ *pvcsz*

3d. Specify reason for visit: *pvreason* _____

_____

_____

_____

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Follow-Up Study and Events Form

4.	**Since the last visit, has the participant visited any physician other than the primary care physician listed in question 3?** *pvotphy*	0 ☐ No *(Go to #5)*	1 ☐ Yes

If yes, complete Section #4

Physician #1

a. Date of additional physician visit: __ __/__ __ /__ __ __ __ *pv2yr1*
pv2mt1 *pv2da1* Month Day Year

b. Were there multiple visits to this physician? *m2vc1* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____ *pv2nme1*

Address: _____ *pv2adds1*

City, State, Zip:_____ *pv2csz1*

d. Specify reason for visit: *pv2reason1*_____

_____

_____

Physician #2

a. Date of additional physician visit: __ __/__ __ /__ __ __ __ *pv2yr2*
pv2mt2 *pv2da2* Month Day Year

b. Were there multiple visits to this physician? *m2vc2* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____ *pv2nme2*

Address: _____ *pv2adds2*

City, State, Zip:_____ *pv2csz2*

d. Specify reason for visit: *pv2reason2*_____

_____

_____

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Follow-Up Study and Events Form

Physician #3

a. Date of additional physician visit: __ __/__ __ /__ __ __ __ *pv2yr3*
pv2mt3 *pv2da3* Month Day Year

b. Were there multiple visits to this physician? *m2vc3* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____ *pv2nme3*

Address: _____ *pv2adds3*

City, State, Zip:_____ *pv2csz3*

d. Specify reason for visit: *pv2reason3*_____

_____

_____

Please continue on the next page

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Follow-Up Study and Events Form

5. **Since the last visit, has the participant been hospitalized?** *hyn*	0 ☐ No **(*Go to #6*)**	1 ☐ Yes
If yes, complete Section #5		
Hospitalization #1		
a. Was this hospitalization unscheduled? *husch1*	0 ☐ No	1 ☐ Yes **(See Note)**

Note: If unscheduled, please report the event to the local IRB and send a copy to the DCIAC

b. Date admitted to hospital: __ __/__ __/__ __ __ __ *hayr1*
hamt1 *hada1* Month Day Year

c. Date discharged from hospital: __ __/__ __/__ __ __ __ *hdyr1*
hdmt1 *hdda1* Month Day Year

d. Length of stay: _____*lenst1*

e. Name and address of hospital:

Name:_____*hnme1*

Address:_____*hadds1*

City, State, Zip:_____ *hacsz1*

f. Name and address of physician treating participant:

Name:_____*phnme1*

Address:_____*phadds1*

City, State, Zip:_____*phcsz1*

g. What was the discharge diagnosis?_____*hdiag1*

h. Was there any renal surgery performed? *rsurgpyn1* *If no, go to Hospitalization #2 or Section 6 if no more hospitalizations*	0 ☐ No	1 ☐ Yes
If yes, was the intent cyst reduction? *ceducyn1*	0 ☐ No	1 ☐ Yes

i. For any renal surgery provide a date and short description:
Date of intervention: __ __/__ __/__ __ __ __ *rsiyr1*
rsimt1 *rsida1* Month Day Year

Description:_____*rsidesc1*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Follow-Up Study and Events Form

Hospitalization #2

a. Was this hospitalization unscheduled? *husch2* 0 ☐ No 1 ☐ Yes **(See Note)**

Note: If unscheduled, please report the event to the local IRB and send a copy to the DCIAC

b. Date admitted to hospital: __ __/__ __/__ __ __ __ *hayr2*
hamt2 *hada2* Month Day Year

c. Date discharged from hospital: __ __/__ __/__ __ __ __ *hdyr2*
hdmt2 *hdda2* Month Day Year

d. Length of stay: _____ *lenst2*

e. Name and address of hospital:

Name:_____ *hnme2*

Address:_____ *hadds2*

City, State, Zip:_____ *hacsz2*

f. Name and address of physician treating participant:

Name:_____ *phnme2*

Address:_____ *phadds2*

City, State, Zip:_____ *phcsz2*

g. What was the discharge diagnosis?_____ *hdiag2*

h. Was there any renal surgery performed? *resurgpyn2* 0 ☐ No 1 ☐ Yes
If no, go to Hospitalization #3 or Section 6 if no more hospitalizations

If yes, was the intent cyst reduction? *ceducyn2* 0 ☐ No 1 ☐ Yes

i. For any renal surgery provide a date and short description:

Date of intervention: __ __/__ __/__ __ __ __ *rsiyr2*
rsimt2 *rsida2* Month Day Year

Description:_____ *rsidesc2*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Follow-Up Study and Events Form

Hospitalization #3

a. Was this hospitalization unscheduled? *husch3* 0 ☐ No 1 ☐ Yes **(See Note)**

Note: If unscheduled, please report the event to the local IRB and send a copy to the DCIAC

b. Date admitted to hospital: __ __/__ __/__ __ __ __ *hayr3*
hamt3 *hada3* Month Day Year

c. Date discharged from hospital: __ __/__ __/__ __ __ __ *hdyr3*
hdmt3 *hdda3* Month Day Year

d. Length of stay: _____ *lenst3*

e. Name and address of hospital:

Name:_____ *hnme3*

Address:_____ *hadds3*

City, State, Zip:_____ *hacsz3*

f. Name and address of physician treating participant:

Name:_____ *phnme3*

Address:_____ *phadds3*

City, State, Zip:_____ *phcsz3*

g. What was the discharge diagnosis?_____ *hdiag3*

h. Was there any renal surgery performed? *rsurgpyn3* 0 ☐ No 1 ☐ Yes
If no, go to Hospitalization #4 or Section 6 if no more hospitalizations

If yes, was the intent cyst reduction? *ceducyn3* 0 ☐ No 1 ☐ Yes

i. For any renal surgery provide a date and short description:

Date of intervention: __ __/__ __/__ __ __ __ *rsiyr3*
rsimt3 *rsida3* Month Day Year

Description:_____ *rsidesc3*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Follow-Up Study and Events Form

Hospitalization #4

a. Was this hospitalization unscheduled? *husch4* 0 ☐ No 1 ☐ Yes **(See Note)**

Note: If unscheduled, please report the event to the local IRB and send a copy to the DCIAC

b. Date admitted to hospital: __ __/__ __/__ __ __ __ *hayr4*
hamt4 *hada4* Month Day Year

c. Date discharged from hospital: __ __/__ __/__ __ __ __ *hdyr4*
hdmt4 *hdda4* Month Day Year

d. Length of stay: _____ *lenst4*

e. Name and address of hospital:

Name:_____ *hnme4*

Address:_____ *hadds4*

City, State, Zip:_____ *hcsz4*

f. Name and address of physician treating participant:

Name:_____ *phnme4*

Address:_____ *phadds4*

City, State, Zip:_____ *phcsz4*

g. What was the discharge diagnosis?_____ *hdiag4*

h. Was there any renal surgery performed? *rsurgpyn4* 0 ☐ No 1 ☐ Yes
(Go to #6)

If yes, was the intent cyst reduction? *ceducyn4* 0 ☐ No 1 ☐ Yes

i. For any renal surgery provide a date and short description:

Date of intervention: __ __/__ __/__ __ __ __ *rsiyr4*
rsimt4 *rsida4* Month Day Year

Description:_____ *rsidesc4*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Follow-Up Study and Events Form

6. Prescribed medications changes:

6a. Since the last visit, have prescribed drugs been added? *payn* 0 ☐ No 1 ☐ Yes ***(Go to #6b)***

If yes, then please record:

Prescribed Medications **added**	Date (month/year)
pma1	*dpmamt1* ___/___ *dpmadate1*
pma2	*dpmamt2* ___/___ *dpmadate2*
pma3	*dpmamt3* ___/___ *dpmadate3*
pma4	*dpmamt4* ___/___ *dpmadate4*
pma5	*dpmamt5* __/__ *dpmadate5*

6b. Since the last visit, have prescribed drugs been stopped/discontinued? *pdyn* 0 ☐ No 1 ☐ Yes ***(Go to #7a)***

If yes, then please record:

Prescribed Medications **discontinued**	Date (month/year)
pmd1	*dpmdmt1* ___/___ *dpmddate1*
pmd2	*dpmdmt2* ___/___ *dpmddate2*
pmd3	*dpmdmt3* ___/___ *dpmddate3*
pmd4	*dpmdmt4* ___/___ *dpmddate4*
pmd5	*dpmdmt5* __/__ *dpmddate5*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Follow-Up Study and Events Form

7. Over-the-counter medications changes:

7a. Since the last visit, have OTC drugs been added? *oayn* 0 ☐ No 1 ☐ Yes ***(Go to #7b)***

If yes, then please record:

OTC Medications **added**	Date (month/year)
oma1	*domamt1* __ __/__ __ __ __ *domadate1*
oma2	*domamt2* __ __/__ __ __ __ *domadate2*
oma3	*domamt3* __ __/__ __ __ __ *domadate3*
oma4	*domamt4* __ __/__ __ __ __ *domadate4*
oma5	*domamt5* __ __/__ __ __ __ *domadate5*

7b. Since the last visit, have OTC drugs been stopped/discontinued? *odyn* 0 ☐ No 1 ☐ Yes ***(Go to#8b)***

If yes, then please record:

OTC Medications **discontinued**	Date (month/year)
omd1	*domdmt1* __ __/__ __ __ __ *domddate1*
omd2	*domdmt2* __ __/__ __ __ __ *domddate2*
omd3	*domdmt3* __ __/__ __ __ __ *domddate3*
omd4	*domdmt4* __ __/__ __ __ __ *domddate4*
omd5	*domdmt5* __ __/__ __ __ __ *domddate5*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Follow-Up Study and Events Form

8. Natural Product Use Changes:

8a. Since the last visit, have Natural Products/Protein Supplements been added? *pnayn* 0 ☐ No *(Go to #13b)* 1 ☐ Yes

If yes, then please record:

Natural Products/Protein Supplements **added**	Date (month/year)
nps1	*dnmamt1* __ __/__ __ __ __ *dnmadate1*
nps2	*dnmamt2* __ __/__ __ __ __ *dnmadate2*
nps3	*dnmamt3* __ __/__ __ __ __ *dnmadate3*
nps4	*dnmamt4* __ __/__ __ __ __ *dnmadate4*
nps5	*dnmamt5* __ __/__ __ __ __ *dnmadate5*

8b. Since the last visit, have Natural Products/Protein Supplements been stopped/discontinued? *pndyn* 0 ☐ No *(Stop)* 1 ☐ Yes

If yes, then please record:

Natural Products/Protein Supplements **discontinued**	Date (month/year)
npds1	*dnmadmt1* __ __/__ __ __ __ *dnmaddate1*
npds2	*dnmadmt2* __ __/__ __ __ __ *dnmaddate2*
npds3	*dnmadmt3* __ __/__ __ __ __ *dnmaddate3*
npds4	*dnmadmt4* __ __/__ __ __ __ *dnmaddate4*
npds5	*dnmadmt5* __ __/__ __ __ __ *dnmaddate5*

Please review all contact information on the Identification Form including phone number and email address.

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Follow-Up Study and Events Form

Contents of Formed Reviewed by Principal Investigator *(required signature):*_____
pinum

Date Principal Investigator Signed __ __/__ __/__ __ __ __ *pidate*

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit - Labs

This form is to be completed at the participant's visit during years 6 and 8.

1. **Date of visit:** *dvdate* ☐☐/☐☐/☐☐☐☐

2. **Specify Laboratory processing samples:**_____ *labname*

BLOOD WORK:

3. **Serum creatinine concentration:** _____ mg/dL *creatclr*

Date creatinine collected: *ccdate* ☐☐/☐☐/☐☐☐☐

Duplicate serum collected for storage: 0 ☐ No 1 ☐ Yes
dupser

4. **Date remaining blood samples were collected:** *rbdate* ☐☐/☐☐/☐☐☐☐

5. **Electrolyte:** Sodium _____ *sod* Potassium_____ *pot* Chloride _____ *chlo* CO_2 _____ *co2*

6. **Serum total cholesterol** (mg/dL) _____ *schole*

Serum triglycerides (mg/dL) _____ *strig*

Serum HDL cholesterol (mg/dL) _____ *shdl*

Serum LDL cholesterol (mg/dL) _____ *sldl*

7. **Serum samples collected for storage:** **Collection Date:** *ssdate* ☐☐/☐☐/☐☐☐☐

20 mL in two SST tubes (tiger-top, 10mL each)
16 mL in two PST tubes (green/grey-top, 8 mL each
____. Centrifuged and shipped to Fisher Bioservices on day of collection _____

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit - Labs

8.	**Urine or Serum Pregnancy test** *(check)* *urpreg*	0 ☐ positive	1☐ negative	2☐ test not performed
	If test not performed, then specify reason: _____ *urreas*			
9.	**Urine albumin** (mg/dL) _____ *urabu*			
	Urine creatinine (mg/dL) _____ *urcreat*			
	Urine albumin/creatinine ratio _____ *urratio*			
10.	**Urine sample collected for storage:**	**Collection Date:** *urvdate* ☐☐/☐☐/☐☐☐☐		
	20 mL poured into four 5mL tubes each Urine pellet for DNA/RNA Frozen and batched shipped to Fisher Bioservices			

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

This form is to be completed at each Biannual Clinic Visit.

1. **Date of visit** *dvdate* | | | / | | | / | | | | |

2. **Since the last visit, has the participant had any illnesses ?** *ilyn* 0 ☐ No (*Go to #3*) 1 ☐ Yes

If yes, **please specify briefly:** *ill*_____

_____

_____

3. **Since the last visit, has the participant visited their primary care physician?** *pvyn* 0 ☐ No (*Go to #4*) 1 ☐ Yes

If yes, complete Section 3

3a. Date of physician visit: __ __/__ __ /__ __ __ __ *pvyr*
pvmt *pvda* Month Day Year

3b. Were there multiple visits to this physician? *mvci* 0 ☐ No 1 ☐ Yes

3c. Name and address of physician treating participant:

Name: _____ *pvnme*

Address: _____ *pvadds*

City, State, Zip: _____ *pvcsz*

3d. Specify reason for visit: *pvreason* _____

_____

_____

_____

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

4. Since the last visit, has the participant visited any physician other than the primary care physician listed in question 3? *pvotphy* 0 ☐ No *(Go to #5)* 1 ☐ Yes

If yes, complete Section #4

Physician #1

a. Date of additional physician visit: __ __/__ __ /__ __ __ __ *pv2yr1*
pv2mt1 *pv2da1* Month Day Year

b. Were there multiple visits to this physician? *m2vc1* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____ *pv2nme1*

Address: _____ *pv2adds1*

City, State, Zip:_____ *pv2csz1*

d. Specify reason for visit: *pv2reason1*_____

_____

_____

Physician #2

a. Date of additional physician visit: __ __/__ __ /__ __ __ __ *pv2yr2*
pv2mt2 *pv2da2* Month Day Year

b. Were there multiple visits to this physician? *m2vc2* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____ *pv2nme2*

Address: _____ *pv2adds2*

City, State, Zip:_____ *pv2csz2*

d. Specify reason for visit: *pv2reason2*_____

_____

_____

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

Physician #3

a. Date of additional physician visit: __ __/__ __ /__ __ __ __ *pv2yr3*
pv2mt3 *pv2da3* Month Day Year

b. Were there multiple visits to this physician? *m2vc3* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____ *pv2nme3*

Address: _____ *pv2adds3*

City, State, Zip:_____ *pv2csz3*

d. Specify reason for visit: *pv2reason3*_____

_____

_____

Please continue on the next page

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

5. **Since the last visit, has the participant been hospitalized?** *hyn*	0 ☐ No **(*Go to #6*)**	1 ☐ Yes

If yes, complete Section #5

Hospitalization #1

a. Was this hospitalization unscheduled? *husch1*	0 ☐ No	1 ☐ Yes **(See Note)**

Note: If unscheduled, please report the event to the local IRB and send a copy to the DCIAC

b. Date admitted to hospital: __ __/__ __/__ __ __ __ *hayr1*
hamt1 *hada1* Month Day Year

c. Date discharged from hospital: __ __/__ __/__ __ __ __ *hdyr1*
hdmt1 *hdda1* Month Day Year

d. Length of stay (in days) : _____ *lenst1*

e. Name and address of hospital:

Name:_____ *hnme1*

Address:_____ *hadds1*

City, State, Zip:_____ *hcsz1*

f. Name and address of physician treating participant:

Name:_____ *phnme1*

Address:_____ *phadds1*

City, State, Zip:_____ *phcsz1*

g. What was the discharge diagnosis?_____ *hdiag1*

h. Was there any renal surgery performed? *rsurgpyn1* *If no, go to Hospitalization #2 or Section 6 if no more hospitalizations*	0 ☐ No	1 ☐ Yes
If yes, was the intent cyst reduction? *ceducyn1*	0 ☐ No	1 ☐ Yes

i. For any renal surgery provide a date and short description:
Date of intervention: __ __/__ __/__ __ __ __ *rsiyr1*
rsimt1 *rsida1* Month Day Year

Description:_____ *rsidesc1*

Hospitalization #2

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

a. Was this hospitalization unscheduled? *husch2* 0 ☐ No 1 ☐ Yes **(See Note)**

.

Note: If unscheduled, please report the event to the local IRB and send a copy to the DCIAC

b. Date admitted to hospital: __ __/__ __/__ __ __ __ *hayr2*
hamt2 *hada2* Month Day Year

c. Date discharged from hospital: __ __/__ __/__ __ __ __ *hdyr2*
hdmt2 *hdda2* Month Day Year

d. Length of stay (in days) : _____*lenst2*

e. Name and address of hospital:

Name:_____*hnme2*

Address:_____*hadds2*

City, State, Zip:_____ *hacsz2*

f. Name and address of physician treating participant:

Name:_____*phnme2*

Address:_____*phadds2*

City, State, Zip:_____*phcsz2*

g. What was the discharge diagnosis?_____*hdiag2*

h. Was there any renal surgery performed? *resurgpyn2* 0 ☐ No 1 ☐ Yes
If no, go to Hospitalization #3 or Section 6 if no more hospitalizations

If yes, was the intent cyst reduction? *ceducyn2* 0 ☐ No 1 ☐ Yes

i. For any renal surgery provide a date and short description:

Date of intervention: __ __/__ __/__ __ __ __ *rsiyr2*
rsimt2 *rsida2* Month Day Year

Description:_____*rsidesc2*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

Hospitalization #3

a. Was this hospitalization unscheduled? *husch3* 0 ☐ No 1 ☐ Yes **(See Note)**

Note: If unscheduled, please report the event to the local IRB and send a copy to the DCIAC

b. Date admitted to hospital: __ __/__ __/__ __ __ __ *hayr3*
hamt3 *hada3* Month Day Year

c. Date discharged from hospital: __ __/__ __/__ __ __ __ *hdyr3*
hdmt3 *hdda3* Month Day Year

d. Length of stay (in days) : _____ *lenst3*

e. Name and address of hospital:

Name:_____ *hnme3*

Address:_____ *hadds3*

City, State, Zip:_____ *hacsz3*

f. Name and address of physician treating participant:

Name:_____ *phnme3*

Address:_____ *phadds3*

City, State, Zip:_____ *phcsz3*

g. What was the discharge diagnosis?_____ *hdiag3*

h. Was there any renal surgery performed? *rsurgpyn3* 0 ☐ No 1 ☐ Yes
If no, go to Hospitalization #4 or Section 6 if no more hospitalizations

If yes, was the intent cyst reduction? *ceducyn3* 0 ☐ No 1 ☐ Yes

i. For any renal surgery provide a date and short description:

Date of intervention: __ __/__ __/__ __ __ __ *rsiyr3*
rsimt3 *rsida3* Month Day Year

Description:_____ *rsidesc3*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

Hospitalization #4

a. Was this hospitalization unscheduled? *husch4* 0 ☐ No 1 ☐ Yes **(See Note)**

Note: If unscheduled, please report the event to the local IRB and send a copy to the DCIAC

b. Date admitted to hospital: __ __/__ __/__ __ __ __ *hayr4*
hamt4 *hada4* Month Day Year

c. Date discharged from hospital: __ __/__ __/__ __ __ __ *hdyr4*
hdmt4 *hdda4* Month Day Year

d. Length of stay (in days) : _____*lenst4*

e. Name and address of hospital:

Name:_____*hnme4*

Address:_____*hadds4*

City, State, Zip:_____*hacsz4*

f. Name and address of physician treating participant:

Name:_____*phnme4*

Address:_____*phadds4*

City, State, Zip:_____*phcsz4*

g. What was the discharge diagnosis?_____*hdiag4*

h. Was there any renal surgery performed? *rsurgpyn4* 0 ☐ No 1 ☐ Yes *(Go to #6)*

If yes, was the intent cyst reduction? *ceducyn4* 0 ☐ No 1 ☐ Yes

i. For any renal surgery provide a date and short description:

Date of intervention: __ __/__ __/__ __ __ __ *rsiyr4*
rsimt4 *rsida4* Month Day Year

Description:_____*rsidesc4*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

6. Smoking and Tobacco:

6a. Has the participant ever smoked cigarettes? *csyn* 0 ☐ No **(*Go to# 6e*)** 1 ☐ Yes

6b. *If yes,* *csevsm*

1 ☐ Current ***(Go to #6d)***
2 ☐ Former, quit since last visit ***(Go to #6c)***
3 ☐ Former, quit prior to last visit ***(Go to #6c)***

6c. If former smoker, quit date: __ __/__ __ __ __ ***(Go to #6e)***
qsm Month Year *qsy*

6d. If current smoker, how many packs per year does the participant smoke? *ppy*
__ __ __ __

6e. Has the participant used any other types of tobacco since last visit? *otytob* 0 ☐ No **(*Go to #7a*)** 1 ☐ Yes

6f. *If yes*, **which types?**

6g. Cigars 0 ☐ No *cigar* 1 ☐ Yes

6h. *If yes*, **how many cigars since the last visit?** __ __ *cignm*

6i. Pipe 0 ☐ No *pipeyn* 1 ☐ Yes

6j. Chewing Tobacco/Snuff 0 ☐ No *chewyn* 1 ☐ Yes

7. Caffeinated Beverages:

7a. Does the participant drink caffeinated coffee or tea? *cucaff* 0 ☐ No **(Go to #7b)** 1 ☐ Yes

If yes, check time interval and enter the average number of caffeinated 8 ounce cups per Interval: *cupcaf*

1 ☐ Per day
2 ☐ Per week **Number of 8 ounce cups per interval__ __** *ccafunit*
3 ☐ Per month

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

7b. Does the participant drink other caffeinated beverages? *cafotbv* 0 ☐ No 1 ☐ Yes
(Go to #7c)

If yes, check time interval and enter the average number of caffeinated 12 ounce portions per interval: *glassc*

1 ☐ Per day
2 ☐ Per week **Number of 12 ounce portions per interval** __ __ *scafunit*
3 ☐ Per month

7c. Does the participant drink alcohol? *alcdr* 0 ☐ No 1 ☐ Yes
(Go to #8)

If yes, check time interval and enter the average number of alcoholic drinks per interval: *nad*

(1 drink=any of the following: 12 ounces of beer, 4 ounces of wine, 1.5 ounces liquor)

1 ☐ Per day
2 ☐ Per week **Number of drinks per interval** __ __ *alconit*
3 ☐ Per month

8. Analgesic Use History: *Record the average number per month over the last year. 0=Participant doesn't use*

8a. Acetaminophen tablets: __ __ __ *acett*
Avg. number per month

8b. Aspirin Tablets: __ __ __ *asprt*
Avg. number per month

8c. Combination analgesics: __ __ __ *combot*
Avg. number per month

8d. NSAIDs: __ __ __ *nsaidt*
Avg. number per month

8e. Medical use of marijuana: __ __ __ *dum*
Avg. Number per month

8f. Cox2 Inhibitors __ __ __ *cox2*
Avg. number per month

9. Has the participant used illicit drugs in the last year? *illdrg* 0 ☐ No 1 ☐ Yes

If yes, check all that apply

☐ Heroin *duh*
☐ Marijuana *duma*
☐ Methamphetamine *dumeth*
☐ Cocaine *duc*
☐ Other *duo*

If other, specify:_____ *othr*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

If this is Visit 8 do not complete this page. Go to # 11.

If this is Visit 6,

10. **List all current prescription medications, over the counter medications and all natural products/protein supplements,**

and then ***STOP***

Prescribed Medications	*pres1*
	pres2
	pres3
	pres4
	pres5
	pres6
	pres7
	pres8

Over the Counter Medications	*oct1*
	oct2
	oct3
	oct4
	oct5
	oct6
	oct7
	oct8

All Natural Products/ Protein Supplements	*npp1*
	npp2
	npp3
	npp4
	npp5
	npp6
	npp7
	npp8

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

For Visit 6, do not complete this page.
For Visit 8, complete this page.

11. Prescribed medications changes:

11a. Since the last visit, have prescribed drugs been added ? *payn* 0 ☐ No 1 ☐ Yes ***(Go to #11b)***

If yes, then please record:

Prescribed Medications **added**	Date (month/year)
pma1	*dpmamt1* __ __/__ __ __ __ *dpmadate1*
pma2	*dpmamt2* __ __/__ __ __ __ *dpmadate2*
pma3	*dpmamt3* __ __/__ __ __ __ *dpmadate3*
pma4	*dpmamt4* __ __/__ __ __ __ *dpmadate4*
pma5	*dpmamt5* __ __/__ __ __ __ *dpmadate5*

11b. Since the last visit, have prescribed drugs been stopped/discontinued? *pdyn* 0 ☐ No 1 ☐ Yes ***(Go to#12a)***

If yes, then please record:

Prescribed Medications **discontinued**	Date (month/year)
pmd1	*dpmdmt1* __ __/__ __ __ __ *dpmddate1*
pmd2	*dpmdmt2* __ __/__ __ __ __ *dpmddate2*
pmd3	*dpmdmt3* __ __/__ __ __ __ *dpmddate3*
pmd4	*dpmdmt4* __ __/__ __ __ __ *dpmddate4*
pmd5	*dpmdmt5* __ __/__ __ __ __ *dpmddate5*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

For Visit 6, do not complete this page.
For Visit 8, complete this page.

12. Over-the-counter medications changes:

12a. Since the last visit, have OTC drugs been added? *oayn* 0 ☐ No 1 ☐ Yes
(Go to #12b)

If yes, then please record:

OTC Medications **added**	Date (month/year)
oma1	*domamt1* __ __/__ __ __ __ *domadate1*
oma2	*domamt2* __ __/__ __ __ __ *domadate2*
oma3	*domamt3* __ __/__ __ __ __ *domadate3*
oma4	*domamt4* __ __/__ __ __ __ *domadate4*
oma5	*domamt5* __ __/__ __ __ __ *domadate5*

12b. Since the last visit, have OTC drugs been stopped/discontinued ? *odyn* 0 ☐ No 1 ☐ Yes
(Go to #13a)

If yes, then please record:

OTC Medications **discontinued**	Date (month/year)
omd1	*domdmt1* __ __/__ __ __ __ *domddate1*
omd2	*domdmt2* __ __/__ __ __ __ *domddate2*
omd3	*domdmt3* __ __/__ __ __ __ *domddate3*
omd4	*domdmt4* __ __/__ __ __ __ *domddate4*
omd5	*domdmt5* __ __/__ __ __ __ *domddate5*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Biannual Clinic Visit/Meds and Events

For Visit 6, do not complete this page.
For Visit 8, complete this page.

13. Natural Product Use Changes:

13a. Since the last visit, have Natural Products/Protein Supplements been added? *pnayn* 0 ☐ No *(Go to #13b)* 1 ☐ Yes
If yes, then please record:

Natural Products/Protein Supplements **added**	Date (month/year)
nps1	*dnmamt1* __ __/__ __ __ __ *dnmadate1*
nps2	*dnmamt2* __ __/__ __ __ __ *dnmadate2*
nps3	*dnmamt3* __ __/__ __ __ __ *dnmadate3*
nps4	*dnmamt4* __ __/__ __ __ __ *dnmadate4*
nps5	*dnmamt5* __ __/__ __ __ __ *dnmadate5*

13b. Since the last visit, have Natural Products/Protein Supplements been stopped/discontinued? *pndyn* 0 ☐ No *(Stop)* 1 ☐ Yes
If yes, then please record:

Natural Products/Protein Supplements **discontinued**	Date (month/year)
npds1	*dnmadmt1* __ __/__ __ __ __ *dnmaddate1*
npds2	*dnmadmt2* __ __/__ __ __ __ *dnmaddate2*
npds3	*dnmadmt3* __ __/__ __ __ __ *dnmaddate3*
npds4	*dnmadmt4* __ __/__ __ __ __ *dnmaddate4*
npds5	*dnmadmt5* __ __/__ __ __ __ *dnmaddate5*

Please review all contact information on the Identification Form including phone number and email address.

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ *deidnum* Date: __ __/__ __/__ __ __ __ *dedate*

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Lab Visit – Years 7 and 9

This form is to be completed at the participant's lab visit during years 7 and 9.

1. **Date of visit:** *dvdate* __/__/____

2. **Specific location where samples were obtained:** _____ *sploc*

If not PCC, specify laboratory name and address:

_____ *name*

_____ *addr*

_____

3. **Specify laboratory processing samples:** _____ *samp*

BLOOD WORK:

Date creatinine collected: *dtcrecol* __/__/____

4. **Serum creatinine concentration:** _____ mg/dL *sercret*

5. **Date duplicate blood sample was collected and stored:** *dupdtcol* __/__/____

PI Signature: _____ *pinum* **Date Signed:** __/__/____ *pidate*

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __/__/__ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ *deidnum* Date: __/__/__ *dedate*

Secondary Entered by: _____ Date __/__/__

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Scan Evaluation Form

1. MR Accession Number _____ *accn*

2. Date of Scan: *dvdate* ☐☐/☐☐/☐☐☐☐

(Check all that apply)

3. Studies Included: 1 ☐ Kidney *kid* 2 ☐ Liver *liv* 3 ☐ Renal Blood Flow *renalbf*

4. Date Received at IAC: *recdate* ☐☐/☐☐/☐☐☐☐

5. Quality Control Date: *qcondate* ☐☐/☐☐/☐☐☐☐

Evaluation Key:

1. Poor - unacceptable
2. Not adequate, coverage incomplete
3. Adequate, acceptable
4. Very good, coverage complete, good contrast
5. Excellent

KIDNEY

6. Is the quality of the images acceptable? Score _____ *kidacep*

Comment: _____ *kidcom*

_____

7. Was the protocol followed? Score _____ *kidprot*

Comment: _____ *kidprcom*

_____

8. Is a rescan necessary? *kdres* 0 ☐ No 1 ☐ Yes *If yes, specify tspec*
   1 ☐ T1
   2 ☐ T2 3mm

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Scan Evaluation Form

Evaluation Key:

1. Poor - unacceptable
2. Not adequate, coverage incomplete
3. Adequate, acceptable
4. Very good, coverage complete, good contrast
5. Excellent

LIVER

9. Is the quality of the images acceptable? Score _____ *livacep*

Comment: _____ *livcom*

_____

10. Was the protocol followed? Score _____ *livprot*

Comment: _____ *livprcom*

_____

11. Is a rescan necessary? *livres* 0 ☐ No 1 ☐ Yes

RENAL BLOOD FLOW

12. Is the quality of the images acceptable? Score _____ *rbacep*

Comment: _____ *rbcom*

_____

13. Was the protocol followed? Score _____ *rbprot*

Comment: _____ *rbprcom*

_____

14. Is a rescan necessary? *rbres* 0 ☐ No 1 ☐ Yes

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Scan Evaluation Form

DATA TRANSMISSION
15. **Were there problems with the transmission?** 0 ☐ No 0 ☐ Yes *dttrans*
Indicate any problem below: _____ *dtprob*

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Women OB-GYN History Form

1. Date of visit: *dvdate*

/ /

2. Age at Menarche: *mena* ☐☐ 3. Age at Menopause: *menage* ☐☐ ☐ N/A *menagena*

4. Pregnancy: *preg*

If visit 6, Have you ever been pregnant?
If visit 8, Have you had any pregnancies since the last visit?

0☐ No – Go to #5 1☐ Yes – Go to #4a

4a. Number of pregnancies _____ *pregnum*

Number of deliveries _____ *pregdel*

Dates of deliveries:

delmt1___/_____delyr1	*delmt2___/_____delyr2*	*delmt3___/_____delyr3*
delmt4___/_____delyr4	*delmt5___/_____delyr5*	*delmt6___/_____delry6*
delmt7___/_____delyr7	*delmt8___/_____delyr8*	*delmt9___/_____delyr9*
delmt10___/_____delyr10	*delmt11___/_____delyr11*	*delmt12___/_____delyr12*

Number of still births _____ *pregbirth*

Number of abortions _____ *pregabort*

Number of miscarriages _____ *pregmis*

Pregnancy related complication? *pregcomp*

0☐ No – Go to #5 1☐ Yes – Check all that apply

☐ 1. Pre-eclampsia *pregcomp1*	☐ 6. Intrauterine Growth Retardation (IUGR) *pregcomp6*
☐ 2. Pregnancy-associated proteinuria *pregcomp2*	☐ 7. Prematurity *pregcomp7*
☐ 3. Pregnancy-induced hypertension *pregcomp3*	☐ 8. Gestational diabetes *pregcomp8*
☐ 4. Hypertension *pregcomp4*	☐ 9. Other, Specify: *pregcomp9*
☐ 5. Pre-term labor *pregcomp5*	_____ *pregcompot*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Women OB-GYN History Form

5. Hormone Exposure: *hormonexp*

If visit 6, Have you ever used contraception?
If visit 8, Have you used contraception since the last visit?

0☐ No – Go to #5b 1☐ Yes – Complete section #5a

5a. Contraception:

	Start Date of Treatment	Duration of Treatment # Months	# Years	Medicine
☐ Oral *contoral*	*oralmt*____/_____*oraltxyr*	_____*ordumt*	_____*orduyr*	_____*oraltx*
☐ Injection *continject*	*injmt*____/_____*injecttxyr*	_____ *injdumt*	_____*injduyr*	_____*injecttx*
☐ Patch *contpatch*	*patmt*____/_____*patchtxyr*	_____ *patdumt*	_____*patduyr*	_____*patchtx*
☐ NovaRing *contring*	*ringmt*____/_____*ringtxyr*	_____ *ringdmt*	_____*ringdyr*	_____*ringtx*
☐ Other *conotcont*	Specify _____ *othsp*			

5b. Fertility Treatment: *fertiltx*

If visit 6, Have you ever had fertility treatment(s)?
If visit 8, Have you had any fertility treatment(s) since the last visit?

0☐ No – Go to #5c 1☐ Yes – Complete section #5b

Number of Treatments: _____ *fertntx*

Date of Treatment	Medicine
*fertlmt1*____/_____ *fertiltxyr1*	_____ *fertiltxmed1*
*fertlmt2*____/_____ *fertiltxyr2*	_____ *fertiltxmed2*
*fertlmt3*____/_____ *fertiltxyr3*	_____ *fertiltxmed3*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Women OB-GYN History Form

5c. Perimenopausal Hormone Therapy: *pmhtherapy*

If visit 6, Have you ever had hormone exposure?
If visit 8, Have you had hormone exposure since the last visit

0☐ NO – Go to #6 1☐ Yes – Complete section #5c

	Start Date of Treatment	Duration of Treatment # Months	# Years	Medicine
☐ Oral *pmhoral*	*pmormt*____/_____*pmhoraltxyr*	____*pmordmt*	____ *pmordyr*	_____*pmhoraltx*
☐ Injection *pmhinject*	*pminjmt*____/_____*pmhinjecttxyr*	____*pminjdmt*	____*pminjdyr*	_____*pmhinjecttx*
☐ Patch *pmhpatch*	*pmpatmt*____/_____*pmhpatchtxyr*	____*pmpatdmt*	____*pmpatdyr*	_____*pmhpatchfx*
☐ Other *pmother*	Specify _____ *pmspc*			

6. Gynecologic Surgery: *gynsurgery*

If visit 6, Have you ever had gynecologic surgery?
If visit 8, Have you had gynecologic surgery since the last visit?

0☐ No – STOP 1☐ Yes – Complete section #6

		Age at Surgery
0☐ No 1☐ Yes	Hysterectomy *hysyn*	_____ *hysynage*
0☐ No 1☐ Yes	Unilateral oophorectomy *unioopyn*	_____ *unioopynage*
0☐ No 1☐ Yes	Bilateral oophorectomy *biloopyn*	_____ *biloopynage*
0☐ No 1☐ Yes	Hysterectomy and oophorectomy *hysynoopyn*	_____ *hysynoopynage*
0☐ No 1☐ Yes	Tubal Ligation *tlyn*	_____ *tlynage*
0☐ No 1☐ Yes	Other *hypother* Specify _____ *otsurgspc*	

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ *deidnum* Date: __ __/__ __/__ __ __ __ *dedate*

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Quality of Life Questionnaire (SF-36v2 Health Survey)

This survey asks for your views about your health, how you feel and how well you are able to do your usual activities. Answer every question by checking the appropriate response. There are no right or wrong answers. If you are unsure about how to answer a question, please give the best answer you can.

Date of visit *dvdate* ☐☐/☐☐/☐☐☐☐

1. In general, would you say your health is: *health*

Excellent	Very Good	Good	Fair	Poor
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

2. Compared to one year ago, how would you rate your health in general now? *rthlth*

Much better	Somewhat better	About the same	Somewhat worse	Much worse
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous activities. *vgract*	1 ☐	2 ☐	3 ☐
b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf *mdract*	1 ☐	2 ☐	3 ☐
c. Lifting or carrying groceries *logroc*	1 ☐	2 ☐	3 ☐
d. Climbing several flights of stairs *cmstair*	1 ☐	2 ☐	3 ☐
e. Climbing one flight of stairs *csstair*	1 ☐	2 ☐	3 ☐
f. Bending, kneeling, or stooping *bdknstp*	1 ☐	2 ☐	3 ☐
g. Walking more than a mile *wlkml*	1 ☐	2 ☐	3 ☐
h. Walking several hundred yards *wlkyd*	1 ☐	2 ☐	3 ☐

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Quality of Life Questionnaire (SF-36v2 Health Survey)

	Yes, limited a lot	Yes, limited a little	No, not limited at all
i. Walking one hundred yards *wlkoyd*	1 ☐	2 ☐	3 ☐
j. Bathing or dressing yourself *bthdrs*	1 ☐	2 ☐	3 ☐

4. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health ?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the amount of time you spent on work or other activities *cuttm*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
b. Accomplished less than you would have liked *dolss*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
c. Were limited in the kind of work or other activities *lmtknd*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
d. Had difficulty performing the work or other activities (for example, it took extra effort) *diffwrk*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

5. During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down the amount of time you spent on work or other activities *ecuttm*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
b. Accomplished less than you would like *edolss*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
c. Did your work or activities less carefully than usual *elsscr*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups? *extent*

Not at all	Slightly	Moderately	Quite a bit	Extremely
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Quality of Life Questionnaire (SF-36v2 Health Survey)

7. How much bodily pain have you had during the past 4 weeks? *pnxtnt*

None	Very mild	Mild	Moderate	Severe	Very severe
1 ☐	2 ☐	3 ☐	4☐	5 ☐	6 ☐

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? *pnintf*

Not at all	Slightly	Moderately	Quite a bit	Extremely
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the Past 4 weeks....	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life? *flife*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
b. Have you been very nervous? *nervs*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
c. Have you felt so down in the dumps that nothing could cheer you up? *edown*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
d. Have you felt calm and peaceful? *ecalm*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
e. Did you have a lot of energy? *fenrgy*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
f. Have you felt downhearted and depressed? *edprss*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
g. Did you feel worn out? *wrnout*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
h. Have you been happy? *ehppy*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
i. Did you feel tired? *etred*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)? *sinterf*

All of the time	Most of the time	Some of the time	A little of the time	None of the time
1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Quality of Life Questionnaire (SF-36v2 Health Survey)

11. How TRUE or FALSE is each of the following statements for you?					
	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
a. I seem to get sick a little easier than other people *esysck*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
b. I am as healthy as anybody I know *hlthy*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
c. I expect my health to get worse *hlthwrs*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
d. My health is excellent *hlthgd*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Pain Questionnaire

Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains and toothaches). We are interested in finding out if you have pain or other symptoms related to your polycystic kidney disease. We also want to find out if the pain affects you day to day.

Please answer each question by marking the appropriate response with an "X",
Thank you for your help.

Date of visit: *dvdate* ☐☐ / ☐☐ / ☐☐☐☐

1. Since your diagnosis of PKD, have you **ever** experienced nagging or chronic pain in the following locations?

(Choose one response for each line)

Location		
Back *backpn*	0 ☐ No	1 ☐ Yes
Back radiating into buttocks, hips or legs *radipn*	0 ☐ No	1 ☐ Yes
Abdomen *abdopn*	0 ☐ No	1 ☐ Yes

2. For each location above, please indicate whether you believe the pain is related to your polycystic kidney disease. *Choose "N/A" (not applicable) for locations that you marked "NO" in question **#1**. If you answered "NO" to* **all** *locations in* **#1**, *please go to* **#3.**

Location			
Back *backpkd*	0 ☐ No	1 ☐ Yes	☐ N/A
Back, radiating into buttocks, hips, or legs *radipkd*	0 ☐ No	1 ☐ Yes	☐ N/A
Abdomen *abdopkd*	0 ☐ No	1 ☐ Yes	☐ N/A

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Pain Questionnaire

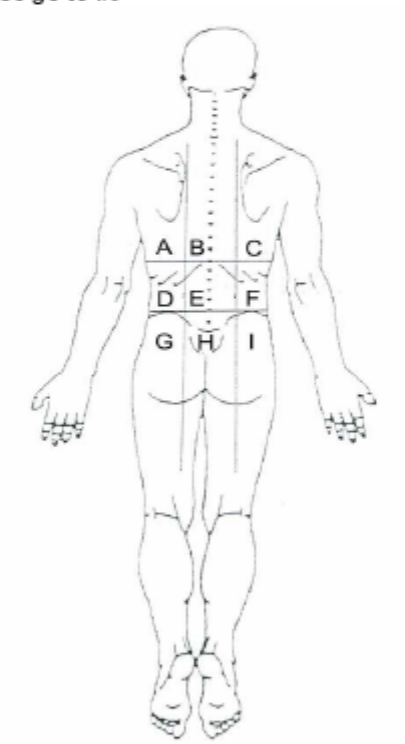
BACK PAIN

3. **Over the past 3 months,** how <u>often</u> did you experience back pain? *bkpnfrq*

(Choose one response only)

1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
Never	Rarely	Sometimes	Often	Usually	Always
(Go to #9)					

If you answered "Never" ***please go to #9***



4. Choose one or more letters from the diagram above that indicate where your back pain was located **over the past 3 months.**

☐ A	☐ B	☐ C	☐ D	☐ E	☐ F	☐ G	☐ H	☐ I	☐ Unsure
bklloca	*bkllocb*	*bkllocc*	*bkllocd*	*bklloce*	*bkllocf*	*bkllocg*	*bklloch*	*bklloci*	*bkllocu*

If you choose only one letter in ***#4, please go to #6***

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Pain Questionnaire

5. If you chose more than one letter in **#4,** is **one** location the **primary** or main location? *bkprim*

0 ☐ No 1 ☐ Yes ☐ Unsure
(Go to #6)

If "YES", indicate one letter that is the **primary** location of your pain. *bkprmloc*

☐ A ☐ B ☐ C ☐ D ☐ E ☐ F ☐ G ☐ H ☐ I

6. Check the <u>one</u> number that best describes how you would rate your back pain <u>at its worst</u> **in the past 3 months.** *(A rating of 10 would indicate pain so severe as to prohibit all activity: the worst pain you can imagine.)* *bkpnwrst*

No Pain ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Pain as bad as you can imagine

7. Check the <u>one</u> number that best describes how you would rate your back pain <u>on average</u> **in the past 3 months.** *bkpnavg*

No Pain ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Pain as bad as you can imagine

8. Was your back pain associated with visible blood in the urine (that you saw yourself) **in the past 3 months?** *bkpnbld*

0 ☐ No 1 ☐ Yes

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Pain Questionnaire

BACK PAIN RADIATING TO YOUR BUTTOCKS, HIPS OR LEGS

9. **Over the past 3 months,** how often did you experience back pain radiating to your buttocks, hips or legs? *rdpnfrq*

(Choose one response only)

1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
Never	Rarely	Sometimes	Often	Usually	Always

(Go to #12)

If you answered "Never", ***please go to #12***

10. Check the one number that best describes how you would rate your back pain radiating into your buttocks, hips or legs at its worst **in the past 3 months.** *rdpnwrst*

	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10	
No Pain												Pain as bad as you can imagine

11. Check the one number that best describes how you would rate your back pain radiating into your buttocks, hips or legs on average **in the past 3 months.** *rdpnavg*

	☐ 0	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9	☐ 10	
No Pain												Pain as bad as you can imagine

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Pain Questionnaire

ABDOMINAL PAIN

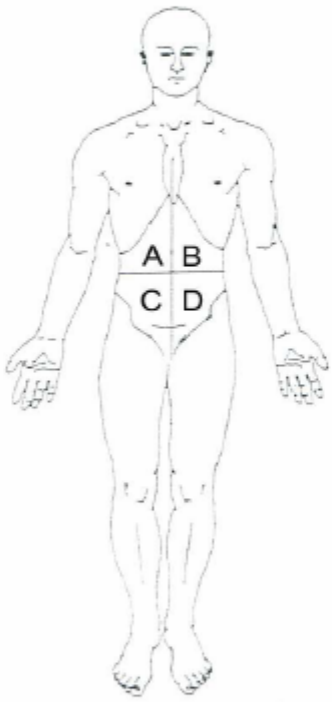
12. **Over the past 3 months,** how often did you experience abdominal pain? *abpnfrq*

(Choose one response only)

1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
Never	Rarely	Sometimes	Often	Usually	Always

(Go to #18)

If you answered "Never", ***please go to #18***



13. Choose one or more letters from the diagram above to indicate the location of your abdominal pain **over the past 3 months.**

☐	☐	☐	☐	☐
A	B	C	D	Unsure
ablocа	*ablocb*	*ablocc*	*ablocd*	*ablocu*

If you chose one letter only in ***#13, please go to #15***

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Pain Questionnaire

14. If you chose more than one letter in **#13**, indicate the **primary** location of your pain **over the past 3 months.** *abprmloc*

☐ A ☐ B ☐ C ☐ D ☐ **Unsure**

15. Check the one number that best describes how you would rate your abdominal pain at its worst **in the past 3 months.** *abpnwrst*

No Pain ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Pain as bad as you can imagine

16. Check the one number that best describes how you would rate your abdominal pain on average **in the past 3 months.** *abpnavg*

No Pain ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Pain as bad as you can imagine

17. Was your abdominal pain associated with visible blood in the urine (that you saw yourself) **in the past 3 months?** *abpnbld*

0 ☐ No 1 ☐ Yes

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Pain Questionnaire

ABDOMINAL FULLNESS

18. How often did abdominal fullness interfere with your ability to perform your usual physical activities **over the past 3 months?** *abflfrq*

(Choose one response only)

1 ☐ Never 2 ☐ Rarely 3 ☐ Sometimes 4 ☐ Often 5 ☐ Usually 6 ☐ Always

19. How often did you eat less than your usual meal size because of abdominal fullness **in the past 3 months?** *eatles*

(Choose one response only)

1 ☐ Never 2 ☐ Rarely 3 ☐ Sometimes 4 ☐ Often 5 ☐ Usually 6 ☐ Always

20. How often was your appetite poor because of nausea **in the past 3 months?** *nausea*

(Choose one response only)

1 ☐ Never 2 ☐ Rarely 3 ☐ Sometimes 4 ☐ Often 5 ☐ Usually 6 ☐ Always

21. Has your abdomen gotten bigger since this time last year? For example, have your required an increase in clothing size? *gotbig*

0 ☐ No 1 ☐ Yes

22. If you experience abdominal fullness, do you think that is caused by your polycystic kidney disease? *abflpkd*

0 ☐ No 1 ☐ Yes ☐ Unsure

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Pain Questionnaire

PAIN TREATMENT

23. What medications or treatments are you receiving for your pain?

(Choose all that apply)

1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐
No treatment *pnmeda* ***(Go to #26)***	Over the counter medications *pnmedb*	Prescription pain medications *pnmedc*	Massage therapy *pnmedd*	Acupuncture *pnmede*	Heat or cold applied locally *pnmedf*	Surgery *pnmedg*

☐ Other *pnmedh* Other specify:_____ *pnmedhdes*

If you answered "No Treatment", ***please go to #26***

24. Check the one number that best describes how much relief is provided by the pain medications or treatments that you use. *pnrelif*

No Relief ☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 Complete Relief

25. In general, how satisfied are you with:

(Choose one response for each line)

	Completely dissatisfied	Very dissatisfied	Somewhat dissatisfied	Somewhat satisfied	Very satisfied	Completely satisfied
a. Your current treatment of your pain? *curtrtpn*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
b. Your physical ability to do what you want to? *dowhtwnt*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐

26. **During the past 3 months** how much did pain (all locations) interfere with the following things:

(Choose one response for each line)

	Not at all	A little bit	Moderately	Quite a bit	Extremely
Mood *pnintrfr1*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
Relations with other people *pnintrfr2*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
Walking ability *pnintrfr3*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
Sleep *pnintrfr4*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Pain Questionnaire

		Not at all	A little bit	Moderately	Quite a bit	Extremely
	Work (part or full time job, homemaker, student, etc.) *pnintrfr5*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
	Strenuous physical activity (jogging, heavy lifting, etc.) *pnintrfr6*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
	Social activities or hobbies *pnintrfr7*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
	Enjoyment of life *pnintrfr8*	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐
27.	Do you have any other comments about pain or its effect on your daily life that this questionnaire did not address? *pncmmnt*					

_____

_____

_____

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

Family Instructions

Included in this packet are 15 copies of the '**Family History – Individual Family Member Questionnaire'**. This form is needed to collect information on your family history as it relates to kidney and liver disease. Please complete one sheet for *each* biological relative you have (biological relative: relative **not adopted** and **not related by marriage**). The names and contact information of your family members is requested but we will not contact your relative without permission from you to approach them. If you have more than 15 biological relatives for whom you would like to provide information, this process can be completed in the clinic when you come in for your (CRISP II) initial visit. Thank you for your cooperation.

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

Family Member ID _____*fammbr*

visit:

Family History –Individual Family Member Questionnaire

Family Member Name: _____

Last name, First name, MI

Relationship:

Please specify this family member's relationship to you: ***(Check only one box)*** *relat*

Parent
- ☐ Mother
- ☐ Father

Grandparent
- ☐ Grandmother mother's side
- ☐ Grandmother father's side
- ☐ Grandfather mother's side
- ☐ Grandfather father's side

Brother or Sister
- ☐ Full sibling
- ☐ Half sibling mother's side
- ☐ Half sibling father's side

Aunt or Uncle
- ☐ Aunt mother's side
- ☐ Aunt father's side
- ☐ Uncle mother's side
- ☐ Uncle father's side

Son or Daughter
- ☐ Son
- ☐ Daughter

Other
- ☐ Grand-Uncle mother's side
- ☐ Grand-Uncle father's side
- ☐ Grand-Aunt mother's side
- ☐ Grand-Aunt father's side
- ☐ Cousin mother's side
- ☐ Cousin father's side
- ☐ Nephew mother's side
- ☐ Nephew father's side
- ☐ Niece mother's side
- ☐ Niece father's side

Address:

_____
Street 1

_____
Street 2

_____
City, State, Zip

Date of birth: _____/_____/_____ *dob* Gender: *gender* ☐ Male ☐ Female

Is this relative living? *live* 0 ☐ No 1 ☐ Yes 2 ☐ Don't Know

If deceased:
Age at death: _____ *aged*

Cause of death? *cause* _____

_____

If deceased:
Did he/she have kidney or liver disease? *dis*

0 ☐ No 1 ☐ Yes 2 ☐ Don't Know

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II, Family History Questionnaire Individual Relative Information, Form 44
Version 4, 08/02/2007 Page 1 of 1

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Visit Checklist

Once the forms below have been completed and entered for the participant's visit during Year 6 and Year 8, the PI should review check off each form that has been completed and entered and sign below.

#	Form Description	Completed	Entered	Comments
44	Family History (visit 6 only)	☐ *fahcp*	☐ *fahent*	*fahcom*
2	Registration (visit 6 only)	☐ *reacp*	☐ *regent*	*regcom*
28	Biannual Meds & Events	☐ *bimcp*	☐ *biment*	*bimcom*
27	Biannual Labs	☐ *bialabcp*	☐ *bialabent*	*bialabcom*
41	Quality of Life (SF-36v2)	☐ *qufcp*	☐ *qufent*	*qufcom*
42	Pain	☐ *paincp*	☐ *painent*	*paincom*
12	Symptoms	☐ *sympco*	☐ *sympent*	*sympcom*
11	Physical Findings	☐ *phyfcp*	☐ *phyent*	*phycom*
40	Women's OB-GYN	☐ *obcp*	☐ *obent*	*obcom*
9	GFR Collection	☐ *gfrcp*	☐ *gfrcent*	*gfrcom*
10	GFR Reporting	☐ *gfrepcp*	☐ *gfrepent*	*gfrepcom*
55	MRI Status Verification (Visit 8 only)	☐ *mvrcp*	☐ *mrvent*	*mrvcom*
7	MR Session/Renal Blood Flow	☐ *mrcp*	☐ *mrent*	*mrcom*
53	Archived Blood Sample	☐ *arbscp*	☐ *arbsent*	*arbscom*
47	Archived Urine Sample	☐ *arcurcp*	☐ *arcurent*	*arcurcom*
48	Shipping Manifest: Repository – Serum Plasma Samples	☐ *shsercp*	☐ *shserent*	*shsercom*
49	Shipping Manifest: Repository – Urine Samples	☐ *shurcp*	☐ *shurent*	*shurcom*
50	Shipping Manifest: Repository – Cleveland Clinic	☐ *shclcp*	☐ *shclent*	*shclcom*
56	Shipping Manifest: Repository – Rutgers	☐ *shrucp*	☐ *shruent*	*shrucom*

Investigator Signature *(sign within 30 days of this visit):* By signing this form, investigator attests that he/she has reviewed all forms for this visit, as well as any additional forms entered since the previous visit, and that the data is complete and accurate.

☐ **PI Signature:** _____ *pinum* **Date Signed:** __ __/__ __/__ __ __ __ *pidate*

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II, Visit Checklist, Form 46
Version 5, 09/20/2007

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Archived Urine Sample Collection Form

This form is to be completed at visit 6 and 8.

ARCHIVED URINE SAMPLES FOR THE NIDDK BIOSAMPLE REPOSITORY

Collection: A freshly voided urine sample will be collected. The urine specimens will be centrifuged in 50 mL tubes at 500 g for 5 minutes as soon as possible, with volume, processing times and voiding times noted (processing times should be no longer than 20-30 minutes from the time of acquisition). Tubes will be kept in ice throughout the process. The bottom 250 µL pellet (sometimes barely- or non-visible) will be transferred with a 1.0 mL pipette to a 1.5 mL eppendorf tube previously prepared with 750 µL of TriReagent and inverted several times and put on ice prior to freezing at -80° C.

Voiding Time: _____ *voidtime* Volume: _____ *volume* Processing Time: _____ *proctime*

The remaining urine samples will then be transferred to 10 mL polypropylene (not polystyrene) Falcon culture tubes, stored in six 5 mL aliquots.

Storage Instructions: Samples are to be stored at the site (-80C) for up to four months after collection.

Shipping Instructions: Samples are to be batch-shipped quarterly on at least five pounds of dry ice. Send the freshly voided urine samples to the NIDDK Biosample Repository at Fisher Bioservices. Use pre-printed Fed Ex airbills. Do not ship on Friday.

1. **LABELS**:

Type of Sample	Bar Code Label
A. Freshly Voided Urine Biosample	Place Label Here
B. Freshly Voided Urine Pellet	Place Label Here

2. **Comments:** _____ *comm*

Shipping Instructions: Complete Shipping Manifest and pre-printed Fed Ex airbill addressed to Fisher BioServices Coorporation (NIDDK Biosample Repository). Ship samples on dry ice per guidelines provided by Fisher.

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ *deidnum* Date: __ __/__ __/__ __ __ __ *dedate*

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Shipping Manifest: Serum/Plasma Samples

This form is to be completed for the serum and plasma samples to be collected from the study participant and shipped to NIDDK Repository at Fisher Bioservices.

To complete the form:

1. Verify the number of tubes per sample and enter in the appropriate field below.
2. Number the pages in sequence (lower right hand corner).
3. When shipping, check the field in the appropriate column below. If, or any reason, a sample will *never* be shipped to the repository (if it was lost, destroyed, or never collected), the reason must be provided in the appropriate field below.
4. Copies of completed forms are to be retained at the collection site.

Date of Collection: ____/____/_____ *dtcoll*

I. Sample Information

	Sample Type	Tube Size	Number of Tubes	Check When Shipped	Reason Sample Will Never Be Sent
1	**SST** Tiger-top for serum			*ttsh* ☐	
2	**SST** Green/gray for plasma			*gssh* ☐	

II. Shipping Information

Number the pages in sequence and staple the packet to create manifest for shipment. The shipping information below is only required on the *first* page of the manifest per shipment. Copies of all completed pages are to be copied and retained at the site. The originals are to be included in the shipment. Refer to the Manual of Procedures for shipping instructions.

Samples are to be shipped via next-day service to:

Heather Higgins
Fisher Bioservices
20301 Century Blvd.
Bldg. 6, Suite 400
Germantown, MD 20874
Phone: (240) 686-4703

FedEx Air Bill Number: _____ *fedexnum* **Date of Shipment:** ____/____/____ *shipdt*

Name of Shipper/Form Completer: _____ **E-mail Address:** _____

Phone: (_____)_____ **Fax:** (_____)_____

Temperature: _____ *temp* ☐ Celsius ☐ Fahrenheit *celfah* **Number of Boxes:** _____ *numbox* **Page** _____ **of** ____

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ *deidnum* Date: __ __/__ __/__ __ __ __ *dedate*

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Archived Urine Sample Collection Form

This form is to be completed at visit 6 and 8.

ARCHIVED URINE SAMPLES FOR THE NIDDK BIOSAMPLE REPOSITORY

Collection: A freshly voided urine sample will be collected. The urine specimens will be centrifuged in 50 mL tubes at 500 g for 5 minutes as soon as possible, with volume, processing times and voiding times noted (processing times should be no longer than 20-30 minutes from the time of acquisition). Tubes will be kept in ice throughout the process. The bottom 250 µL pellet (sometimes barely- or non-visible) will be transferred with a 1.0 mL pipette to a 1.5 mL eppendorf tube previously prepared with 750 µL of TriReagent and inverted several times and put on ice prior to freezing at -80° C.

Voiding Time: _____ *voidtime* Volume: _____ *volume* Processing Time: _____ *proctime*

The remaining urine samples will then be transferred to 10 mL polypropylene (not polystyrene) Falcon culture tubes, stored in six 5 mL aliquots.

Storage Instructions: Samples are to be stored at the site (-80C) for up to four months after collection.

Shipping Instructions: Samples are to be batch-shipped quarterly on at least five pounds of dry ice. Send the freshly voided urine samples to the NIDDK Biosample Repository at Fisher Bioservices. Use pre-printed Fed Ex airbills. Do not ship on Friday.

1. **LABELS**:

Type of Sample	Bar Code Label
A. Freshly Voided Urine Biosample	Place Label Here
B. Freshly Voided Urine Pellet	Place Label Here

2. **Comments:** _____ *comm*

Shipping Instructions: Complete Shipping Manifest and pre-printed Fed Ex airbill addressed to Fisher BioServices Coorporation (NIDDK Biosample Repository). Ship samples on dry ice per guidelines provided by Fisher.

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ *deidnum* Date: __ __/__ __/__ __ __ __ *dedate*

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II, Archived Urine Sample Collection, Form 47
Version 2, 6/25/2007

CRISP II

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Shipping Manifest: Cleveland Clinic

This form is to be completed for the serum creatinine samples to be collected from the study participant and shipped to the reference laboratory at Cleveland Clinic. Samples are to be stored at the collection site (-20 degrees Celsius or colder) and shipped to Cleveland Clinic on a quarterly basis. This form must be completed at the time of collection and kept in sequential order to reflect samples being stored at the site.

Specimen: CRETS
Account#: 7395

To complete this form:

1. Verify the number of tubes per sample and enter it in the appropriate field below.
2. Number the pages in sequence (lower right hand corner) and store then in the PCC freezer until time of shipment.
3. When shipping, check the field in the appropriate column below. If, or any reason, a sample will *never* be shipped to the lab (if the sample was lost, destroyed, or not collected), the reason must be provided in the appropriate field below.
4. Copies of completed forms are to be retained at the collection site. The originals are to be sent with the shipment.

Date of Collection: ____/____/_____ *dtcoll*

I. Sample Information

	Sample Type	Number of Tubes	Check when Shipped	Provide Reason if Sample Will Never be Shipped
1	Serum for Creatinine			

II. Shipping Information

Number the pages in sequence and staple the packet to create a single manifest per shipment. The shipping information below is only required on the *first* page of the manifest per shipment. Retain copies of all completed pages at the site. The originals are to be included in the shipment. Refer to the Manual of Procedures for shipping instructions.

Samples are to be shipped to:

Cleveland Clinic Reference Library
9500 Euclid Avenue, L15
Cleveland, OH 44195
(216) 444-8108

FedEx Air Bill Number: _____ *clfedexnm* **Date of Shipment** ____/____/_____ *clshipdt*

Name of Shipper/Form Completer: _____ **E-mail Address:** _____

Phone: (_____)_____ **Fax:** (_____)_____

Temperature: _____ ☐ Celsius ☐ Fahrenheit **Number of boxes** _____ **Page** ____**of** ___

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Archived Blood Sample Collection Form

This form is to be completed at visit 6 and 8. Samples must be shipped on the day of collection to the NIDDK Biosample Repository at Fisher BioServices.

LABELS:
The specimen labels will be provided by the repository.
Affix the "SST" and "PST" labels to this form.
Affix corresponding labels on both tubes per sample.

1. **Serum Sample: Collect 2 SST tubes of blood (tiger-top, 10 ml each). Gently invert 5 times, but do not shake. Allow to clot in a vertical position for 30 minutes. Centrifuge at 1300 RCF (g) for 15 minutes (within 1-2 hours of collection). Refrigerate samples. No decanting is necessary. Ship sample on the day of collection per instructions below.**

2. **Plasma Sample: Collect 2 PST tubes (green/grey cap, 8 ml each). Gently invert 8-10 times, but do not shake. No clotting time is necessary. Centrifuge at 1300 RCF (g) for 10 minutes (within 1-2 hours of collection). Refrigerate samples. No decanting is necessary. Ship sample on the day of collection per instructions below.**

Type of Sample	Collection Time 24hr	Bar Code Label
A. Serum Sample Label: "SST"	: *sertime*	Place Label Here
B. Plasma Sample Label: "Bio-plasma"	: *plastime*	Place Label Here

3. **Comments:** _____ *comm*

Shipping Instructions: Complete Shipping Manifest and pre-printed Fed Ex airbill addressed to Fisher BioServices Corporation (NIDDK Biosample Repository). Ship samples on cold packs, per IATA 650 guidelines, but do not allow samples to freeze.

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

MRI Status Verification

This form is to be completed for all participants at visit 8, prior to administration of the MRI.

Date of visit: *dvdate* ☐☐ / ☐☐ / ☐☐☐☐

1. Eligible but Modified Criteria – Part I

*Review **all** possible conditions listed in section 1 with the participant. Check any that apply. If **any** of the MR contraindications in Part 1 are checked, go to section 3 and check **Eligible but Modified** for Participant Status. **Do not** complete section 2.*

If none are checked, go to section 2.

- ☐ Weight > 158.6 kg (350 lbs) *weight*
- ☐ Pregnant *preg*
- ☐ Cardiac Pacemaker *cardpac*
- ☐ Implanted cardioverter defibrillator (ICD) *cardef*
- ☐ Neurostimulation system *neuron*
- ☐ Claustrophobia *claust*
- ☐ Spinal cord stimulator *spinal*

2. Eligible but Modified Criteria – Part II

*Review **all** possible conditions listed in section 2 (continued on the next 2 pages) with the participant. Check any that apply. If **any** are checked, please discuss the condition(s) with the radiologist to determine if an MRI may be administered.*

*If none are checked, go to section 3 and check **Eligible and Enrolled.***

- ☐ Bone growth/bone fusion stimulator *bonfus*
- ☐ Cochlear, otologic, or other ear implant *earimp*
- ☐ Insulin or other infusion pump *insul*
- ☐ Implanted drug infusion device *druginf*
- ☐ Eyelid spring or wire *eyel*
- ☐ Tissue expander (e.g. breast) *tissex*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

MRI Status Verification

☐ Hx of working with metal *hxwkmet*
☐ Hx of metal in eyes *hxmeteye*
☐ Aneurysm Clip(s) *aneu*
☐ Hearing aid *hearaid*
☐ Embolization coils *emcoil*
☐ Internal electrodes or wires *wires*
☐ Any type of prosthesis (eye, penile, etc.) *prost*
☐ Heart valve prosthesis *heart*
☐ Metallic stent, filter, or coil *metst*
☐ Artificial or or prosthetic limb *proslim*
☐ Shunt (spinal or intraventricular) *shunt*
☐ Vascular access port and/or catheter *vascath*
☐ Radiation seeds or implants *radseim*
☐ Swan-Ganz or thermodilution catheter *swan*
☐ Medication patch (Nicotine, Nitroglycerine) *patch*
☐ Any metallic fragment or foreign body *metfrag*
☐ Wire mesh implant *wimeim*
☐ Surgical staples, clips or metallic sutures *surstcl*
☐ Joint replacement (hip, knee, etc.) *jorep*
☐ Bone/joint pin, screw, nail, wire, plate, etc. *bojpin*
☐ IUD, diaphragm or pessary *iud*
☐ Dentures or partial plates *denppl*
☐ Tattoo or permanent makeup *tattoo*
☐ Body piercing jewelry *bopierc*
☐ Other implant *otimp*
Please specify: _____ *impsp*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

MRI Status Verification

☐ Breathing problem *breatpr*
☐ Other *other*
Please specify:_____ *othersp*

3.	**Status:** *finenro* *(Check only one)*
3 ☐	Eligible but Modified – **Continue, no MRI**
4 ☐	Eligible and Enrolled – **Continue**

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

NIDDK – CRISP Genetics Initiative Phlebotomy Form

SHIP AT ROOM TEMPERATURE IN SAFETY MAILER
ENCLOSE A COPY OF THIS FORM WITH BLOOD KIT

FOR RU LAB USE ONLY:

TO: DR. DOUGLAS FUGMAN/GENETICS
RUTGERS UNIV./CELL REPOSITORY
DIV. LIFE SCIENCES – NELSON LABS
604 ALLISON ROAD (RM. C120A)
PISCATAWAY, NJ 08854-8082

FAX: (732) 445-1149
PHONE: (732) 445-1498

WEB FORM: http://rucdr.rutgers.edu/shippingblood

INITIAL: _____

YELLOW ML: _____

ID#: _____

FROM (NIDDK-CRISP SITE):

SHIPMENT TO INCLUDE BLOOD SAMPLES FOR CELL LINES

YELLOW TOP TUBES: ____

NIDDK-CRISP STAFF: PLACE TUBE LABEL HERE OR COMPLETE BY HAND
(VERIFY INFO AGAINST INFO ON BLOOD TUBES!!!)

SEX: M___ F___ AGE: _____

ALTERNATE ID#: _____

CRISP-NIDDK-ID#: _____

TO BE COMPLETED AT COLLECTION SITE:

DATE BLOOD DRAWN: _____ - ____ - ____ (MONTH – DAY – YEAR) *bldrdt*

TIME DRAWN: _____ (24 HOURS) *timedr*

DRAWN BY: _____

CONTACT THE RUTGERS CELL & DNA REPOSITORY TO CONVEY PACKAGE TRACKING NO./DATE OF SHIPMENT (SEE BELOW). IF BLOOD IS SHIPPED ON A FRIDAY FOR SATURDAY DELIVERY, NOTIFY RUTGERS AND CHECK FEDEX FORM FOR SATURDAY DELIVERY.

EMAILED/FAXED/ CALL IN BY: _____ (SEE RUTGERS FAX/PHONE #S ABOVE)

____/____/____ DATE *emfxdt*

_____AM/PM TIME

PACKAGE TRACKING #: _____ *packtrk* (CHECK SATURDAY DELIVERY ON DELIVERY FORM IF APPLICABLE)

TO BE COMPLETED BY RUTGERS UNIVERSITY CELL & DNA REPOSITORY

PRIOR NOTIFICATION REC'D: YES ____ NO ____ - IF YES, DATE/TIME ____/____/____ _____AM/PM

CONFIRMATION OF RECEIPT OF BLOOD SAMPLE TO NIDDK SITE SENT BY: _____ DATE/TIME ____/____/____

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ *deidnum* Date: __ __/__ __/__ __ __ __ *dedate*

Secondary Entered by: _____ Date __ __/__ __/__ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

Death Notification Form

This form is to be completed for any participant who dies after enrollment in the study. As soon as CRISP clinic personnel are aware of the participant's death, this form must be completed. When available, send copy of autopsy report to the DCIAC. Any patient identifying information should be obliterated from the copies sent to the DCIAC and replaced with CRISP ID number.

1. **Date of last contact:** *lacodate* | | | / | | | / | | | | |

2. **Date of death:** *dtdeath* | | | / | | | / | | | | |

3. **Cause of death:** *(Check all that apply)*
   1 ☐ Cardiovascular Disease *caucards* 2 ☐ Septicemia *causep* 3 ☐ Cancer *caucanc* 4 ☐ Trauma *cautrau* 5 ☐ Suicide *causui*
   6 ☐ Renal Disease *caurends* 7 ☐ Respiratory Disease *cauresds* 8 ☐ Cerebrovascular Accident *caucerac* ☐ Unknown *cauunk*
   9 ☐ Other Specify: _____ *cauoth* *causspe*

4. **Has the autopsy been performed?** *auto* 0 ☐ No 1 ☐ Yes ☐ Unknown

5. **Location of Death:** *locodet* 1 ☐ During hospitalization 2 ☐ At home 3 ☐ At work 4 ☐ En route To Hospital ☐ Unknown
   5 ☐ Other Specify_____ *sploc*

6. **How was information regarding participant's death confirmed?** *infconf* 1 ☐ Family Member 2 ☐ Medical Record
   3 ☐ Other Specify: _____ *infsp*

7. **Comments:** *detcom*_____
   _____

PI Signature: _____ *pinum* **Date Signed:** __ __/__ __/__ __ __ __ *pidate*

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ *deidnum* Date: __ __/__ __/__ __ __ __ *dedate*

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

:

Transfer Form

This form is to be completed by the Study Coordinator whenever a participant transfers between clinics. The destination clinic should complete this form. Please contact the clinic of origin to coordinate date of transfer and other participant information. BEFORE completing this form, and before the destination clinic prepares any visit forms for the patient, you must contact the DCIAC via email (crispii@pitt.edu) to obtain confirmation of the new transfer ID. You cannot generate pre-printed forms from the website with the new ID until the DCIAC confirms that the new ID is in the system.

1.	**Original Participant ID:** *orpkdid* __ __ __ __ __ __				
2.	**Original Clinic:** *orclinic*	1 ☐ Emory	2 ☐ KUMC	3 ☐ Mayo	4 ☐ UAB
3.	**Destination Clinic:** *destcli*	1 ☐ Emory	2 ☐ KUMC	3 ☐ Mayo	4 ☐ UAB
4.	**Date of Transfer:** *transdte*	__ __ / __ __ / __ __ __ __			
5.	**Modified Participant ID:** *(provided by data entry system)* *modpkdid* __ __ __ __ __ __				
PI Signature: _____ *pinum* **Date Signed** __ __/__ __/__ __ __ __ *pidate*					

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Study Withdrawal/Lost to Follow-up Form

This form is to be completed if the participant is lost to follow-up, becomes ineligible, or withdraws from the study.

1.	Date of last contact with participant or family member: *contdate*	☐☐/☐☐/☐☐☐☐	
2.	Is this participant lost to follow-up? *ltfyn* *If yes, STOP*	0 ☐ No	1 ☐ Yes **STOP**
3.	Has the participant withdrawn? *parwd*	0 ☐ No **(Go to 14)**	1 ☐ Yes
4.	Date of withdrawal: *wddte*	☐☐/☐☐/☐☐☐☐	
5.	Are the reasons for the participant's withdrawal known? *rwkyn* *If yes, then please complete items 6-13*	0 ☐ No **STOP**	1 ☐ Yes
6.	The participant has moved to a location which is not near a CRISP Clinical Center. *moveyn*	0 ☐ No	1 ☐ Yes
7.	The participant's physician has asked him or her to withdraw from the study. *doctoryn*	0 ☐ No	1 ☐ Yes
8.	The participant is unwilling to miss school/work. *schwork*	0 ☐ No	1 ☐ Yes
9.	The participant is unwilling to travel to clinic for visits. *travcl*	0 ☐ No	1 ☐ Yes
10.	The participant is unwilling to make a follow-up commitment. *fucom*	0 ☐ No	1 ☐ Yes
11.	The participant has a new job or a new work situation which makes participation burdensome. *newjobyn*	0 ☐ No	1 ☐ Yes
12.	The participant has an illness or hospitalization of self or family. *illyn*	0 ☐ No	1 ☐ Yes
13.	There is another circumstance that in the discretion of the principal investigator is a valid reason for withdrawal. *otenr* *If yes, please specify briefly: otensp* _____	0 ☐ No	1 ☐ Yes

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Study Withdrawal/Lost to Follow-up Form

14.	**Is the participant ineligible?** *inelig*	0 ☐ No	1 ☐ Yes
	If yes, please complete items 15-18		
15.	**The participant has a current psychiatric or addiction non-compliance disorder that in the discretion of the principal investigator indicates that they will not successfully complete the study.** *curpsyc*	0 ☐ No	1 ☐ Yes
	If yes and the participant volunteers the information, please specify:		
	_____ *curpsycspc*		
16.	**The participant has a current medical problem that in the discretion of the principal investigator would make unsafe their participation in the study.** *cur*	0 ☐ No	1 ☐ Yes
	If yes and the participant volunteers the information, please specify:		
	_____ *curspc*		
17.	**The participant has another condition that in the discretion of the principal investigator makes the participant ineligible.** *otcrit*	0 ☐ No	1 ☐ Yes
	If yes, please specify: _____ *otcritsp*		
18.	**Date found ineligible:** *ineldt*	__/__/____	
	PI Signature: _____ *pinum* **Date Signed:** __ __/__ __/__ __ __ __ *pidate*		

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ *deidnum* Date: __ __/__ __/__ __ __ __ *dedate*

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Missed Visit Form

This form is to be completed if, despite the best efforts of CRISP personnel, a follow-up clinic visit or telephone interview cannot be completed within the time window specified by the appointment schedule.

1.	**Date of scheduled follow-up visit or telephone interview:** *dsvdate*	☐☐/☐☐/☐☐☐☐
2.	**Was the participant or family member contacted for this visit?** *parcont*	0 ☐ No 1 ☐ . *If no, enter reason and* **STOP** _____ *reas*
	If yes, enter **Date of last contact** *and go to #3* *dlcdate*	☐☐/☐☐/☐☐☐☐
3.	**Are the reasons for the participant's missed follow-up visit known?** *rkyn*	0 ☐ No **STOP** 1 ☐ Yes
	If yes, then please complete items 5-11	
4.	**There were scheduling difficulties, personal or job related:** *sdpyn*	0 ☐ No 1 ☐ Yes
6.	**There were scheduling difficulties within the clinic:** *sdcyn*	0 ☐ No 1 ☐ Yes
6.	**The participant refused:** *pryn*	0 ☐ No 1 ☐ Yes
7.	**The participant had transportation problems:** *typn*	0 ☐ No 1 ☐ Yes
8.	**The participant was ill or incapacitated:** *iiyn*	0 ☐ No 1 ☐ Yes
9.	**Other** *other*	0 ☐ No 1 ☐ Yes
	Please specify briefly: *otheryn*_____	
10.	**Is it likely the participant will return for the next scheduled annual clinic visit?** *rvyn*	0 ☐ No 1 ☐ Yes
	If no, **please explain:** *norturn* _____	

PI Signature: _____ *pinum* **Date Signed:** __ __/__ __/__ __ __ __ *pidate*

CRISP Member completing this form_____ *cdidnum*

Date Form Completed __ __/__ __/__ __ __ __ *cddate*

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate* *deidnum*

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Identification Form

This form is to be completed at the participant's first clinic visit and kept in confidence at the PCC. Information on this form will NOT be sent to the DCIAC. This form is to be updated with each visit or telephone contact.

1. **Participant ID:** __ __ __ __ __ __

2. **Participant's Name:** _____, _____ __ __ __
   Last First Middle

3. **Address:** _____ _____ _____
   Street P. O Box Apartment

   _____ _____ __ __ __ __ __
   City State/Province Zip

4. **Social Security Number:** __ __ __ - __ __ - __ __ __ __

5. **Telephone:** Home: (__ __ __)__ __ __-__ __ __ __ Work: (__ __ __)__ __ __-__ __ __ __

   Fax: (__ __ __)__ __ __-__ __ __ __ Cell: (__ __ __)__ __ __-__ __ __ __

6. **Email:** _____

7a. **Primary Care or Referring Physician information**

   Name: _____

   Phone: (__ __ __)__ __ __-__ __ __ __ Fax: (__ __ __)__ __ __-__ __ __ __

   Address: _____ _____ _____
   Street P.O. Box Suite

   _____ _____ __ __ __ __ __
   City State/Province Zip

7b. **Nephrologist or Other Physician caring for participant:**

   Name: _____

   Phone: (__ __ __)__ __ __-__ __ __ __ Fax: (__ __ __)__ __ __-__ __ __ __

   Address: _____ _____ _____
   Street P.O. Box Suite

   _____ _____ __ __ __ __ __
   City State/Province Zip

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Identification Form

8. **Contact Persons** *(NOTE: For participants under 18 years of age, you must list a parent or guardian):*

A) Name: _____ , _____
Last Name First Name

Phone: (__ __ __)__ __ __ - __ __ __ __ Relationship to Participant: _____

Address:_____ _____ _____
Street P.O. Box Apartment

_____ _____ __ __ __ __ __
City State/Province Zip

B) Name: _____ , _____
Last Name First Name

Phone: (__ __ __)__ __ __ - __ __ __ __ Relationship to Participant: _____

Address:_____ _____ _____
Street P.O. Box Apartment

_____ _____ __ __ __ __ __
City State/Province Zip

9. **Contact Notes for Participant:** _____

_____

_____

_____

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

CRISP II

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

CRISP II Data Change Form

Visit *visit*	Date Found *dcdtfound*	Form Number *formid*	Variable Name *dcvarname*	Prior Value *dcprival*	New Value *dcnewval*	Comments (Please include Question Number) *dccomm*

CRISP Member completing this form_____
cdidnum
Date Form Completed __ __/__ __/__ __ __ __

Data Entry Status: Please check to indicate that the above information has been entered ☐

Data Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

CRISP -FORM #

CRISP Information and Web Access Form

Please complete the following information for anyone involved with the CRISP Study. Note that the bottom portion of the page "Application and Authorization for CRISP Web Access" needs to be completed if the staff member will need Internet access to the CRISP information.

Fax the completed form to: Johana Schafer, Project Research Coordinator, at 412-641-2582.

Full Name of Person Requesting Access (please print): _____

Clinic: _____

Title or Role in CRISP: _____

Primary Phone Number: _____

Fax Number: _____

E-mail Address: _____

Application and Authorization for CRISP Web Access

Description of Web Access:
The Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) has made some administrative information accessible to authorized users through the Internet. Study codes are used to protect patient anonymity. All CRISP study data are privileged and confidential.

Internet access to CRISP information is restricted to certified CRISP study personnel who have specifically been granted authorization for CRISP study Internet access by the Data Coordinating Image Analysis Center (DCIAC). Web access to the study information is restricted by a unique user ID and password for each staff member. Each clinic will be able to access only its clinic's data.

Terms of Agreement for Web Access:
I agree not to release any information from the CRISP web access system to anyone outside of the CRISP study or to any CRISP study certified personnel from other clinics. I agree to safeguard my user ID and password and not make them available to any other person. I understand that upon leaving the study or for other reasonable causes, my user ID and password will be deactivated.

Applicant Signature: _____ Date: _____

PI Signature: _____ Date: _____

For DCIAC Use Only:

User ID: _____ Temporary Password: _____

Date Assigned: _____ Date Removed: _____

Comments:

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit:

Missing Data Report

1.	**Date of Visit:** *dvdate*			/		/				
2.	**Form Id:** *formid*_____
3.	**Enter variable name:** *form_var* _____
4.	**Re-Enter variable name:** *form_var* _____
5.	**Reason missing:** *reason* _____

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

CRISP II, Missing Date Report, Form 54
Version 1, 07/25/2007

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit: Family Member ID _____ *fammbr*

Lifestyle Form – Family Member

1. Date of visit *dvdate* ☐☐/☐☐/☐☐☐☐

2. Smoking and Tobacco:

2a. Has the participant ever smoked cigarettes? *csyn* 0 ☐ No (*Go to# 2e)* 1 ☐ Yes

2b. *If yes,* *csevsm*
1 ☐ Current *(Go to #2d)*
2 ☐ Former *(Go to #2c)*

2c. If former smoker, quit date: __ __/__ __ __ __ *(Go to #2e)*
qsm Month Year *qsy*

2d. If current smoker, how many packs per year does the participant smoke? *ppy*
__ __ __ __

2e. Has the participant used any other types of tobacco? *otytob* 0 ☐ No (*Go to #3a)* 1 ☐ Yes

2f. *If yes*, **which types?**

2g. Cigars 0 ☐ No 1 ☐ Yes *cigar*

2h. *If yes*, **how many cigars ?** __ __ *cignm*

2i. Pipe 0 ☐ No 1 ☐ Yes *pipeyn*

2j. Chewing Tobacco/Snuff 0 ☐ No 1 ☐ Yes *chewyn*

3. Caffeinated Beverages:

3a. Does the participant drink caffeinated coffee or tea? *cucaff* 0 ☐ No (Go to #3b) 1 ☐ Yes

If yes, check time interval and enter the average number of caffeinated 8 ounce cups per interval: *cupcaf*

1 ☐ Per day
2 ☐ Per week **Number of 8 ounce cups per interval**__ __ *ccafunit*
3 ☐ Per month

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit: Family Member ID _____*fammbr*

Lifestyle Form – Family Member

3b. Does the participant drink other caffeinated beverages? *cafotbv* 0 ☐ No 1 ☐ Yes
(Go to #3c)

If yes, check time interval and enter the average number of caffeinated 12 ounce portions per interval: *glassc*

1 ☐ Per day
2 ☐ Per week **Number of 12 ounce portions per interval __ __** *scafunit*
3 ☐ Per month

3c. Does the participant drink alcohol? *alcdr* 0 ☐ No 1 ☐ Yes
(Go to #4)

If yes, check time interval and enter the average number of alcoholic drinks per interval: *nad*

(1 drink=any of the following: 12 ounces of beer, 4 ounces of wine, 1.5 ounces liquor)
1 ☐ Per day
2 ☐ Per week **Number of drinks per interval __ __** *alconit*
3 ☐ Per month

4. Analgesic Use History: *Record the average number per month over the last year. 0=Participant doesn't use*

4a. Acetaminophen tablets: __ __ __ *acett*
Avg. number per month

8b. Aspirin Tablets: __ __ __ *asprt*
Avg. number per month

4c. Combination analgesics: __ __ __ *combot*
Avg. number per month

8d. NSAIDs: __ __ __ *nsaidt*
Avg. number per month

4e. Medical use of marijuana: __ __ __ *dum*
Avg. Number per month

8f. Cox2 Inhibitors __ __ __ *cox2*
Avg. number per month

5. Has the participant used illicit drugs in the last year? *illdrg* 0 ☐ No 1 ☐ Yes

If yes, check all that apply
☐ Heroin *duh*
☐ Marijuana *duma*
☐ Methamphetamine *dumeth*
☐ Cocaine *duc*
☐ Other *duo*

If other, specify:_____*othr*

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit: Family Member ID _____*fammbr*

Lifestyle Form – Family Member

6. List all current prescription medications, over the counter medications and all natural products/protein supplements,

Prescribed Medications	*pres1*
	pres2
	pres3
	pres4
	pres5
	pres6
	pres7
	pres8

Over the Counter Medications	*oct1*
	oct2
	oct3
	oct4
	oct5
	oct6
	oct7
	oct8

All Natural Products/ Protein Supplements	*npp1*
	npp2
	npp3
	npp4
	npp5
	npp6
	npp7
	npp8

CRISP II

Attention - DO NOT enter patient data on this form if the header does not contain *preprinted* CRISP ID number, clinical center ID, and visit number.

Participant ID:_____ *pkdid* Clinical Center: _____ *pccn*

visit: Family Member ID _____*fammbr*

Lifestyle Form – Family Member

CRISP Member completing this form_____
cdidnum

Date Form Completed __ __/__ __/__ __ __ __
cddate

Data Entry Status: Please check to indicate that the above information has been entered ☐

Primary Entered by: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

Secondary Entered by: _____ Date __ __/__ __/__ __ __ __

LIST OF MEDICATIONS THAT SHOULD BE AVOIDED
BY CRISP PKD STUDY PARTICIPANTS

PLEASE NOTE: These medicines should not be taken for at least ONE week prior to Enrollment and each subsequent Visit in the CRISP Study.

****Extra-Strength Tylenol® is acceptable for pain or discomfort.**

Names of some of the more-common Non-Steroidals (NSAIDS)

1. **Salicylates (Aspirin, Empirin, Midol)**
2. **Fioricet**
3. **FiorinaL**
4. **Phrenilin Forte**
5. **Ibuprofen/Excedrin/Advil**
6. **Motrin**
7. **Nuprin**
8. **Naproxen Sodium/Naprosyn/Anaprox/Aleve**
9. **Diclofenac**
10. **Indomethacin**
11. **Sulindac**
12. **Tolmetin**
13. **Celecoxib**
14. **Rofecoxib**
15. **Meclofenamate**
16. **Mefanamic Acid**
17. **Nambumetone**
18. **Piroxicam**
19. **Fenoprofen**
20. **Ketaprofen (Extended Release)**
21. **Oxaprozin**
22. **Etodolac**
23. **Ketorolac**
24. **Toradol**
25. **Celebrex**
26. **Viox**
27. **C0X^2 Inhibitors**
28. ***NOTE: Hydrochlorthiazide (any Diuretics) should not be started as a NEW antihypertensive treatment < 2 wks prior to Enrollment Visit. (If it is necessary for you to start this medication, Enrollment should be delayed for 2 weeks).**
29. **The following medications also interfere with Creatinine excretion and should not be used for 4 days prior to each Visit:**
    - **Trimethoprim (Bactrim/Septra)**
    - **Cimetidine/Tagamet.**

PLEASE REVIEW THIS LIST. If you have any questions or are taking any of these medicines, PLEASE CALL your Physician or your Nurse Study Coordinator.

Thanks.

APPLICATION FOR A CRISP ANCILLARY STUDY

Background

The Consortium of Radiologic Imaging Studies of PKD (CRISP) is conducting a multicenter descriptive study of non-azotemic adult subjects over an 8 year time frame. Initial published studies based on the first four years (*Kidney Int. 64:1035-45, 2003; N Engl J Med. 354:2122-30, 2006; J Am Soc Nephrol. 2006;17:3013-9*) were drawn from history and physical examinations of 241 subjects and recorded annual conventional laboratory data together with measurements of iothalamate clearance, total kidney volume, total cyst volume, cyst number (left kidney mid-slice, one time only), PKD genotype and specific mutations and the rate of change in TKV and TCV over a three year interval.

CRISPII is underway and will extend CRISP another 4 years allowing additional conventional and new clinical and laboratory determinations to be made. In addition, serum, plasma, urine and DNA samples will continue to be placed in an NIH Repository to be used by CRISP investigators as well as those non-CRISP investigators who make application for an Ancillary Study.

The Specific Aims for CRISPII investigators are:

Aim 1: Extend the preliminary observations of CRISPI to ascertain the extent to which quantitative (kidney volume and hepatic and kidney cyst volume) or qualitative (cyst distribution and character) structural parameters predict renal insufficiency.

Aim 2: Extend the preliminary observations of CRISPI to ascertain the extent to which age and sex-adjusted measurements of renal blood flow by MR technology predict the rate of renal growth; and, renal blood flow and kidney volume predict the rate of renal function decline in ADPKD.

Aim 3: Exhaustively analyze the living database and stored biologic samples derived from CRISPI and the CRISPII extension to develop and test new metrics to quantify and monitor disease progression.

CRISPII site specific aims include:

Mayo/UAB: Collect DNA samples and clinical information from CRISP family members known to have ADPKD for use in future studies to examine genotype-phenotype correlations and to identify genetic modifiers

Emory*:* To determine the contribution of blood pressure phenotype (24 hour ambulatory blood pressure levels) and circulatory measures of the renin-angiotensin-aldosterone system to the prediction of disease severity defined as renal and cyst volume and change in renal and cyst volume over time in CRISPII participants.

University of Pittsburgh: Determine the growth of individual renal cysts from serial MR images and compare it with models of cyst growth and changes in the total kidney and renal cyst volumes.

Kansas University: Extend the analysis of monocyte chemotactic protein-1 (MCP-1) excretion to determine if absolute levels of urinary MCP-1 excretion and changes in the rates of excretion bear relation to specific morbid events (e.g. gross hematuria, new onset hypertension urinary tract infection, renal stone, nonspecific renal pain, and worsening renal function (declining GFR or increased albuminuria).

Members of the ***CRISP Steering Committee*** include (Patient Care Site PIs noted in bold): W. M. Bennett (chair), **A..B.Chapman,** J.E. Bost, **J.J.Grantham, L.M. Guay-Woodford**, C.M. Meyers, **V.E. Torres**.

Investigators with an interest and expertise in PKD may submit preliminary proposals to utilize this unique and precious database and repository of biologic samples provided they do not conflict with existing aims of CRISP investigators. In addition, new investigators may propose additional clinical data gathering in support of new hypotheses addressed to the clinical diagnosis, clinical manifestations of ADPKD or clinical progression of ADPKD. Successful applicants will be expected to work in collaboration with one or more CRISPII patient care site investigators.

OVERVIEW

Participation in, and approval of an ancillary study is subject to review by the CRISP Ancillary Studies chair, and formal approval by the CRISP Steering Committee.

To facilitate application the investigator should send a preliminary draft of the proposal to the chair of the Ancillary Studies Committee, Jared J. Grantham M.D., jgrantha@kumc.edu. Proposals should be submitted electronically in MS Word format/Arial font 12. Limit to 5 single spaced pages. Preliminary data validating new biomarker assays (plasma or urine) in PKD subjects versus controls is essential.

The chair will consult other members of the CRISP Steering Committee to determine if the proposal fits within the guidelines and capabilities of the CRISP protocol.

Format outline

1. Title of study
2. Principal Investigator and co-investigators
3. Institution, department, telephone, fax, email
4. Suggested CRISPII primary care site collaborator (excludes chair)
5. Planned start date (Note: Preliminary application must be made at least two months before any grant submission deadline.)
6. Brief background (with references), rationale and importance.
7. Hypothesis and Specific aims
8. Specific analytical methods used to analyze repository samples, if assay new to CRISP, and clinical data collection methodology, including questionnaires in an appendix, if applicable.
9. Funding plans and estimated costs. (Note: No funds are provided by CRISPII; moreover, if the collection of unusual samples or patient-specific information is planned, then PCC sites must be reimbursed for coordinator costs and supplies).
10. Are there any potential burdens to participants?
11. How many participants are required? Has a power analysis been done?
12. How will subject confidentiality be assured?
13. What CRISP core data and/or analysis are needed? Repository plasma, serum, DNA, or urine only? Will you need fresh blood or urine samples collected in the PCC?
14. What quantities of specimens will be needed? Repository plasma, serum, DNA, or urine only? Will you need fresh blood or urine samples collected in the PCC?
15. Sources of funding

After preliminary review and provisional acceptance, more detailed information may be requested before final approval.

SOME THINGS TO CONSIDER

- An ancillary study is one based on information from the CRISP study participants or study data in an investigation or analysis that is relevant to, yet not described in the Study protocol, and derives support from non-CRISP funds.
- Screening studies, i.e. to survey a microarray or proteomics database, will not be eligible. Rather, steering committee support of CRISP ancillary studies will require well-developed analytic tools based on preliminary studies.
- Proposals requesting only access to de-identified stored urine and plasma/serum samples and derived data e.g. DNA, GFR measurements, total kidney volume and kidney growth rate may not require local IRB approval, but investigators are encouraged to check with their local IRB.
- Once the proposal passes CRISP review you will be able to contact the Repository where samples from 2001-2005 are stored, and new samples will be added.
- An ancillary study applicant may propose the collection of additional data not collected or analyzed as part of the routine CRISP study data set provided that the samples can be collected at a regularly scheduled visit and funds are available from the investigator to cover the costs.
- All Ancillary Studies must include at least one Steering Committee member as a collaborating investigator who will not participate in the final merit review of the proposal.
- The proposed study must meet the standard of highest scientific merit.
- The proposed study must not interfere with the completion of the main objectives of the CRISP Study.
- The proposed study must be acceptable to the research subjects (consideration of time, discomfort, privacy).
- The proposed study must put minimal demand on scarce CRISP Study resources such as blood samples.
- The proposed study must require the unique characteristics of the CRISP Study cohort to accomplish its goals.
- The proposed study must not create a serious diversion of CRISP study resources (personnel, equipment or study samples) or investigator/staff time.
- The investigator must abide by the rules and regulation for CRISP covered in the Manual of Procedures that will be provided to successful applicants.

Memorandum of Understanding (MOU)

Memorandum of Understanding
CRISP & HALT-PKD Consortia
December 2007

This Memorandum of Understanding (MOU) is between the **Consortium for Renal Imaging Studies of Polycystic Kidney Disease** (CRISP) Steering Committee and the **Halt Polycystic Kidney Disease** (HALT-PKD**)** Steering Committee. This MOU has been formally reviewed and approved by all voting members of both the HALT-PKD (-----) and the CRISP steering committees (13 December 2007).

The CRISP is an NIDDK-funded prospective, longitudinal study to evaluate the accuracy and validity of magnetic resonance imaging to determine disease progression in autosomal dominant form of Polycystic Kidney Disease (ADPKD) that has now entered a second phase (CRISP II). The CRISP observational study does not exclude participants from enrolling in interventional studies such as HALT-PKD.

The HALT-PKD is an NIDDK-funded two treatment trial of patients with PKD; Study A is for patients with early disease and Study B is for patients with more advanced disease.

Subjects participating in both CRISP-II and HALT-PKD Study A or HALT-PKD Study B, will be asked to sign consent forms that permit sharing of their de-identified data between the investigators in both studies. The data to be shared between CRISP-II and HALT-PKD investigators meet current definitions and criteria of "de-identified" with the exception of date of enrollment into either study. Only data on consenting subjects will be shared between the Parties. Participating sites with both CRISP and HALT-PKD patients will advise the Data Coordinating Centers of corresponding ID numbers for the two studies, and will provide the Data Coordinating Centers with verification that informed consent has been obtained for data sharing between the two study groups.

This agreement outlines the understanding between the two steering committees regarding dual subject participant involvement, data sharing and use of data, confidentiality, publications and ancillary studies that utilize both CRISP and HALT-PKD subject data.

The steering committees agree to the following:

- The HALT-PKD Data Coordinating Center will provide the CRISP Data Coordinating Center with HALT-PKD Study A and Study B baseline visit data throughout the conduct of the HALT-PKD Study A and Study B, on a mutually agreed upon schedule. The baseline visit data that will be provided will include: imaging, biochemical, genetic and pertinent clinical data to be designated by the Steering Committee prior to transfer.
- The CRISP Consortium will analyze the baseline visit data in accordance with the current CRISP protocol analytical plan and will not use the data for any other purpose. The CRISP Data Coordinating Center will not provide the HALT-PKD patient data to any third parties for any purpose.

- Subsequent HALT-PKD Study A and Study B patient data will be provided by the HALT-PKD Data Coordinating Center to the CRISP Data Coordinating Center after submission of the initial publication on the primary end-points of HALT-PKD Study A and Study B, respectively. The subsequent visit data that will be provided will include: all imaging, biochemical, genetic and pertinent clinical data to be designated by the Steering Committee prior to transfer.
- The CRISP Data Coordinating Center will provide the HALT-PKD Data Coordinating Center with the CRISP-I and CRISP-II data for subjects who participate in HALT-PKD Study A and HALT-PKD Study B at the conclusion (within 90 days of last HALT-PKD patient visit) of the HALT-PKD Study A and HALT-PKD Study B, respectively. The CRISP I and CRISP II data that will be provided to HALT-PKD Study A and HALT-PKD Study B will include: all imaging, biochemical, genetic and pertinent clinical data.
- The HALT-PKD Data Coordinating Center will analyze the data in accordance with the current HALT-PKD protocol analytical plan and will not use the data for any other purpose. The HALT-PKD Data Coordinating Center will not provide the CRISP study data to any third parties for any purpose
- There is an existing CRISP/HALT-PKD Liaison Committee with the following representative members: CRISP Steering Committee Chairperson, HALT-PKD Steering Committee Chairperson, NIDDK CRISP and HALT-PKD Program Officials, the Principal Investigator from the CRISP Data Coordinating Center, the Principal Investigator from the HALT-PKD Data Coordinating Center, and two Principal Investigators involved in both the CRISP and HALT-PKD studies.
- The CRISP/HALT-PKD Liaison Committee will review all ancillary study applications and manuscript/publications proposals that involve both CRISP and HALT-PKD subject data. Review and approval by the CRISP/HALT-PKD Liaison Committee will be required prior to submission to the Ancillary/Publication subcommittees of CRISP and HALT-PKD.
- All ancillary studies that utilize both CRISP and HALT-PKD subject data will be reviewed by both CRISP and HALT-PKD Ancillary Studies committees with clarification from the applicant that both data sets are being requested after approval by the CRISP/HALT-PKD Liaison Committee.
- All manuscript/abstract/presentation proposals that utilize both CRISP and HALT-PKD subject data will be reviewed by both CRISP and HALT-PKD Publications committees after approval by the CRISP/HALT Liaison Committee.
- The period of this MOU will be in effect for six (6) years from the above-listed date of this agreement.

CRISP II Study Biosample Repository

Assembling the Refrigerated Laboratory Shipper

1. Insert the Vacutainers into the bubble wrap pouch.

2. Roll up and place the bubble wrap pouch into the zip-lock biohazard bag with a white absorbent sheet. Squeeze the air out of the bag and seal it.

3. Place a frozen gel pack in the bottom of the foam cooler.

4. Place the zip-lock bag on top of the frozen gel pack. If necessary, add additional packing to prevent contents from shifting

5. Put the lid on the foam cooler, and place a copy of the specimen shipment form on top of the cooler lid.

6. Close and seal the outer box with packing tape.

7. Affix the “UN 3373 Biological Substance Category B” label on the top of the box in the upper right corner.

8. Affix the repository address label on the same side of the box in the upper left corner.

9. Use the pre-printed Fed Ex air bill to ship specimens to the NIDDK Repository:

   a. Section 1, From: Fill in your name, return address, phone number and the date. Leave “Sender’s FedEx Account Number” blank.

   b. Section 5, Packaging: Place a check mark in the “Other” box.

   c. Section 6, Special Handling: Place a check mark in the “No” box, indicating no dangerous goods are in the shipment.

   d. Section 7, Payment: Enter “1” under “Total Packages” and the total weight of the package.

Follow the peel-and-stick instructions on the back of the air bill to affix it to the box as shown.

10. Call Federal Express, 1-800-GO-FEDEX (1-800-463-3339). Give them the account number (in Section 7, Payment) on the preprinted FedEx air bill and your pickup address. FedEx will dispatch a courier to pick up the package. Please schedule shipments Monday through Thursday. **Do not ship specimens on Fridays; the repository is closed on weekends.**

11. Send a shipment notification to the repository via email at BIO-NIDDKRepository@thermofisher.com or fax (301-515-4049) on the day the package is picked up by FedEx. Include the 12-digit FedEx tracking number in the notification.

12. Contact the NIDDK Repository via email or call Heather Higgins (240-793-0353) or Sandra Ke (240-686-4702) regarding questions about packaging and shipping.

Assembling the STP 320 Repository Shipper

1. Upon receipt of the empty shipping kit from the repository, remove the “EMPTY PACKAGING” cover from the outer box.

2. Place the specimen box and the absorbent strip inside the plastic bag. Seal the bag.

3. Place the plastic bag inside the white Tyvek envelope. Seal the envelope.

4. Place the Tyvek envelope in the cardboard inner box. If only one or two specimen boxes are being shipped, fill the rest of the space inside the cardboard inner box with packing material (e.g., bubble wrap) or an empty specimen box to prevent movement during shipment. Tape the box and place it in the middle of the cooler.

5. Fill the remainder of the space between the inner cardboard box and the inner walls of the cooler with dry ice.

6. Place the lid on the cooler. Place the “EMPTY PACKAGING” cover and shipping form on top of the cooler lid.

7. Close and tape the outer cardboard box.

8. Place a checkmark in the block on the outer cardboard box next to “BIOLOGICAL SUBSTANCE, CATEGORY B”. Do not cover this marking with labels.

9. Affix a label with your name and return address to the side of the box in the “Shipper:” block.

10. Affix the repository address label to the side of the box in the “Consignee:” block.

11. Affix the dry ice label below the repository address label. Enter the weight of dry ice on the label in kilograms.

12. Affix the “UN3373 BIOLOGICAL SUBSTANCE, CATEGORY B” label to the right of the dry ice label.

13. Use the pre-printed Fed Ex air bill to ship specimens to the NIDDK Repository:

Section 1: Fill in your name, return address, phone number and the date. Leave “Sender’s FedEx Account Number” blank.

Section 6, Special Handling: Check “Yes, Shippers Declaration not required”. Check the “Dry Ice” block; enter “1” and the weight of dry ice in kg.

Section 7: Enter “1” under “Total Packages” and the total weight of the package.

Follow the peel-and-stick instructions on the back of the air bill. As shown, affix the air bill to a side of the box adjacent to the labeled side.

14. Call Federal Express, 1-800-GO-FEDEX (1-800-463-3339). Give them the account number (in Section 7, Payment) on the preprinted FedEx air bill and your pickup address. FedEx will dispatch a courier to pick up the package. Please schedule shipments Monday through Wednesday to avoid weekend shipment delays. **Do not ship frozen packages on Friday; the repository is closed on weekends.**

15. Send a shipment notification to the repository via email at BIO-NIDDKRepository@thermofisher.com or fax (301-515-4049) on the day the package is picked up by FedEx. Include the 12-digit FedEx tracking number in the notification.

16. Contact the NIDDK Repository via email or call Heather Higgins (240-793-0353) or Sandra Ke (240-686-4702) regarding questions about packaging and shipping.

Emory letter goes here…

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

National Institute of Diabetes,
Digestive and Kidney Diseases
Bethesda, Maryland 20892-5458
(301) 594-6007
(301) 480-3510 Fax

May 22, 2007

Dr. Vincent Torres
Mayo Clinic Rochester
200 First Street Southwest
Rochester, Minnesota 55905

Dear Dr. Torres

The informed consent from your site in the "**Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease" (CRISP II) (Relatives)** study has been reviewed by the NIDDK Central Repository office and has been approved.

Consent Version Date	**Page Numbers**	**Comments:**
April 12, 2007	**5-7**	**X, Approved as Written**

Please revise the consent and send me the IRB-approved revised version. Should you have any further questions or concerns, please do not hesitate to contact me.

Sincerely,

Jeanette Hammond, RN
Repository Specialist

Cc: Kristin Cornwell, RN
Heather Higgins, ThermoFisher
Dana Witt, Rutgers
Dr. Catherine Meyers

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

National Institute of Diabetes,
Digestive and Kidney Diseases
Bethesda, Maryland 20892-5458
(301) 594-6007
(301) 480-3510 Fax

June 14, 2007

Dr. Lisa M. Guay-Woodford
University of Alabama at Birmingham
701 20th Street South
Birmingham, AL 35294

Dear Dr. Guay-Woodford,

The informed consent from your site in the **"Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPDK): Extension" (CRISP II)** study has been reviewed by the NIDDK Central Repository office and has been approved.

Consent Version Date	Page Numbers	Comments:
February 1, 2007	**8-9**	**X, Approved as Written**

Should you have any further questions or concerns, please do not hesitate to contact me.

Sincerely,

Jeanette Hammond, RN
Repository Specialist

Cc: Mary Virginia Gaines
Heather Higgins, ThermoFisher
Dana Witt, Rutgers
Dr. Catherine Meyers

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

National Institute of Diabetes,
Digestive and Kidney Diseases
Bethesda, Maryland 20892-5458
(301) 594-6007
(301) 480-3510 Fax

May 30, 2007

Dr. Jared Grantham
The University of Kansas Medical Center
Kansas City, KS 66160

Dear Dr. Grantham,

The informed consent from your site in the "**Consortium for Radiological Imaging Studies of PKD" (CRISP II)** study has been reviewed by the NIDDK Central Repository office and has been approved.

Consent Version Date	**Page Number**	**Comments:**
May 8, 2007	**4**	**x, Approved as Written**

Should you have any further questions or concerns, please do not hesitate to contact me.

Sincerely,

Jeanette Hammond, RN
Repository Specialist

Cc: Mary Virginia Gaines
Heather Higgins, ThermoFisher
Dana Witt, Rutgers
Dr. Catherine Meyers

CRISP II Study IRB Approval Letters

Data Coordinating Center Image Analysis Center (University of Pittsburgh) IRB Approval Letter

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Ground Level
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)

MEMORANDUM

TO: Kyongtae Ty Bae, MD, PhD

FROM: Christopher Ryan, PhD, Vice Chair

DATE: November 6, 2007

SUBJECT: IRB #0610092: Renal Imaging to Assess Progression n Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP II)

Your renewal with modifications of the above-referenced proposal has received expedited review and approval by the Institutional Review Board under 45 CFR 46.110 (7).

Please include the following information in the upper right-hand corner of all pages of the consent form:

Approval Date: November 5, 2007
Renewal Date: November 5, 2008
University of Pittsburgh
Institutional Review Board
IRB #0610092

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. The IRB Reference Manual (Chapter 3, Section 3.3) describes the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Event Coordinator at 412-383-1504.

The protocol and consent forms, along with a brief progress report must be resubmitted at least **one month prior** to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

CR:kh

Data Coordinating Center Image Analysis Center (Washington University) IRB Approval Letter

Washington University in St.Louis

Human Research Protection Office

Barnes-Jewish Hospital
St. Louis Children's Hospital
Washington University

April 12, 2007

Fred Prior, PhD
Radiology (General)
Box 8131

RE: 00-0976
Data Coordinating and Image Analysis for CRISP II

Dear Dr. Prior:

The above-stated protocol was reviewed and approved by the Human Research Protection Office (HRPO). Following please find specifics of the approval:

Approval Date:	4/12/2007
Date released for accrual:	4/12/2007
Expiration Date:	4/11/2008
Research Risk Level:	Minimal
Type of Review:	Minimal Risk Cont. Review (Expedited 9)
Reviewing Committee:	08 MRCR
HIPAA Compliance:	Exempt

A subcommittee of WU HRPO members have been designated by the HRPO Chair to review all submissions that meet the criteria for "Expedited" review. All actions and recommendations of the subcommittees are reported to a full board committee in accordance with regulatory requirements for "Expedited" review.

The WU HRPO complies with the regulations outlined in 45 CFR 46, 45 CFR 164, 21 CFR 50, 21 CFR 56. The OHRP Federal Wide Assurance numbers for WUSM, BJH, and SLCH are FWA00002284, FWA00002281, and FWA00002282 (respectively).

If further information is necessary, please contact the HRPO office at (314) 633-7400.

Sincerely,

Philip Ludbrook, M.D.
Associate Dean and Chair

CC: Mary Virginia Gaines

Emory University IRB Approval Letter

FROM: Susan M. Ray, MD
Vice Chair
Emory University IRB

TO: Arlene Chapman, MD
Principal Investigator

CC:

Han	Yoosun	MedRenal
Langley	Sharon	MedRenal
Watkins	Diane	MedRenal
Wilkening	Beth	MedRenal
Martin Diego	Radiology - Main	
Rahbari Oskoui Frederic	MedRenal	

DATE: April 20, 2007

RE: **Notification of Full Board Approval**
IRB00002998
RENAL IMAGING TO ASSESS PROGRESSION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): EXTENSION (CRISP II)

This is your notification that your above referenced study was reviewed and APPROVED under the Full Board review process by Committee IV, per pediatric category 45 CFR 46.404. This approval is valid from **3/28/2007 until 3/27/2008** . Thereafter, continued approval is contingent upon the submission of a renewal form that must be reviewed and approved by the IRB prior to the expiration date of this study.
Any reportable events (serious adverse events, breaches of confidentiality, protocol deviation or protocol violations) or issues resulting from this study should be reported immediately to the IRB and to the sponsoring agency (if any). Any amendments (changes to any portion of this research study including but not limited to protocol or informed consent changes) must have IRB approval before being implemented.
All correspondence and inquiries concerning this research study must include the IRB ID, the name of the Principal Investigator and the Study Title.
Sincerely,
Susan M. Ray, MD
Vice Chair
Emory University Institutional Review Board
This letter has been digitally signed

Emory University
1256 Briarcliff Road, NE Room 307N - Atlanta, Georgia 30306
Tel: 404.712.0720 - Fax: 404.727.1358 - Email: irb@emory.edu - Web: http://www.emory.edu/irb

Mayo Clinic IRB Approval Letter

From: IRBe [irbe@mayo.edu]
Sent: Thursday, April 12, 2007 1:43 PM
To: Spencer, Dorothy C.
Subject: A Protocol has been Approved by IRB

Principal Investigator Notification:

From: IRB

To: Vicente Torres

CC: Study Team Members that are marked as wishing to receive correspondence regarding the protocol/grant application

Re: Application # 06-009502
Click the link below to access the protocol/grant application information in your IRBe workspace, as well as the approved consent document(s)/Rough Word consent document(s) that need to be used when submitting consent changes as part of a modificaiton request (if applicable) under the Documents tab:

06-009502

Please note that all correspondence (modifications, progress reports, reportable events (SAEs/Deviations) related to this study/grant application must be submitted electronically in the IRBe system.
The following is an excerpt from the minutes of the Full-Blue Thursday of the Mayo Clinic Institutional Review Boards meeting dated 4/12/2007:

The Committee reviewed and (8-0) approved the protocol entitled "Renal Imaging To Assess Progression In Autosomal Dominant Polycystic Kidney Disease (Adpkd): Extension (Crisp II) " from Dr. Vicente Torres (Principal Investigator, PI) and colleagues. This approval is valid for exactly one year unless during the year the IRB determines that it is appropriate to halt or suspend the study earlier. A maximum of 358 adult participants (ages 18-75) with Polycystic Kidney Disease is approved for target accrual in this protocol at Mayo Clinic Rochester. The Committee noted justification for not having a DSMB was appropriate because this is not an interventional trial. The Committee noted Biospecimens Subcommittee approval dated March 8, 2007, and Nephrology Research Committee approval dated December 20, 2006. In accordance with 45 CFR 46.306, the Committee determined that prisoners are not appropriate for enrollment in this protocol as the study offers no benefit to participants. The questionnaires, patient contact letters, and telephone scripts were approved for use in the study, as written. The Committee noted $300 remuneration will be provided to participants who have successfully completed study interventions and determined this is acceptable. Funding for the study will be provided by the National Institute of Diabetes and Digestive and Kidney Diseases. Due to HIPAA regulations, if an investigator will obtain protected health information to recruit subjects into non-therapeutic studies on or after April 14, 2003, he or she must submit a “Review Preparatory to Research” form before obtaining such information.
The form can be found on the IRB website at http://resis.mayo.edu/resis/myprojects/irb_preparatory.cfm. The Committee noted a request to waive HIPAA authorization in order to collect protected health information on deceased family members. The Committee noted verification from Dr. Torres that all criteria for waiver of HIPAA authorization are met for this protocol. The Committee therefore approves waiver of HIPAA authorization in accordance with applicable HIPAA regulations and waiver of informed consent in accordance with 45 CFR 46.116(d). The Committee approved the participant consent form with revisions, including updates to the current Mayo template. The IRB office will provide the final approved consent form on the IRBe workspace for this item. 06-009502.

Rubin, Joseph M.D. , Chair
Aimee Gabrielson , Specialist
Mayo Clinic Institutional Review Boards
Full-Blue Thursday

University of Alabama-Birmingham IRB Approval Letter

UAB SCHOOL OF MEDICINE

James A. Pittman General Clinical Research Center

July 11, 2007

Lisa Guay-Woodford, MD
KAUL 740, zip 0024

RE: GCRC Protocol #1311 "Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP II)" IRB Protocol #F070226008"

At the Scientific Advisory Committee Meeting held on July 10, 2007 your protocol listed above was approved for implementation on the General Clinical Research Center as follows.
Study Classification: A
Priority Score: 1.48
# of inpatients: 31
# of inpatient days: 62
# of outpatients: 31
# of outpatients visits: 62
Award: $1,685.63 for inpatient and $123.69 for outpatient annually for serum creatinine, total electrolyte, lipid panel, B-HCG qualitative urine pregnancy test, random urine albumin, random urine creatinine, random urine albumin/creatinie ratio, and GFR test pharmacy charge.

Additional Comments:
The GCRC requires that an approved IRB and consent form be on file in the GCRC office before initiating the protocol. The GCRC requires any revisions to the consent form that are submitted to the IRB also be sent to the GCRC. All protocol correspondence submitted to and received from the IRB should be copied to the GCRC's Research Subject Advocate, Kathleen Powell. This includes renewals, amendments, revised consents, and reports from data safety monitors. All SAEs and unexpected AEs should be received by the GCRC within 10 days of occurrence.

NIH REQUESTS THAT YOU CREDIT GCRC GRANT #M01-RR00032 AS PROVIDING SUPPORT FOR THIS PROTOCOL IF ANY INFORMATION (JOURNAL ARTICLE, BOOK, ABSTRACT) IS PUBLISHED AS A RESULT OF THIS STUDY.

Prior to initiation of this protocol you must schedule an in-service *at least two weeks before your first subject is enrolled* with the GCRC nursing staff. Please contact Jolene Lewis at 4-6669 to schedule this in-service.

We look forward to working with you on this protocol. If you have questions please call me at 4-4852.

Sincerely,

Decarlos Wright
Administrative Manager

My signature below signifies that I understand the stipulations as outlined regarding GCRC awards. I agree to abide by these requirements. Please return a signed copy of this letter to the GCRC administrative office.

Lisa Guay-Woodford, MD

M907 Medical Education Building
1813 6th Avenue South
205.934.4852
Fax 205.975.6616
http://www.gcrc.uab.edu

The University of
Alabama at Birmingham
Mailing Address:
MEB M907
619 19TH ST S
BIRMINGHAM AL 35249-6909

University of Alabama-Birmingham IRB Approval Letter (continue)

OMB No. 0990-0263
Approved for use through 11/30/2008

Protection of Human Subjects
Assurance Identification/IRB Certification/Declaration of Exemption
(Common Rule)

Policy: Research activities involving human subjects may not be conducted or supported by the Departments and Agencies adopting the Common Rule (56FR28003, June 18, 1991) unless the activities are exempt from or approved in accordance with the Common Rule. See section 101(b) of the Common Rule for exemptions. Institutions submitting applications or proposals for support must submit certification of appropriate Institutional Review Board (IRB) review and approval to the Department or Agency in accordance with the Common Rule. Institutions must have an assurance of compliance that applies to the research to be conducted and should submit certification of IRB review and approval with each application or proposal unless otherwise advised by the Department or Agency.

1. Request Type	2. Type of Mechanism	3. Name of Federal Department or Agency and, if known, Application or Proposal Identification No.
[X] ORIGINAL [ ] CONTINUATION [ ] EXEMPTION	[ ] GRANT [ ] CONTRACT [ ] FELLOWSHIP [ ] COOPERATIVE AGREEMENT [ ] OTHER:	

4. Title of Application or Activity	5. Name of Principal Investigator, Program Director, Fellow, or Other
Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP II)	GUAY-WOODFORD, LISA M

6. Assurance Status of this Project *(Respond to one of the following)*

[X] This Assurance, on file with Department of Health and Human Services, covers this activity:
Assurance Identification No. FWA00005960, the expiration date 2/14/09 IRB Registration No. IRB00000726

[ ] This Assurance, on file with *(agency/dept)* _____, covers this activity.
Assurance No. _____, the expiration date _____ IRB Registration/Identification No. _____ *(if applicable)*

[ ] No assurance has been filed for this institution. This institution declares that it will provide an Assurance and Certification of IRB review and approval upon request.

[ ] Exemption Status: Human subjects are involved, but this activity qualifies for exemption under Section 101(b), paragraph _____.

7. Certification of IRB Review (Respond to one of the following IF you have an Assurance on file)

[X] This activity has been reviewed and approved by the IRB in accordance with the Common Rule and any other governing regulations.
by: [X] Full IRB Review on (date of IRB meeting) 5/9/2007 or [ ] Expedited Review on (date) _____
[ ] If less than one year approval, provide expiration date _____

[ ] This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by the Common Rule will be reviewed and approved before they are initiated and that appropriate further certification will be submitted.

8. Comments	Title FD70226008
Protocol subject to Annual continuing review.	Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP II)

IRB Approval Issued: 05-29-07

9. The official signing below certifies that the information provided above is correct and that, as required, future reviews will be performed until study closure and certification will be provided.	10. Name and Address of Institution
11. Phone No. *(with area code)* (205) 934-3789 12. Fax No. *(with area code)* (205) 934-1301 13. Email: smoore@uab.edu	University of Alabama at Birmingham 701 20th Street South Birmingham, AL 35294
14. Name of Official Albert Oberman, M.D., MPH	15. Title Vice Chair, IRB
16. Signature Albert Oberman, MD, MPH / JEM	17. Date 05-29-07

Authorized for local Reproduction — Sponsored by HHS

Public reporting burden for this collection of information is estimated to average less than an hour per response. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: OS Reports Clearance Officer, Room 503 200 Independence Avenue, SW., Washington, DC 20201. *Do not return the completed form to this address.*

University of Kansas IRB Approval Letter

The University of Kansas Medical Center

Human Research Protection Program

May 14, 2007

Project Number:	10824
Project Title:	Consortium For Radiologic Imaging Studies Of Polycystic Kidney Disease (CRISPII)
Sponsor:	National Institutes of Health
Protocol Number:	QG816940
Primary Investigator:	Jared J Grantham, M.D.
Department	Internal Medicine
Meeting Date:	5/8/2007
HSC Approval Date:	5/8/2007
HSC Expiration Date:	5/7/2008
Type of Approval:	Full Committee Review – New Protocols

Dear Investigator:

This is to certify that your research proposal involving human subject participants has been reviewed and **approved** by the KU Human Subjects Committee. This approval is based upon the assurance that you will protect the rights and welfare of the research participants, employ approved methods of securing informed consent from these individuals, and not involve undue risk to the human subjects in light of potential benefits that can be derived from participation. It is the investigator's responsibility to only use those informed consent documents bearing the correct approval and expiration dates when obtaining informed consent from research participants."

Approval of this research is contingent upon your agreement to:

(1) Adhere to all KUMC Policies and Procedures Relating to Human Subjects, as written in accordance with the Code of Federal Regulations (45 CFR 46).
(2) Maintain copies of all pertinent information related to the research study including, but not limited to, video and audio tapes, instruments, copies of written informed consent agreements, and any other supportive documents in accordance with the KUMC Research Records Retention Policy.
(3) Report unanticipated problems to the HSC by completing the Internal or External HSC Unanticipated Problem/Adverse Event reporting form, as applicable.
(4) Submit deviations from previously approved research activities which were necessary to eliminate apparent and immediate dangers to the subjects by using the KUMC Protocol Deviation Report.
(5) Submit Amendments to the HSC for any proposed changes from the previously approved project using the Request for Amendment form. Changes may not be initiated without prior HSC review and approval, unless a delay in implementation would place subjects at risk.
(6) Submit Continuing Review Form (CR Form) to the KUMC HSC before the expiration date. Federal regulations and HSC policies require continuing review of research at intervals appropriate to the degree of risk, but not less than once per year.

If you have any questions regarding the human subject protection process, please do not hesitate to contact our office.

Very truly yours,

Daniel J. Voss, M.S., J.D.
IRB Administrator

RECEIVED
MAY 16 2007
Clinical Research Administration

Mail-Stop 1032, 3901 Rainbow Blvd., Kansas City, KS 66160
Phone: (913) 588-1240 Fax: (913) 588-5771 humansubjects@kumc.edu

CRISP II Study Consent Forms

Emory University Consent Form

Study No.: IRB00002998 | **Emory University IRB** IRB use only | Document Approved On: 10/30/2007 Project Approval Expires On: **3/27/2008**

CONSENT TO PARTICIPATE IN A RESEARCH STUDY AT EMORY UNIVERSITY SCHOOL OF MEDICINE

TITLE OF STUDY: CONSORTIUM FOR RADIOLOGIC IMAGING STUDIES OF POLYCYSTIC KIDNEY DISEASE (CRISP II)

INVESTIGATORS' NAMES, DEPARTMENTS, PHONE NUMBERS

Arlene B. Chapman, M. D.	**Internal Medicine**	**(404) 727-2525**
Frederic Rahbari Oskoui, MD	**Internal Medicine**	**(404) 727-2525**
Diego Martin, MD, PhD	**Radiology**	**(404) 778-3800**
George Baramidze, MD	**Internal Medicine**	**(404) 727-2525**

COORDINATORS' NAMES, DEPARTMENTS, PHONE NUMBERS

Yoosun Han	**Internal Medicine**	**(404) 727-2525**
Beth Wilkening, PA-C	**Internal Medicine**	**(404) 686-8280**
Diane Watkins	**Internal Medicine**	**(404) 727-2525**
Bijan Ahrari	**Internal Medicine**	**(404) 727-2525**
Sharon Langley, MS	**Internal Medicine**	**(404) 727-2525**

PURPOSE:

You have been invited to volunteer for a research project funded by the National Institutes of Health. You are being asked to participate because you have polycystic kidney disease (PKD), and you participated in the original Consortium for radiologic imaging studies of polycystic kidney disease (CRISP) study. The purpose of this study is to continue following you for another four years to determine if pictures of your kidneys using magnetic resonance imaging (MRI) can detect change in kidney size over a short period of time. If you enroll, you will participate for 48 months (4 years).

If you decide to volunteer and participate in this study, a number of tests will be done that are outlined below. Eligible subjects are being enrolled at other sites in the U.S.A., and include the Mayo Foundation, University of Kansas Medical Center and University of Alabama at Birmingham. It is expected that all 73 subjects who participated in CRISP at Emory will be enrolled and at least 220 subjects will be enrolled altogether. At this site, all studies will be performed at the General Clinical Research Center (GCRC) inpatient or outpatient unit at Emory University Hospital and the Satellite GCRC at Emory Crawford Long Hospital.

PROCEDURES:

The CRISP II protocol includes participants that enroll in other interventional trials. If CRISP II participants are recruited into an interventional trial (e.g. HALT clinical trial that also requires imaging studies) the visits for CRISP II and for the interventional trial will be coordinated to avoid duplication of tests and undue burden on you. You will, however, complete the necessary studies of CRISP II that are not included in HALT or any other interventional study.

If you are also a participant in the National Institutes of Health (NIH) sponsored HALT clinical trial or any other interventional study, please read the following statements and make your choice:

1. I permit the deidentified information (identified by CRISP ID number only) collected for the CRISP study to be provided to the HALT or any other interventional trial investigators

☐Yes ☐No Please initial here: _____Date: _____

2. I permit deidentified information (identified by HALT ID number or any other interventional study number) collected for the study to be provided to the CRISP investigators

☐Yes ☐No Please initial here: _____Date: _____

A: ELIGIBILITY DETERMINATION:

You are eligible if you participated in the original CRISP cohort study. Initially, a medical history and a complete physical exam will be done to determine your overall health. The physical exam will include height, weight, and blood pressure measurements. If you have serious heart, liver, lung or other medical conditions, you may not participate in this extended CRISP II study. Included in your medical history, a family tree (pedigree) will be done. We may request information about your family and ask for your help in getting this information. Once the needed pieces of information are obtained, and if you are eligible, you will be enrolled into the study and admitted to the General Clinical Research Center (GCRC) at Emory University Hospital for testing.

B: GENERAL CLINICAL RESEARCH CENTER (GCRC) STAY at years 1 and 3:

You will spend as few as one and as many as two days at the inpatient or outpatient GCRC at Emory University Hospital. These visits will occur years 1 and 3 throughout the study. You will be asked to give a medication history. You will also have blood pressures measured at least nine times. This will be done in the same arm that was used in CRISP I. A special test with blood and urine collections to measure your kidney function will be done, and special pictures of your kidneys using MRI/MRA will be done.

Bi: LABORATORY TESTS:

The freshly void urine will be collected during your GCRC stay. The results from this test will determine your kidney function and the amount of protein in your urine. A urine test to determine pregnancy will be performed on women with child-bearing potential prior to undergoing any tests. You will be told if you are pregnant. Blood samples will be obtained during your visit to determine your chemistry and cholesterol profile, and other markers that may identify risk for renal failure in PKD. About 50 ml or 4 tablespoons of blood will be taken for these tests. Some of blood and urine samples will be sent to the NIDDK Central Repositories (a central repository, Fisher BioServices, and the NIDDK Center for Genetic Studies, Rutgers University Cell and DNA Repository), a research resource supported by the National Institutes of Health. The Repository collects, stores, and distributes biological samples and associated data from people with many kinds of disorders, from unaffected family members, and from other healthy people. The purpose of this collection is to make samples available for use in research for the study of Autosomal Dominant Polycystic Kidney Disease,

after the current study is completed. Sending samples to the Repository may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to prevent Autosomal Dominant Polycystic Kidney Disease.

De-identified (identified by CRISP ID number only) blood and urine samples will be shared with other CRISP site investigators.

Bii RADIOLOGY TESTS:

An MRI/MRA of your kidneys will be done. When you have an MRI/MRA, you will lie still in the scanner (a hollow tube) for up to 90 minutes. While you are in the scanner, you will be moved slowly and pictures of your kidneys will be made. You will be asked to hold your breath for 30 seconds when each picture is taken. There is no radiation exposure associated with this procedure.

Biii GLOMERULAR FILTRATION RATE (GFR) TEST:

Your kidney function will be measured using a special test called a GFR test. GFR is a test of how well the kidney filters and cleans the blood. During this test you will not eat food but you will drink water a number of times so that you make enough urine. Iothalamate meglumine will be injected under your skin in the upper arm at the beginning of the test. This is absorbed into the blood and carried to the kidneys to be filtered. During the test, two blood samples (1 teaspoonful each) will be obtained. The duration of the test will be approximately two hours. You will be asked to go to the bathroom at least three times during the test. An ultrasound of your bladder will be done after you go to the bathroom to be sure that your bladder empties. Gel will be placed on the skin above your bladder and a probe will be moved over the skin. If you do not empty your bladder completely after you go to the bathroom, you will be asked to go to the bathroom again. If you cannot empty your bladder during the test, it will be stopped and repeated on another day.
Each of the tests mentioned above, (the GFR test and the MRI/MRA) will be done once every two years over a four-year period. Blood for gene testing or DNA analysis if needed, will be obtained once.

C: Optional General Clinical Research Center (GCRC) VISIT at years 2 and 4:

At years 2 and 4, you will have 20 ml of blood samples (2 tablespoon) collected either at the GCRC or at your local clinic to measure your kidney function. Your local lab will be contacted directly with the procedure to be followed, and your blood samples will be shipped to the GCRC to process.

OUTPATIENT FOLLOW-UP :

After the GCRC tests are done, you will be discharged from the GCRC, and continue under the care of your own primary physician. We ask that you keep track of any change in your medications, whether prescribed or over the counter. We will contact you and your doctor's office every six months between GCRC visits. At this time, we will talk with you on the phone to determine if any medication changes, illnesses, or hospitalizations have occurred. These phone calls will not be longer than 45 minutes. We may request information obtained by your doctor during this time. If you have been hospitalized, we request permission to receive medical records from your hospitalization. If you have any surgery performed, we request access to medical records from those surgeries. If you have any radiology tests performed such as an x-ray, CT scan,

ultrasound, or other test, we request permission to obtain those records. By signing this informed consent form, you are giving us permission to obtain these records.

ALTERNATIVES:

The alternative to consenting to participate in this study is not to participate at all. If this were the case and you decide not to participate, there will not be changes in your treatment and you will continue to receive your usual medical care.

RISKS:

Due to the investigational nature of this study there may be unforeseeable risks.

If you are a woman of childbearing potential you will undergo a urinary pregnancy test prior to undergoing the GFR test. If you know that you are pregnant you must inform the principal investigator and not participate in this study. If you become pregnant after completion of the first visit of this study, you need to inform the principal investigator to determine if and when you should be studied again.

There are risks related to blood drawing that include pain, bruising and infection. Risks related to intravenous catheter placements are also present and include pain, bruising and infection. Given that the intravenous line is in place for an extended amount of time (between 2 and 6 hours), mild discomfort may be present for a few days after the test.

There are no known risks from the magnetic resonance imaging. However, the hollow tube is narrow and some people have anxiety related to being closed in or claustrophobia. This occurs in approximately 12% of people. If you have any pacemakers or metal objects that are not compatible with a magnetic resonance image you may not participate in this study.

BENEFITS:

There are no direct benefits to you for participating in this study. Information regarding your level of kidney involvement may help to determine how fast you are progressing with PKD. This information will be made available to your treating physician. You will continue to receive your usual treatment by your primary physician. No changes to your usual care will be instituted by this study. If you are thinking about participating in another clinical study or trial, you need to discuss this with the Study Coordinator and the Principal Investigator before you can participate.

CONFIDENTIALITY:

All information concerning you will be kept private. In particular, given the hereditary nature of PKD, extra care will be taken to maintain your anonymity. All subject records will be filed based on a special unique identifier other than your name. As well, all data will be kept in a computer database that is internet, hospital and medical insurance inaccessible. Ultimately, research records of the hospital, like hospital charts, may be obtained by court order. If information about you is published, it will be written in a way that you cannot be recognized.

By signing this form, you are giving permission for your physician to allow the study sponsor, and any regulatory body to review the information regarding your participation in the study and your medical records. All data and medical records associated with your participation in this study will be kept confidential except

where noted, and as may be required by law. You will be identified by a unique identifier and not your name, including to the sponsor and regulatory body.

People other than those doing the study may look at both medical charts and study records. Agencies and Emory departments and committees that make rules and policy about how research is done have the right to review these records. So do companies and agencies that pay for the study. The government agencies and units within Emory responsible for making sure that studies are conducted and handled correctly that may look at your study records in order to do this job including the Food and Drug Administration, the Office for Human Research Protections, the sponsor(s), the Emory University Institutional Review Board, the Emory Office of Research Compliance, the Clinical Trials Office, etc. Companies and other groups that pay for studies and that are listed in consent and authorization documents also will have the right to look at your records. In addition, records can be opened by court order or produced in response to a subpoena or a request for production of documents. We will keep any records that we produce private to the extent we are required to do so by law. We will use a study number rather than your name on study records where we can. Your name and other facts that might point to you will not appear when we present this study or publish its results.

If you are or have been a patient at an Emory Healthcare facility, then you will have an Emory Healthcare medical record. If you have never been an Emory Healthcare patient, then you will not have an Emory Health medical record and no medical record will be created for you just because you are participating in a study.

Due to confidentiality considerations, the Emory IRB has determined that the results from following tests and procedures that are done during the research study should not be included in any medical record you have. The researchers will take steps to make sure that these results are not placed in any Emory Healthcare medical record that you may have, and the results will not be made available to any other healthcare providers who may be giving you treatment. It will be up to you to let your healthcare providers know that you are in a clinical trial. These results will be kept by the researchers in a research record.

Results from other tests and procedures done during the study that are performed, analyzed and/or read at or for Emory Healthcare facilities that can be used for healthcare purposes and that are not listed above, will be included in any Emory Healthcare medical record that you have. Persons who have access to your medical record will be able to have access to all results that are placed there, and the results may be used by Emory Healthcare facilities to help provide you with medical care. Any results that are kept as part of your medical record are not covered by certain state and federal laws and regulations that may prevent the disclosure of research data. However, the confidentiality of the results in the medical record will be governed by laws such as HIPAA that concern medical records.

Emory University does not have any control over results from tests and procedures performed and/or analyzed or read at non-Emory Healthcare facilities. These results are NOT routinely included in medical records at Emory Healthcare facilities, and they will not necessarily be available to Emory Healthcare providers. Emory University also does not have control over any other medical records that you may have with other healthcare providers and will not send any test or procedure results from the study to these providers. It is up to you to let these healthcare providers know that you are participating in a clinical trial.

Some tests and procedures that may be performed during this study by Emory Healthcare or other facilities or persons MAY NOT BE LOOKED AT OR READ FOR ANY HEALTHCARE TREATMENT OR DIAGNOSTIC PURPOSES. THESE TESTS AND PROCEDURES WILL ONLY BE LOOKED AT FOR

RESEARCH PURPOSES AND THE RESULTS WILL NOT BE REVIEWED TO MAKE DECISIONS ABOUT YOUR PERSONAL HEALTH OR TREATMENT.

Due to confidentiality considerations, the Emory IRB has determined that a copy of your signed Informed Consent form and signed HIPAA Authorization form should not be included in your medical record. Accordingly, if you have an Emory Healthcare medical record, copies of these forms will not be placed there. However, the following information will be included in any Emory Healthcare medical record you have in lieu of including copies of these documents: (a) statement that you are enrolled in a research study and your informed consent has been obtained; (b) list of the contact information for the researcher who is in charge of the study; (c) description of any intervention required by other health care professionals to deal with any potential medical problems arising from the study; and (d) description of when and how health care providers may gain access to research information that may be necessary for the provision of medical treatment, and a statement that such research information will be provided to health care providers upon request.

COSTS AND COMPENSATION:

There are no costs to you for participating in this study. There is no financial reimbursement for participating in this study. In the event that injury occurs as a result of this research, medical treatment will be available. However, you will not be provided with reimbursement for medical care other than what your insurance carrier may provide, nor will you receive other compensation. Emory University, Emory University Hospital, The Emory Clinic, Emory Crawford Long Hospital, and Children's Healthcare of Atlanta have made no provisions for payment of costs associated with any injury resulting from participation in this study. For more information concerning the research and research related risks or injuries, you can contact Dr. Chapman, the investigator in charge at (404) 727-2525.

VOLUNTARY PARTICIPATION/WITHDRAWAL:

Participation in this study is voluntary. You are free to withdraw your participation at any time. Your decision to participate or not participate will in no way affect your current or future treatment. There will be no medical consequences if you decide not to participate or if you withdraw from the study. The investigator retains the right to withdraw subjects from the study if she thinks that it is in your or the study's best interest. If your participation is stopped, you will be notified in person. All information regarding this study will be made available to your treating physician.

CONTACT PERSONS:

To make inquiries concerning this study, contact Dr. Arlene Chapman at (404) 727-2525. If you have any questions or concerns about your rights as a participant in this research study, you may contact Colleen DiIorio, PhD, Chair, Emory University Institutional Review Board at (404) 712-0720.

NEW FINDINGS:

In the event that any significant new findings are developed during the course of the research, this information will be provided to you.

A copy of this consent form will be given to you. Your signature below indicates that you consent to volunteer for this study.

Subject's Name_____

Study No.: IRB00002998 **Emory University IRB** IRB use only Document Approved On: 10/30/2007 Project Approval Expires On: **3/27/2008**

I have read this authorization form and have been given the chance to ask questions about it. I am signing this form voluntarily and I understand that by signing I will be authorizing the Researchers to use and disclose my PHI as described in this form.

_____ _____ _____
Patient/Subject Signature Date Time

_____
Patient/Subject Printed Name

_____ _____ _____
Legal Guardian Signature Date Time

_____ _____ _____
Witness Date Time

_____ _____ _____
Signature of Person Obtaining Consent Date Time

_____
Printed Name of Person Obtaining Consent

Study No.: IRB00002998 | Emory University IRB IRB use only | Document Approved On: 10/30/2007 Project Approval Expires On: 3/27/2008

EMORY UNIVERSITY SCHOOL OF MEDICINE
INFORMED CONSENT FORM

TITLE: RENAL IMAGING TO ASSESS PROGRESSION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): EXTENSION (CRISP II)

Principal Investigator:	Arlene B. Chapman, MD	Internal Medicine	(404) 727-2525
Co-investigator:	Diego Martin, MD, PhD	Radiology	(404) 778-3800
Sub-investigator:	Frederic Rahbari Oskoui, MD	Internal Medicine	(404) 727-2525
	George Baramidze, MD	Internal Medicine	(404) 727-2525
Study Coordinator:	Yoosun Han	Internal Medicine	(404) 727-2525
Study Personnel:	Beth Wilkening, PA-C	Internal Medicine	(404) 686-8280
	Diane Watkins	Internal Medicine	(404) 727-2525
	Bijan Ahrari	Internal Medicine	(404) 727-2525
	Sharon Langley, MS	Internal Medicine	(404) 727-2525

Introduction:

You are being asked to take part in this research study because you have polycystic kidney disease (PKD) and you are a relative of a participant in the original Consortium for Radiologic Imaging Studies of Polycystic kidney disease (CRISP Study). The purpose of this study is to collect more exhaustive family histories of all CRISP I patients to draw an electronic pedigree of each family and to identify genetic factors that influence the severity of the cystic disease. Up to 370 affected relatives of CRISP I participants will be enrolled in the study at Emory University, Atlanta, GA (approximately five affected relatives for each of the 73 CRISP I participants studied at Emory University). Additional affected relatives will be enrolled at the other CRISP I sites including, the Mayo Clinic in Rochester, Minnesota, University of Alabama, Birmingham, and Kansas University Medical Center, Kansas City, MO. The National Institutes of Health are funding the study.

What will I be asked to do?

A blood sample (30 mL or approximately two tablespoonfuls) will be obtained by venipuncture for a measurement of serum creatinine and extraction of DNA. You will be asked to complete a lifestyle questionnaire (smoking history, caffeine use, estrogen use, and levels of physical activity) and a family history questionnaire. You will be asked to sign a release form to have the last imaging study (CT scan, MRI or ultrasound) of your kidneys sent to the investigator (Dr. Chapman) for her review. The entire procedure should take 15 minutes. Your blood will be processed in several ways for this study, one of which will include making an unlimited source of material for future study. By making an unlimited source, we will be able to continue this study for a long time without needing to ask for any fresh blood samples from you. Any biological products that are made from your sample will be stored at the NIDDK Central Repository. In order to protect your privacy, all samples and products made from your blood will be assigned an identification code that does not include any of your personal information. Your sample will be stored for as long as it is useful, unless you ask

us to destroy it sooner. You may request that your sample be destroyed at any time, simply by contacting the Principal Investigator (Arlene B. Chapman, MD at 404-727-2525 or 101 Woodruff Circle, suite 338, Atlanta, GA 30322) The Principal Investigator of this study may also share stored samples with other scientists for research purposes, but your name will not be given to them.

Are there any risks?

Collecting blood from a vein in your arm is a standard medical procedure, although sometimes there may be some discomfort or bruising. Because we will be looking at genetic information in your blood, there may also be other risks that we currently don't recognize or expect. For more information concerning potential research-related risks or injuries, you can contact Arlene B. Chapman, MD, the Principal Investigator for this study (404-727-2525 or 101 Woodruff Circle, suite 338, Atlanta, GA 30322).

Are there any benefits?

Although your participation in this study may not directly help you or your relatives, the results of this research project should help us understand more about polycystic kidney disease (PKD).

What about results or new findings?

The information that is learned from studies of your samples may be used scientifically, and may be used by the sponsor in other research. The results of our studies of your samples WILL NOT be made available to you or to your referring health care professional because your blood will be assigned an identification code that does not include any of your personal information and your name will not be given to scientists for research purposes.

What about my privacy?

All information about you will be kept private. Please understand, however, that research records, like hospital charts, can be obtained by court order. Also, the study's sponsor, The National Institutes of Health, including the Emory University Institutional Review Board, may review the information regarding your participation in this study. All information and medical records associated with your participation in this study will be kept private, except as explained above, or as specifically authorized by you in future communication. You will be identified by a unique code whenever possible. If information about you is published, we will write it in such a way that you cannot be recognized. Unless you disagree (see below), the Principal Investigator will keep a private list that links your sample code with your name, allowing him/her to know which samples were collected from you. You can request that we do not keep any information linking your name with your sample, but please understand that once we lose the ability to know which sample(s) came from you, we also lose the ability to destroy your samples upon request, or to respond to any future requests you may make regarding results or new information.

Please initial the line before "do" or "do not" to indicate your wishes.

I _____ do _____ do not want the Principal Investigator to retain information that links my sample with my name.

Will there be any costs or payments?

Study No.: IRB00002998 **Emory University IRB** IRB use only Document Approved On: 10/30/2007 Project Approval Expires On: **3/27/2008**

There will be no extra costs to you or your insurance company for participating in this study. The research aspects of this project are funded by The National Institutes of Health. Similarly, you and/or your relatives will not receive any money for participating in this study. You should also understand that blood removed from you for this study may be valuable for scientific, research, or teaching purposes, or for the development of new medical products. By agreeing to participate in this research, you authorize Emory University and members of its staff to use your blood for these purposes. If this future research leads to the development of new diagnostic tests, new medicines, or other uses that may be commercially valuable, you will receive no financial benefits.

What if I am injured?

In the very unlikely event that you are injured as a result of this blood drawing, medical treatment will be made available to you. However, it will be your responsibility and your insurance carrier's responsibility to pay for this care, and you will not receive any other payments. Emory University has not set aside any funds for payment of costs associated with any injury resulting from participation in this study.

What are my options?

Participation in this study is voluntary. You are free not to participate in this study, or to withdraw your participation at any time. Your decision to participate or not participate in this study will in no way affect your current or future medical treatment. Should you wish to withdraw once you have already donated samples, simply notify Arlene B. Chapman, MD at 404-727-2525 or 101 Woodruff Circle, suite 338, Atlanta, GA 30322. Similarly, you do not have to agree to participate in any follow-up activities that may be asked of you at a later time.

Who should I call if I have questions?

If you have any questions about this study, please contact the Principal Investigator, Arlene B. Chapman, MD at 404-727-2525 or 101 Woodruff Circle, suite 338, Atlanta, GA 30322. If you have further questions about your rights as a volunteer, you may contact Dr. Colleen DiIorio, the Chair of the Emory University Institutional Review Board (IRB), at 404-712-0720.

A copy of this consent form will be given to you.

Your signature below indicates that you consent to volunteer either yourself, or the child or adult for whom you serve as guardian (as indicated), for participation in this study.

_____	_____	_____	_____
Signature (patient/subject)	Date/Time	Signature (parent or guardian)	Date/Time

_____	_____
Signature (person obtaining consent)	Date/Time

Subject's Name_____

Study No.: IRB00002998 | Emory University IRB IRB use only | Document Approved On: 10/30/2007 Project Approval Expires On: 3/27/2008

EMORY UNIVERSITY SCHOOL OF MEDICINE INFORMED CONSENT FORM

TITLE: RENAL IMAGING TO ASSESS PROGRESSION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): EXTENSION (CRISP II)

Principal Investigator:	Arlene B. Chapman, MD	Internal Medicine	(404) 727-2525
Co-investigator:	Diego Martin, MD, PhD	Radiology	(404) 778-3800
Sub-investigator:	Frederic Rahbari Oskoui, MD	Internal Medicine	(404) 727-2525
	George Baramidze, MD	Internal Medicine	(404) 727-2525
Study Coordinator:	Yoosun Han	Internal Medicine	(404) 727-2525
Study Personnel:	Beth Wilkening, PA-C	Internal Medicine	(404) 686-8280
	Diane Watkins	Internal Medicine	(404) 727-2525
	Bijan Ahrari	Internal Medicine	(404) 727-2525
	Sharon Langley, MS	Internal Medicine	(404) 727-2525

Introduction:

You are being asked to take part in this research study because you have polycystic kidney disease (PKD) and you are a relative of a participant in the original Consortium for Radiologic Imaging Studies of Polycystic kidney disease (CRISP Study). The purpose of this study is to collect more exhaustive family histories of all CRISP I patients to draw an electronic pedigree of each family and to identify genetic factors that influence the severity of the cystic disease. Up to 370 affected relatives of CRISP I participants will be enrolled in the study at Emory University, Atlanta, GA (approximately five affected relatives for each of the 73 CRISP I participants studied at Emory University). Additional affected relatives will be enrolled at the other CRISP I sites including, the Mayo Clinic in Rochester, Minnesota, University of Alabama, Birmingham, and Kansas University Medical Center, Kansas City, MO. The National Institutes of Health are funding the study.

What will I be asked to do?

A blood sample (30 mL or approximately two tablespoonfuls) will be obtained by venipuncture for a measurement of serum creatinine and extraction of DNA. You will be asked to complete a lifestyle questionnaire (smoking history, caffeine use, estrogen use, and levels of physical activity) and a family history questionnaire. You will be asked to sign a release form to have the last imaging study (CT scan, MRI or ultrasound) of your kidneys sent to the investigator (Dr. Chapman) for her review. The entire procedure should take 15 minutes. Your blood will be processed in several ways for this study, one of which will include making an unlimited source of material for future study. By making an unlimited source, we will be able to continue this study for a long time without needing to ask for any fresh blood samples from you. Any biological products that are made from your sample will be stored at the NIDDK Central Repository. In order to protect your privacy, all samples and products made from your blood will be assigned an identification code that does not include any of your personal information. Your sample will be stored for as long as it is useful, unless you ask

Study No.: IRB00002998 | Emory University IRB IRB use only | Document Approved On: 10/30/2007 Project Approval Expires On: 3/27/2008

us to destroy it sooner. You may request that your sample be destroyed at any time, simply by contacting the Principal Investigator (Arlene B. Chapman, MD at 404-727-2525 or 101 Woodruff Circle, suite 338, Atlanta, GA 30322) The Principal Investigator of this study may also share stored samples with other scientists for research purposes, but your name will not be given to them.

Are there any risks?

Collecting blood from a vein in your arm is a standard medical procedure, although sometimes there may be some discomfort or bruising. Because we will be looking at genetic information in your blood, there may also be other risks that we currently don't recognize or expect. For more information concerning potential research-related risks or injuries, you can contact Arlene B. Chapman, MD, the Principal Investigator for this study (404-727-2525 or 101 Woodruff Circle, suite 338, Atlanta, GA 30322).

Are there any benefits?

Although your participation in this study may not directly help you or your relatives, the results of this research project should help us understand more about polycystic kidney disease (PKD).

What about results or new findings?

The information that is learned from studies of your samples may be used scientifically, and may be used by the sponsor in other research. The results of our studies of your samples WILL NOT be made available to you or to your referring health care professional because your blood will be assigned an identification code that does not include any of your personal information and your name will not be given to scientists for research purposes.

What about my privacy?

All information about you will be kept private. Please understand, however, that research records, like hospital charts, can be obtained by court order. Also, the study's sponsor, The National Institutes of Health, including the Emory University Institutional Review Board, may review the information regarding your participation in this study. All information and medical records associated with your participation in this study will be kept private, except as explained above, or as specifically authorized by you in future communication. You will be identified by a unique code whenever possible. If information about you is published, we will write it in such a way that you cannot be recognized. Unless you disagree (see below), the Principal Investigator will keep a private list that links your sample code with your name, allowing him/her to know which samples were collected from you. You can request that we do not keep any information linking your name with your sample, but please understand that once we lose the ability to know which sample(s) came from you, we also lose the ability to destroy your samples upon request, or to respond to any future requests you may make regarding results or new information.

Please initial the line before "do" or "do not" to indicate your wishes.

I _____ do _____ do not want the Principal Investigator to retain information that links my sample with my name.

Will there be any costs or payments?

Study No.: IRB00002998 **Emory University IRB** IRB use only Document Approved On: 10/30/2007 Project Approval Expires On: **3/27/2008**

There will be no extra costs to you or your insurance company for participating in this study. The research aspects of this project are funded by The National Institutes of Health. Similarly, you and/or your relatives will not receive any money for participating in this study. You should also understand that blood removed from you for this study may be valuable for scientific, research, or teaching purposes, or for the development of new medical products. By agreeing to participate in this research, you authorize Emory University and members of its staff to use your blood for these purposes. If this future research leads to the development of new diagnostic tests, new medicines, or other uses that may be commercially valuable, you will receive no financial benefits.

What if I am injured?

In the very unlikely event that you are injured as a result of this blood drawing, medical treatment will be made available to you. However, it will be your responsibility and your insurance carrier's responsibility to pay for this care, and you will not receive any other payments. Emory University has not set aside any funds for payment of costs associated with any injury resulting from participation in this study.

What are my options?

Participation in this study is voluntary. You are free not to participate in this study, or to withdraw your participation at any time. Your decision to participate or not participate in this study will in no way affect your current or future medical treatment. Should you wish to withdraw once you have already donated samples, simply notify Arlene B. Chapman, MD at 404-727-2525 or 101 Woodruff Circle, suite 338, Atlanta, GA 30322. Similarly, you do not have to agree to participate in any follow-up activities that may be asked of you at a later time.

Who should I call if I have questions?

If you have any questions about this study, please contact the Principal Investigator, Arlene B. Chapman, MD at 404-727-2525 or 101 Woodruff Circle, suite 338, Atlanta, GA 30322. If you have further questions about your rights as a volunteer, you may contact Dr. Colleen DiIorio, the Chair of the Emory University Institutional Review Board (IRB), at 404-712-0720.

A copy of this consent form will be given to you.

Your signature below indicates that you consent to volunteer either yourself, or the child or adult for whom you serve as guardian (as indicated), for participation in this study.

_____	_____	_____	_____
Signature (patient/subject)	Date/Time	Signature (parent or guardian)	Date/Time

_____	_____
Signature (person obtaining consent)	Date/Time

Subject's Name_____

Version Date(s): 11/07/07

Mayo Clinic Consent Form

MAYO CLINIC

IRB # 06-009502 00
Consent form approved **April 12, 2007**;
This consent valid through **April 11, 2008**;

1. General Information About This Research Study

Study Title: "Consortium for Radiologic Imaging Studies of Polycystic Kidney Diesase (CRISP II)" (Proband)

Name of Principal Investigator on This Study: Dr. V. E Torres and Colleagues

A. Study Eligibility and Purpose

You are being asked to take part in this research study because you have polycystic kidney disease (PKD) and you participated in the original Consortium for Radiologic Imaging studies of polycystic kidney disease (CRISP) Study. The purpose of this study is to continue following you for another four years to determine if pictures of your kidney using magnetic resonance imaging (MRI) can detect change in kidney size over a short period of time. If you enroll, you will participate for 48 months (4 years).

As you read this form describing the study, ask any questions you have. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you decide. You may stop participating at any time during the study. You may decide not to participate. If so, none of your current benefits or normal health care will be affected in any way. When you feel comfortable that all your questions have been answered, and you wish to take part in this study, sign this form in order to begin your participation. If you are agreeing for someone else, you need to sign this form. Your signature means you have been told about the study and what the risks are. Your signature on this form also means that you want yourself to take part in this study.

If you are unclear about anything along the way, please ask until you feel you understand.

B. Number of Participants

At least 210 subjects will be enrolled in this study in the United States. Fifty-eight (58) people will be enrolled at the Mayo Clinic in Rochester, Minnesota. The other sites include Emory University, Atlanta, GA, University of Alabama, Birmingham, and Kansas University Medical Center, Kansas City, MO.

C. Additional Information You Should Know

The NIH is funding the study.
The NIH will pay your study healthcare provider or the institution to cover costs related to your participation in the study.

MAYO CLINIC

2. What Will Happen to You While You Are in This Research Study?

If you agree to be in the study, you will be asked to participate in the following:
You will be scheduled for visits, Baseline (Year 1) and 3 yearly follow-up visits (Year 2. Year 3, and the last visit Year 4)

A. Baseline (Year 1) and Year 3 Visits

For these visits you will be admitted to the In-Patient Clinical Research Unit (CRU) at St. Mary's Hospital. The following tests and examinations will be performed at that visit:

A medical history, medication history, and complete physical exam will be done to determine your overall health. The physical exam will include height, weight, and blood pressure measurements

You will have blood pressures measured at least six times using a technique similar to that used in CRISP I.

A blood test to determine pregnancy will be performed on women with child-bearing potential prior to undergoing any tests. You will be told if you are pregnant. If you are pregnant, your participation in the study will be postponed.

Blood samples will be obtained during your visit to determine your chemistry and cholesterol profile, and other markers that may identify risk for renal (kidney) failure in PKD. About 50 ml or 4 tablespoons of blood will be taken for these tests. A fresh urine sample will be collected for measurements of albumin, creatinine, and other markers that may identify risk for renal failure in PKD. Deidentified blood and urine samples will be stored in a central repository and shared with other CRISP investigators. These samples will be identified only by a special CRISP assigned number.

A specialized test of your kidney function with blood and urine collections will be performed at Year 1 and Year 3. Your kidney function will be measured using a special test called a GFR Test (Glomerular Filtration Rate). This test measures the kidney's ability to filter and clean the blood. A substance called Iothalamate will be injected under your skin in the upper arm. This substance is absorbed from the injection site into the blood and is carried to the kidneys for filtration. Also, during this test two small blood samples (1 teaspoon [5 ml] each) will be obtained by placing a needle in the vein in your arm. Before and during this test you will not be allowed to eat food. However, you will be asked to drink water several times because it is important for the accuracy of the test. You will be asked to complete three urine collections in the course of the test. A small machine, called a Bladder Monitor, will be used to be sure that your bladder empties completely when doing these urine collections. For this examination, jelly will be placed on the skin and a probe that measures bladder volume will be moved over the skin. The GFR test will take approximately two hours to complete.

MAYO CLINIC

A Magnetic Resonance Imaging (MRI) study will be done to determine the size of your kidneys. The MRI will be performed without administration of contrast (gadolinium). An MRI involves lying still in a hollow tube or scanner for short periods of time. The total duration of the MRI will be approximately 45 minutes. You are moved slowly through the scanner while images of your kidneys are made. There is no radiation exposure associated with this procedure. The MRI will be done at Year 1 and Year 3.

At the Year 1visit only, if you have not already done so during your CRISP I study participation, you will be asked to provide a blood sample for genetic testing. This testing requires obtaining approximately 2 tablespoons (30 ml) of blood from your arm. The doctors involved in this study will isolate genetic material (DNA) from the deidentified (identified by CRISP ID number only) blood sample in order to study the family factors, or genes, that are inherited and cause Autosomal Dominant Polycystic Kidney Disease (ADPKD). Because the genetic tests in this study are not used for regular medical care, you will not be told the results of the test(s). The test results will also not be put in your medical record. In addition, if you agree, your blood cells will be put through a process called immortalization, to enable the researchers to have DNA for future research studies related to this project. In case either the DNA isolation or the immortalization process fails you may be asked to provide an additional blood sample to repeat the procedure. When these studies are completed, this procedure will allow researchers access to deidentified blood samples to perform additional tests on samples known to be related to this disease (PKD).

A major part of CRISP II is to collect more complete and updated family histories of all CRISP I patients and create an electronic pedigree for each family. You will be asked to provide contact information and permission to contact family members who might be at risk of having Polycystic Kidney Disease. With this information, we will contact the family members you give us permission to contact. We will ask your family members whether they are known to have Polycystic Kidney Disease and, if so, whether they are interested in participating in the study. Affected family members who agree to participate will sign a consent form and provide a blood sample for serum creatinine and DNA extraction. Affected relatives will also be asked to complete a lifestyle questionnaire (smoking history, caffeine use, estrogen use, and levels of physical activity) and a family history questionnaire. Permission to review their most recent imaging study of the kidneys (preferably CT or MRI; ultrasound if CT or MRI is not available) will also be requested.

B. Year 2 and Year 4 Visits

On Year 2 and 4 you will be asked to provide a blood sample for measurement of serum creatinine in a central laboratory. The blood sample can be obtained either at the Mayo Clinic in Rochester or at a local laboratory near your home. If the blood sample is obtained at a local laboratory, we will provide you with the appropriate tube labeled with the CRISP identification number, and a mailing container with instructions.

MAYO CLINIC

C. Semi-annual telephone interviews.

Every six months, the CRISP study coordinator will contact you to obtain information regarding any medication changes, hospitalizations, doctor visits and outpatient procedures. We will ask your permission to contact and obtain information regarding your health from any physician who has examined or treated you since your last visit or telephone interview.

You will continue to be under the care of your primary physician at home. You will be asked to keep a journal of any change in medications, whether prescribed or over the counter. You will be asked if you have had any medication changes, illnesses, or hospitalizations. These phone calls will not be longer than 30 minutes. Information may also be obtained from your doctor during this time.

You should tell the study coordinator and/or research doctor if you:

Are hospitalized
Have any surgery performed
Have any radiology tests.

If you are hospitalized, have any surgery performed , or radiology tests (such as an x-ray, CT scan, Ultrasound, or other tests) Mayo Researchers will ask you if they may obtain copies of the medical records from *the* hospital that you are located at.

The CRISP II protocol does not exclude participants that enroll in other interventional trials. If, as a CRISP II participant, you are recruited into an interventional trial (e.g. HALT clinical trial that also requires imaging studies) the visits for CRISP II and for the interventional trial will be coordinated to avoid duplication of tests and undue burden on you. You will, however, complete the necessary studies of CRISP II that are not included in HALT.

If you are also a participant in the National Institutes of Health (NIH) sponsored HALT clinical trial, please read the following statements and make your choice:

1. I permit the deidentified information (identified by CRISP ID number only) collected for the CRISP study to be provided to the HALT investigators

☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit deidentified information (identified by HALT ID number only) collected for the HALT study to be provided to the CRISP investigators

☐ Yes ☐ No Please initial here: _____Date: _____

MAYO CLINIC

3. How Long Will You Be in This Research Study?

You will be in this study for four years.

4. Why You Might Want To Take Part in This Research Study

This study will not make your health better. It is for the benefit of research.

The first phase of the CRISP study (CRISP I) in which you participated has helped to understand how polycystic kidney disease progresses. CRISP II will provide more information that will be extremely valuable for the design of clinical trials to test possible treatments. You or your family may benefit from this increased knowledge.

5. What Are the Risks of This Research Study?

The risks of drawing blood include pain, bruising, or rarely, infection at the site of the needle stick.

The risks of intravenous catheter placements (IV) include pain, bruising and infection. Because the intravenous line is in place for an approximately 2 hours for the GFR test, you may have mild discomfort for a few days after the test.

In rare cases (less than 1 in 50,000) there is a risk of allergic reaction to Iothalamate Meglumine used in the GRF test for this study. This amount of iothalamate is not dangerous to the kidney function.

There are no known risks from the Magnetic Resonance Imaging (MRI). Because some concerns have been recently raised about the use of gadolinium (a contrast agent) for MRI in patients with advanced renal insufficiency, MRI examinations for CRISP II will be performed without administration of contrast. The hollow tube in the MRI machine is narrow and some people have experienced anxiety related to feeling closed-in (claustrophobia). This occurs in approximately 12% of people. If you have any pacemakers or metal objects that are not compatible with a Magnetic Resonance Imaging machine, you can be in the study, but will not be permitted to have the MRI.

MAYO CLINIC

A. Pregnancy and Birth Control:

1) Will sexually active, pregnant, and/or nursing women be allowed to participate in this study?

No: There is not enough medical information to know what the risks might be to a breast-fed infant or to an unborn child carried by a woman who takes part in this study. Breast-feeding mothers must stop breast-feeding to take part in this study.

2) Do you have to take a pregnancy test to be part of the study?
Yes: As part of this study a pregnancy test is required for all women who are able to become pregnant.

A blood pregnancy test will be given by taking blood from your arm.

You will be told the results of the pregnancy test. If the pregnancy test is positive, you will not be able to take part in the study.

3) Will men who are sexually active be allowed to participate in this study?

Yes: Men who are sexually active and could impregnate a woman are allowed to take part in this study.

4) What types of birth control are acceptable?
Surgical sterilization
Approved hormonal contraceptives (such as birth control pills, Depo-Provera, or Lupron Depot)
Barrier methods (such as a condom or diaphragm) used with a spermicide
An intrauterine device (IUD)

B. Risk summary

Many side effects go away shortly after the GFR and MRI are stopped, but in some cases side effects can be serious, long lasting, or may never go away. Some side effects may not be known. Side effects may range from mild to life-threatening. Other drugs may be given to make side effects less serious and uncomfortable. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.

6. What Other Choices Do You Have If You Don't Take Part in This Research Study?

This study is only being done to gather information. You may choose not to take part in this study.

MAYO CLINIC

7. Are there Reasons You Might Leave This Research Study Early?

Taking part in this research study is your decision. You may decide to stop at any time. You should tell the researcher if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the researchers, NIH, or Mayo may stop you from taking part in this study at any time:

- if it is in your best interest,
- if you do not follow the study rules,
- if the study is stopped.

8. Will You Need to Pay for Any of the Tests and Procedures?

You will not need to pay for tests and procedures which are done just for this research study. These tests and procedures are:

- MRI
- GFR Test
- Blood tests (Serum Pregnancy tests, Creatinine, blood for DNA/Genetic testing, Chemistry, Cholesterol profile)

However, you and/or your health plan will need to pay for all other tests and procedures that you would normally have as part of your regular clinical care.

9. Will You Be Paid for Participating in this Research Study?

You will be reimbursed for travel expenses including: gas, mileage, parking, hotels, meals, airfare, etc. up to $300. In order to receive reimbursement, you must provide a copy of the original receipts for those expenses.

MAYO CLINIC

10. What Happens if You Are Injured or Ill Because You Were in this Research Study?

If you have side effects from taking part in this study, you need to report them to the researcher and your regular physician, and you will be treated as needed. Mayo will give medical services for treatment for any bad side effects from taking part in this study. Such services will be free if not covered by a health plan or insurance. No additional money will be offered.

11. What Are Your Rights if You Are in This Research Study?

Taking part in this research study will not change your rights and benefits. Taking part in this research study does not give you any special privileges. If you decide to not participate in this study, or stop in the middle of the study, no benefits are taken away from you. Specifically, you do not have to be in this research study to receive or continue to receive medical care from Mayo Clinic.

You will be told of important new findings or any changes in the study or procedures that may affect you or your willingness to continue in the study.

12. What About Your Privacy?

Authorization To Use And Disclose Protected Health Information

Your privacy is important to us, and we want to protect it as much as possible. By signing this form, you authorize Mayo Clinic and the investigators to use any information created or collected in the course of your participation in this research protocol. This information might be in different places, including your original medical record, but we will only disclose information that is related to this research protocol for the purposes listed below.

This information will be given out for the proper monitoring of the study, checking the accuracy of study data, analyzing the study data, and other purposes necessary for the proper conduct and reporting of this study. If some of the information is reported in published medical journals or scientific discussions, it will be done in a way that does not directly identify you.

MAYO CLINIC

This information may be given to other researchers in this study, including those at other institutions, representatives of the company sponsoring the study, including representatives in the USA or other countries, or private, state or federal government parties or regulatory authorities in the USA and other countries responsible for overseeing this research. These may include the Food and Drug Administration, the Office for Human Research Protections, or other offices within the Department of Health and Human Services, and the Mayo Clinic Office for Human Research Protections or other Mayo groups involved in protecting research subjects.

If this information is given out to anyone outside of Mayo, the information may no longer be protected by federal privacy regulations and may be given out by the person or entity that receives the information. However, this information will always be deidentified and Mayo will take steps to help other parties understand the need to keep this information confidential.

You may stop this authorization at any time by writing to the following address:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
200 1st Street SW
Rochester, MN 55905

If you stop authorization, Mayo may continue to use your information already collected as part of this study, but will not collect any new information.

This authorization lasts forever.

13. What Will Happen to Your Samples?

Your sample of blood will be kept at Mayo for use in this study. Researchers at Mayo who are not involved with this study may ask to use your sample for more research. You have a say in how your stored sample is used in future research. You can still take part in the in the data collecting study without giving your sample for future use.

Exceptions when your samples may be used without your permission:

1) When government rules allow your sample to be used without identifying you, even with a code.
2) When use of the sample is not considered human subject research.

At all other times:
-You can let Mayo use your sample.
-You can say NO to have your sample used by Mayo.

Identification information:
If you agree to allow your sample to be used for further research, the sample may be stored forever. The sample will be stored at Mayo and would be given a code (instead of

MAYO CLINIC

your name) while it is stored and when it is used in research. This code allows your sample to be used without anyone knowing that it is your sample just by looking at the label.

There is a very small chance that some commercial value may result from the use of your donated sample. If that happens, you will not be offered a share in any profits.

Risks:
Some future studies may be for testing the genes you inherited from your parents (also known as genetic testing). If a researcher finds that future test results may be useful for your health care, you will be contacted and given the choice to learn the test results. At that time, you will be given general information on the potential risks, benefits, and costs of choosing to learn the test results. The risks of learning genetic test results may include emotional upset, insurance or job discrimination, and/or family conflicts from learning unknown information about your parents or blood relatives. Test results will only be put into your medical record if you chose to learn the results. Sometimes results should be released only through a genetic counselor, who can help explain the possible risks and benefits of learning the results.

Please read the following statements and mark your choice:

1. I permit my sample to be stored and used in future research of autosomal dominant polycystic kidney disease at Mayo:

☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my sample to be stored and used in future research at Mayo to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

Who will use your sample?
If you agree to give your sample, it will be the property of Mayo and may be used for research by Dr. Vicente Torres and other staff at Mayo Clinic. Researchers at other institutions may also ask for a part of your sample for future studies.

How do researchers from other institutions get the sample?
Researchers from universities, hospitals, and other health organizations conduct research using tissue. They may contact Mayo and request samples for their studies. If you approve release of your sample by checking 'yes' below, Mayo may send the tissue sample(s) and some information about you to researchers who request them, but Mayo will not send your name, address, phone number, social security number, or any other identifying information with the sample. If you allow your sample to be given to researchers at other institutions, it will be given to them with a code number rather than your name. If these researchers use the sample for future research and decide that a test result may be useful for your health care, they may contact the Mayo Clinic and Mayo would then contact you to offer you the choice to learn the test results.

MAYO CLINIC

I permit Mayo to give my sample to researchers at other institutions:
Please mark one box:

☐ Yes ☐ No Please initial here: _____Date: _____

Mayo has the right to end storage of the sample without telling you

Researchers at other institutions are asking for a part of your blood sample for research studies. You can still take part in the treatment study or in the data collecting study without giving your sample. If you decide to give your sample, it would be given a code (not your name) when it is given to researchers at other institutions. This code allows your sample to be used without these researchers knowing that it is your sample just by looking at the label. The sample may be used for future research and may be stored forever.

When donating your samples, Mayo will then own them. The Sponsors of this study or researchers at other institutions do not. Some future studies may be for testing the genes you inherited from your parents (also known as genetic testing). If the researchers at other institutions, not commercial sponsors use the sample for future research and decide that a test result may be useful for your health care, they may contact the Mayo Clinic and Mayo would then contact you to ask whether you choose to learn the test results. At that time, you would be given general information on the potential risks, benefits, and costs of choosing to learn the test results. The risks of learning genetic test results may include emotional upset, insurance or job discrimination, and/or family conflicts from learning unknown information about your parents or blood relatives. Sometimes results should be released through a genetic counselor who can help explain the possible risks and benefits of learning this information.

I permit Mayo to give my sample to researchers at other institutions (not a commercial sponsor):

☐ Yes ☐ No Please initial here: _____ Date:

Mayo has the right to end storage of the sample without telling you

If you want your sample destroyed at any time, write to:

Dr. Vicente Torres
Nephrology and Hypertension
Eisenberg Building
200 First Street Southwest
Rochester, MN 55905

MAYO CLINIC

If you move please send your new address to

Mayo Clinic Rochester
Section of Registration
200 First Street Southwest
Rochester, MN 55905

14. What is the Institutional Review Board (IRB) and How Does it Protect You?

The Mayo Clinic IRB is made up of:

- Scientists
- IRB Specialists
- Allied Health Employees
- Local Community Members
- Visitors (Lawyers, Compliance, Administration, and others)

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have been treated unfairly.

15. Who Can Answer Your Questions?

You can call …	At …	If you have questions or concerns about …
Principal Investigator: Dr. Vicente Torres	**Phone:** 507-284-2511 (Mayo Clinic Operators)	**Questions about the study tests and procedures** **Research-related injuries or emergencies** **Any research-related concerns or complaints**
IRB Administrator: Marcia Andresen-Reid	**Phone:** 507-266-4000 **Toll-Free:** 866-273-4681	**Rights of a research subject** **Use of protected health information** **Any research-related concerns or complaints**
Research Billing	**Rochester:** 507-287-1819	**Billing / Insurance Questions**

MAYO CLINIC

16. Summary and Enrollment Signatures

You have been asked to take part in a clinical trial, also called a research study, at Mayo Clinic. The information about this study has been provided to you to inform you about the nature of this IRB approved study.

- I have read the whole consent form, and all of my questions have been answered to my satisfaction.
- I know that joining the study is voluntary and I agree to join the study.
- I know enough about the purpose, methods, risks, and possible benefits of the study to decide that I want to join.
- I know that I can call the investigator and research staff at any time with any new questions or to tell them about side effects.
- I understand that a copy of this form will be put in my medical records and that I will be given a copy of this completed form.
- I understand that I may withdraw from the study at any time.

Please sign and date to show that you have read and understand all of the above guidelines. Please do not sign unless you have read the entire packet of information. If you do not want to sign, you don't have to, but if you don't you cannot participate in this research study.

_____	_____	_____
(Date / Time)	(Printed Name of Participant)	(Clinic Number)

_____
(Signature of Participant)

_____	_____
(Date / Time)	(Printed Name of Individual Obtaining or in Receipt of Consent)

_____
(Signature of Individual Obtaining or in Receipt of Consent)

MAYO CLINIC

IRB # **06-009502 01**
Consent form approved **April 12, 2007**;
This consent valid through **April 11, 2008**;

1. General Information About This Research Study

Study Title: "Consortium for Radiologic Imaging Studies of Polycystic Kidney Diesase (CRISP II)" (Relatives)

Name of Principal Investigator on This Study: Dr. V. E Torres and Colleagues

A. Study Eligibility and Purpose

You are being asked to take part in this research study because you have polycystic kidney disease (PKD) and you are a relative of a participant in the original Consortium for Radiologic Imaging Studies of Polycystic kidney disease (CRISP Study). The purpose of this study is to collect more exhaustive family histories of all CRISP patients and draw an electronic pedigree of each family.

As you read this form describing the study, ask any questions you have. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare provider before you decide. You may stop participating at any time during the study. You may decide not to participate. If so, none of your current benefits or normal health care will be affected in any way. When you feel comfortable that all your questions have been answered, and you wish to take part in this study, sign this form in order to begin your participation. If you are agreeing for someone else, you need to sign this form. Your signature means you have been told about the study and what the risks are. Your signature on this form also means that you want yourself or your child to take part in this study.

If you are unclear about anything along the way, please ask until you feel you understand.

B. Number of Participants

Up to 300 affected relatives of CRISP participants will be enrolled in the study at the Mayo Clinic in Rochester, Minnesota (approximately five affected relatives for each of the 58 CRISP participants studied at the Mayo Clinic). Additional affected relatives will be enrolled at the other CRISP sites including Emory University, Atlanta, GA, University of Alabama, Birmingham, and Kansas University Medical Center, Kansas City, MO.

C. Additional Information You Should Know

The NIH is funding the study. The NIH will pay your study healthcare provider or the institution to cover costs related to your participation in the study.

MAYO CLINIC

2. What Will Happen to You While You Are in This Research Study?

A blood sample (30 mL or approximately two tablespoonfuls) will be drawn for testing and DNA extraction. You will be asked to complete a lifestyle questionnaire (smoking history, caffeine use, estrogen use, and levels of physical activity) and a family history questionnaire. You will be asked to sign a consent form to have the last imaging study (CT scan, MRI or ultrasound) of your kidneys sent to the investigator (Dr. Torres) for his review.

3. How Long Will You Be in This Research Study?

You will be in this study for one day.

4. Why You Might Want To Take Part in This Research Study

This study will not make your health better. It is for the benefit of research. However, your participation in this study will provide information that will help to understand why the progression of polycystic kidney disease varies markedly from patient to patient even within the same family.

5. What Are the Risks of This Research Study?

The risks of drawing blood include pain, bruising, or rarely, infection at the site of the needle stick.

Pregnancy and Birth Control:

1) Will sexually active, pregnant, and/or nursing women be allowed to participate in this study?

   Yes: Women who are sexually active, pregnant, and/or nursing may take part in this study because the risk to an unborn or nursing child appears very small.

MAYO CLINIC

2) Will men who are sexually active be allowed to participate in this study?

Yes: Men who are sexually active and could impregnate a woman are allowed to take part in this study.

The risks of this research study are minimal, which means that we do not believe that they will be any different than what you would experience at a routine clinical visit or during your daily life.

6. What Other Choices Do You Have If You Don't Take Part in This Research Study?

This study is only being done to gather information. You may choose not to take part in this study.

7. Are there Reasons You Might Leave This Research Study Early?

Taking part in this research study is your decision. You may decide to stop at any time. You should tell the researcher if you decide to stop and you will be advised whether any additional tests may need to be done for your safety.

In addition, the researchers, or Mayo may stop you from taking part in this study at any time:

- if it is in your best interest,
- if you do not follow the study rules,
- if the study is stopped.

8. Will You Need to Pay for Any of the Tests and Procedures?

You will not need to pay for tests and procedures which are done just for this research study. These tests and procedures include venipuncture, measurement of serum creatinine and extraction of blood DNA for genetic testing.

You and/or your health plan will need to pay for other tests and procedures that you would normally have as part of your regular clinical care.

MAYO CLINIC

9. Will You Be Paid for Participating in this Research Study?

You will not be paid for taking part in this study.

10. What Happens if You Are Injured or Ill Because You Were in this Research Study?

If you have side effects from taking part in this study, you need to report them to the researcher and your regular physician, and you will be treated as needed. Mayo will give medical services for treatment for any bad side effects from taking part in this study. Such services will be free if not covered by a health plan or insurance. No additional money will be offered.

11. What Are Your Rights if You Are in This Research Study?

Taking part in this research study will not change your rights and benefits. Taking part in this research study does not give you any special privileges. If you decide to not participate in this study, or stop in the middle of the study, no benefits are taken away from you. Specifically, you do not have to be in this research study to receive or continue to receive medical care from Mayo Clinic.

You will be told of important new findings or any changes in the study or procedures that may affect you or your willingness to continue in the study.

12. What About Your Privacy?

Authorization To Use And Disclose Protected Health Information

Your privacy is important to us, and we want to protect it as much as possible. By signing this form, you authorize Mayo Clinic and the investigators to use and disclose any information created or collected in the course of your participation in this research protocol. This information might be in different places, including your original medical record, but we will only disclose information that is related to this research protocol for the purposes listed below.

MAYO CLINIC

This information will be given out for the proper monitoring of the study, checking the accuracy of study data, analyzing the study data, and other purposes necessary for the proper conduct and reporting of this study. If some of the information is reported in published medical journals or scientific discussions, it will be done in a way that does not directly identify you.

Information Disclosed to Study Sponsor
The study data sent by the study doctor to the sponsor does not include your name, address, social security number, or other information that directly identifies you. Instead, the study doctor assigns a code number to the study data and may use your initials. Some study data sent to the sponsor may contain information that could be used (perhaps in combination with other information) to identify you (eg, date of birth). If you have questions about the specific health information that will be sent to the sponsor, you should ask the study doctor.

This information may be given to other researchers in this study, including those at other institutions, representatives of the company sponsoring the study, including representatives in the USA or other countries, or private, state or federal government parties or regulatory authorities in the USA and other countries responsible for overseeing this research. These may include the Food and Drug Administration, the Office for Human Research Protections, or other offices within the Department of Health and Human Services, and the Mayo Clinic Office for Human Research Protections or other Mayo groups involved in protecting research subjects.

If this information is given out to anyone outside of Mayo, the information may no longer be protected by federal privacy regulations and may be given out by the person or entity that receives the information. However, Mayo will take steps to help other parties understand the need to keep this information confidential.

You may stop this authorization at any time by writing to the following address:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
200 1st Street SW
Rochester, MN 55905

If you stop authorization, Mayo may continue to use your information already collected as part of this study, but will not collect any new information.

This authorization lasts forever.

13. What Will Happen to Your Samples?

Your sample of blood will be kept at Mayo for use in this study. Researchers at Mayo who are not involved with this study may ask to use your sample for more research. You

MAYO CLINIC

have a say in how your stored sample is used in future research. You can still take part in the in the data collecting study without giving your sample for future use.

Exceptions when your samples may be used without your permission:

1) When government rules allow your sample to be used without identifying you, even with a code.
2) When use of the sample is not considered human subject research.

At all other times:
-You can let Mayo use your sample.
-You can say NO to have your sample used by Mayo.

Identification information:
If you agree to allow your sample to be used for further research, the sample may be stored forever. The sample will be stored at Mayo and would be given a code (instead of your name) while it is stored and when it is used in research. This code allows your sample to be used without anyone knowing that it is your sample just by looking at the label.

There is a very small chance that some commercial value may result from the use of your donated sample. If that happens, you will not be offered a share in any profits.

Risks:
Some future studies may be for testing the genes you inherited from your parents (also known as genetic testing). If a researcher finds that future test results may be useful for your health care, you will be contacted and given the choice to learn the test results. At that time, you will be given general information on the potential risks, benefits, and costs of choosing to learn the test results. The risks of learning genetic test results may include emotional upset, insurance or job discrimination, and/or family conflicts from learning unknown information about your parents or blood relatives. Test results will only be put into your medical record if you chose to learn the results. Sometimes results should be released only through a genetic counselor, who can help explain the possible risks and benefits of learning the results.

Please read the following statements and mark your choice:

1. I permit my sample to be stored and used in future research of autosomal dominant polycystic kidney disease at Mayo:

☐ Yes ☐ No Please initial here: _____Date: _____

2. I permit my sample to be stored and used in future research at Mayo to learn about, prevent, or treat any other health problems:

☐ Yes ☐ No Please initial here: _____Date: _____

MAYO CLINIC

Who will use your sample?
If you agree to give your sample, it will be the property of Mayo and may be used for research by Dr. Vicente Torres and other staff at Mayo Clinic. Researchers at other institutions may also ask for a part of your sample for future studies.

How do researchers from other institutions get the sample?
Researchers from universities, hospitals, and other health organizations conduct research using tissue. They may contact Mayo and request samples for their studies. If you approve release of your sample by checking 'yes' below, Mayo may send the tissue sample(s) and some information about you to researchers who request them, but Mayo will not send your name, address, phone number, social security number, or any other identifying information with the sample. If you allow your sample to be given to researchers at other institutions, it will be given to them with a code number rather than your name. If these researchers use the sample for future research and decide that a test result may be useful for your health care, they may contact the Mayo Clinic and Mayo would then contact you to offer you the choice to learn the test results.

I permit Mayo to give my sample to researchers at other institutions:
Please mark one box:

☐ Yes ☐ No Please initial here: _____Date: _____

Mayo has the right to end storage of the sample without telling you

Researchers at other institutions are asking for a part of your blood sample for research studies. You can still take part in the treatment study or in the data collecting study without giving your sample. If you decide to give your sample, it would be given a code (not your name) when it is given to researchers at other institutions. This code allows your sample to be used without these researchers knowing that it is your sample just by looking at the label. The sample may be used for future research and may be stored forever.

When donating your samples, Mayo will then own them. The Sponsors of this study or researchers at other institutions do not. Some future studies may be for testing the genes you inherited from your parents (also known as genetic testing). If the researchers at other institutions, not commercial sponsors use the sample for future research and decide that a test result may be useful for your health care, they may contact the Mayo Clinic and Mayo would then contact you to ask whether you choose to learn the test results. At that time, you would be given general information on the potential risks, benefits, and costs of choosing to learn the test results. The risks of learning genetic test results may include emotional upset, insurance or job discrimination, and/or family conflicts from learning unknown information about your parents or blood relatives. Sometimes results should be released through a genetic counselor who can help explain the possible risks and benefits of learning this information.

I permit Mayo to give my sample to researchers at other institutions (not a commercial sponsor):

☐ Yes ☐ No Please initial here: _____ Date:

MAYO CLINIC

Mayo has the right to end storage of the sample without telling you

If you want your sample destroyed at any time, write to:

Dr. Vicente Torres
Nephrology and Hypertension
Eisenberg Building
200 First Street Southwest
Rochester, MN 55905

If you move please send your new address to

Mayo Clinic Rochester
Section of Registration
200 First Street Southwest
Rochester, MN 55905

14. What is the Institutional Review Board (IRB) and How Does it Protect You?

The Mayo Clinic IRB is made up of:

- Scientists
- IRB Specialists
- Allied Health Employees
- Local Community Members
- Visitors (Lawyers, Compliance, Administration, and others)

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have been treated unfairly.

MAYO CLINIC

15. Who Can Answer Your Questions?

You can call …	At …	If you have questions or concerns about …
Principal Investigator: Dr. Vicente Torres	**Phone:** 507-284-2511 (Mayo Clinic Operators)	**Questions about the study tests and procedures** **Research-related injuries or emergencies** **Any research-related concerns or complaints**
IRB Administrator: Marcia Andresen-Reid	**Phone:** 507-266-4000 **Toll-Free:** 866-273-4681	**Rights of a research subject** **Use of protected health information** **Any research-related concerns or complaints**
Research Billing	**Rochester:** 507-287-1819	**Billing / Insurance Questions**

16. Summary and Enrollment Signatures

You have been asked to take part in a clinical trial, also called a research study, at Mayo Clinic. The information about this study has been provided to you to inform you about the nature of this IRB approved study.

- I have read the whole consent form, and all of my questions have been answered to my satisfaction.
- I know that joining the study is voluntary and I agree to join the study.
- I know enough about the purpose, methods, risks, and possible benefits of the study to decide that I want to join.
- I know that I can call the investigator and research staff at any time with any new questions or to tell them about side effects.
- I understand that a copy of this form will be put in my medical records and that I will be given a copy of this completed form.
- I understand that I may withdraw from the study at any time.

MAYO CLINIC

Please sign and date to show that you have read and understand all of the above guidelines. Please do not sign unless you have read the entire packet of information. If you do not want to sign, you don't have to, but if you don't you cannot participate in this research study.

_____	_____	_____
(Date / Time)	(Printed Name of Participant)	(Clinic Number)

_____
(Signature of Participant)

_____	_____
(Date / Time)	(Printed Name of Individual Obtaining or in Receipt of Consent)

_____
(Signature of Individual Obtaining or in Receipt of Consent)

University of Alabama-Birmingham Consent Form

CRISP II CONSENT

Consent Form to Participate in Research at UAB

TITLE OF RESEARCH: "Renal Imaging to Mess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKP): Extension (CRISP II)"

INVESTIGATORS: Lisa M. Guay-Woodford, M.D.
Mark Lockhart M.D.

SPONSOR: National Institutes of Health

PURPOSE OF THE STIJDY

You are being asked to take part in this research study because you have polycystic kidney disease (PKD), and you participated in the original Consortium for Radiologic Imaging Studies of Polycystic kidney disease (CRISP) study. The purpose of this study is to continue following you for another four years to determine if pictures of your kidneys using Magnetic Resonance Imaging (MRI) can detect change in kidney size over a short period of' time. Blood samples will be obtained during your visits to determine your serum chemistries and cholesterol profile, and other markers that may identify risk for renal failure in PKD. If you enroll, you will participate for 48 months (4 years). This study is funded by the National1nstitntes of Health.

If you decide to volunteer and participate in this study, a number of tests will be done that are outlined below. Eligible subjects are being enrolled at other sites in the U.S., including the Mayo Foundation, University of Kansas Medical Center, and Emory University. The data coordinating and imaging analysis center (DCIAC) is located at the University of Pittsburgh.

It is expected that most of the subjects who participated in original CRISP at UAB will be enrolled and at least 210 subjects will be enrolled altogether. At this site, all studies will be performed at the General Clinical Research Center (GCRC) inpatient unit at University of Alabama at Birmingham Hospital.

UAB-IRB
Consent Form Approval 05-29-07
Expiration Date 05-09-08

EXPLANATION OF PROCEDURES

1. ELIGIBILITY DETERMINATION

You are eligible if you participated in the original CRISP study. We will mail you information about the study and a copy of the consent for you to review.
Initially, a medical history and a complete physical exam will be done to determine your overall health. The physical exam will include height, weight, and blood pressure measurements. If you have serious heart, liver, lung or other medical conditions, you may not participate in this extended CRISP II study. Included in your medical history, a family tree (pedigree) will be done. We may request information about your family and ask for your help in getting this information. Once the needed pieces of information are obtained, and if you are eligible, you will be enrolled into the study and admitted to the General Clinical Research Center (OGRC) at University of Alabama at Birmingham Hospital for testing.

2. WHAT WILL HAPPENTO YOU WBILE YOU ARE IN THIS RESEARCH STUDY?

If you agree to participate in the study, you will be scheduled for two visits at baseline (Year 1) and Year 3.
a. Baseline (Year 1) and Year 3 visits

For these visits you will be admitted to the inpatient General Clinical Research Center (GCRC) at University of Alabama at Birmingham Hospital. You will spend as few as one and as many as two days in the GCRC.

Prior to the visit to the GCRC, we will mail you a family history questionnaire. During the OCRC visit, the study coordinator will review the completed questionnaire and the: Information regarding your family history of ADPKD will be updated. The study coordinator will provide you with a letter to your family members with information about the study and contact information so that they may reach us.

A medical history, medication history, and complete physical exam will be done to determine your overall health. The physical exam will include height, weight, and blood pressure measurements.

You will have blood pressure measured at least three times in the same and that was used in CRISP I.

If you are a woman with childbearing potential, a urine pregnancy test to determine if you are pregnant will be performed prior to under going any test. You will be told if you are pregnant.

Blood samples will be obtained during your visit to determine your serum chemistries and cholesterol profile, and other markers that may identify risk for renal failure in PKD. About 50 mL or 4 tablespoons of blood will be taken for these tests. De-identified (identified by CRISP ID number only) blood and urine samples will be stored in a central repository (Fisher BioServices) and shared with other CRISP investigators.

A specialized test of your kidney function with blood and urine collections will be performed at baseline (Year 1) and Year 3. Your kidney function will be measured using a special test called. GFR Test (Glomerular Filtration Rate). This test measures the kidney's ability to filter and clean the blood. Before and during this test you will not be allowed to eat food. However, you will be asked to drink water several times because it is important for the accuracy of the test. A substance called Iotha1amate will be injected under

your skin in the upper arm. This substance is absorbed from the injection site into the blood and it is carried to the kidneys for filtration. You will be asked to void three times in the course of the test to collect urine, A small ultrasound machine, called Bladder Monitor, will be used to be sure that your bladder empties completely when you void. For this examination, jelly will be placed on the skill and a probe that measures bladder volume will be moved over the skin. Two small blood samples (l teaspoon [5mL] each) will be obtained by placing a needle in the vein in your arm. This test will take approximately two hours to complete.

A Magnetic Resonance Imaging (MRI) study will be done to determine the size of your kidneys. An MRI involves lying still in a hollow tube or scanner for short periods of time. The total duration of the MRI will be approximately 30 minutes. You are moved slowly through the scanner while images of your kidneys are made by measuring the magnetic spin of the kidney. There is no radiation exposure associated with this procedure. The MRI will be done at baseline and Year 3 visits.

At the baseline visit only, if you have not already done so, you will be asked to provide a blood sample for genetic testing. This testing requires obtaining approximately 2 tablespoons (30 mL) of blood from your arm. The doctors involved in this study will isolate genetic material (DNA) from the de-identified (identified by CRISP ID number only) blood sample in order to study the family factors, or genes, that are inherited and cause Autosomal Dominant Polycystic Kidney Disease (ADPKD). In addition, if you agree, your blood cells will be put through a process called immortalization to enable the researchers to have DNA for future research studies related to this project.

Because these genetic materials (DNA and immortalized cell lines) will be identified only by the CRISP ID number, the researchers will not be able to directly link you to the sample material These de-identified samples will be stored in a central repository at the NIH (NIDDK Center for Genetic Studies, Rutgers University Cell and DNA Repository). Because the genetic tests in this study are not used for regular medical care, you will not be told the results of the test(s). The results will also not be put in your medical record. In case either the DNA isolation or the immortalization process fails, you maybe asked to provide an additional blood sample to repeat the procedure.

De-identified (identified by CRISP ID number only) DNA samples will be shared with other CRISP site investigators. When these studies are completed, the-researchers may wish to 'perform additional tests on these samples related to this disease.

Should you not wish to participate in the genetic part of the study, you will not be held back from participating in the rest of the study. Given that the identity of these samples will be kept anonymous, the risk of ONA testing with regard to yow: good name, insurability, employability and paternity are minimal, The genetic information obtained in this study will not be shared directly with you and will be kept anonymous.

Please initial the options with which you agree.

(A) _____ I give my permission to have my DNA isolated and my blood cells immortalized. I understand that if the process is successful, additional blood for DNA studies will not be required. However, if the process is not successful, an additional blood sample maybe requested.

(B) _____I do not give my permission for my DNA to be isolated.

(C) _____I do not give my permission for the immortalization process but you way isolate my DNA.

UAB-IRB
Consent Form Approval 05-29-07
Expiration Date 05-09-08

Recruitment of Family Members

A major part of CRISP II is to collect more complete family histories of all CRISP patients and create a filmily tree (pedigree) for each family. We are asking you to share the study information letter (given to you at the GCRC visit) with your relatives who might have Polycystic Kidney Disease and to ask them to contact the Research Nurse Coordinator (Teresa Chacana, RN) if they are interested in participating in the study.

Affected family members who agree to participate will sign a separate consent form and provide a blood sample for serum creatinine and DNA extraction. Affected relatives will also be asked to complete a lifestyle questionnaire (smoking history, caffeine use, estrogen use, and levels of physical activity) and a family history questionnaire, Permission to review their most recent imagining study of the kidneys (preferably Computer Tomography [CT] or Magnetic Resonance Imaging [MRI]; ultrasound if CT or MRI is not available) will be requested.

Please initial the options with which you agree.

(A) _____ I will give the information to my family members

(B) _____ I will not give the information to my family members

b. Year 2 and Year 4 Visits

In Year 2 and 4 you will be asked to provide a blood sample for measurement of serum creatinine in a central laboratory. The blood sample can be obtained either at the GCRC/UAB laboratory or at your local physician's office/laboratory. If the blood sample is obtained at a local laboratory, we will provide you with the appropriate tube labeled with the CRISP identification number, a mailing container and instructions.

c. Semi-annual telephone interviews

Every six months, the CRISP study coordinator will contact you to obtain information regarding any medication changes, hospitalizations, doctor visits and outpatient procedures. We will ask your permission to contact to obtain information regarding your health from any physician who has examined or treated you since your last visit or telephone interview.

3. HOW LONG WILL YOUBE IN THIS RESEARCII STUDY?

This is a four year study. Visits at Baseline (Year 1) and Year 3 will be at the OCRC at University of Alabama at Birmingham Hospital. Visits at Year 2 and Year 4 can be completed with your local physician. There will be telephone follow-up visits 6 months after each yearly visit. You will continue to be under the care of your primary physician at home. You will be asked for a list of your medications and mention any change on them, whether prescribed or over the counter. You will be contacted by telephone for the 6 month follow-up visits. You will be asked if you have had any medication changes, illnesses, or hospitalizations. These phone calls will not be longer than 30 minutes.

You should tell the research doctor if you:

Are hospitalized
Have any surgery performed
Have any radiology tests.

If you are hospitalized, have any surgery or radiology test (such as X-ray, CT scan, Ultrasound, or others tests) performed between your study visits, Dr. Guay-Woodford will ask you if we may obtain copies of the medical records from that hospital after you sign a release of health information form.

RISKS AND DISCOMFORTS

Due to the investigational nature of this study there may be unforeseeable risks. If you are a woman of childbearing age, for each visit you will undergo a urine test for pregnancy prior to undergoing any tests. If you know that you are pregnant you must inform the principal investigator and not participate in this study. If you become pregnant after completion of the first visit of this study, you need to inform Dr. Guay-Woodford and she will determine if and when you should be studied again. There are risks related to blood drawing that include pain, bruising and infection. Risks related to intravenous catheter placements are also present and include pain, bruising and infection. Given that the intravenous line is in place for an extended amount of time (between 2 and 6 hours), mild discomfort may be present for a few days lifter the test.

The risk of allergic reaction to iothalamate meglumine is less than I in 50,000.h with any infusion there is a 5% risk of in filtration (leaking outside the vein). If this occurs there may be temporary discomfort in your arm.

There are no known risks from the magnetic resonance imaging. However, the hollow tube is narrow and some people have anxiety related to being closed in, also called claustrophobia. This occurs in approximately 12% of people. If you have any pacemakers or metal objects that are not compatible with a magnetic resonance Imaging you can be in the study, but will not be permitted to have the MRI.

There is not enough medical information to know what the risks might be to a breast-fed infant or to an unborn child in a woman who takes part in this study. Therefore, pregnant or lactating women cannot participate in the study. If you are a woman, who can become pregnant and is sexually active, you or your sexual partners while in this study must use one of the following birth control measures: tubal ligation, birth control pill, or vasectomy. If you are a woman, at each visit you must have a pregnancy test (urine test) before taking part in this study. You will be told the results of the pregnancy test. If the pregnancy test is positive, the studies will need to be postponed.

There is a risk of breaches in confidentiality for your family member. To minimize this risk we will not contact them directly but rather provide you with an informational letter to share with them. If, after reviewing the information, they want to participate in this study, they should contact Ms. Chacana, the Research Nurse Coordinator.

PAYMENT FOR PARTICIPATION IN RESEARCH:

You will not be paid for taking part in this study. However, reimbursement for travel expenses at a rate of 48 cents per mile plus $6.00 per day for parking up to amount of $250.00 will be offered to you.

PAYMENT FOR RESEARCH RELATED INJURIES

UAB and the NIH have made no provision for monetary compensation in tile event of injury resulting from the research and in the event of such injury, treatment is provided, but is not provided free of charge.

QUESTIONS

If you have any questions about the research or a research related injury, Dr. Guay-Woodford or Ms. Chacana, the Research Nurse Coordinator, will be glad to answer them, Dr. Guay-Woodford's number is 205·934-7308 and Teresa Chacana's number is 205-934-7649. Ms. Chacana may be reached Monday through Friday, between the hours of 8:00 a.m. and 5:00 p.m. CT.

If you have questions about your rights as a research participant, you may contact Ms. Sheila Moore, Director of the Office of the Institutional Review Board for Human Use (IRB). Ms. Moore may be reached at (205) 934-3789 or 1-800-822-8816, press the option for an operator/attendant and ask for extension 4-3789 between the hours of 8:00 a.m. and 5:00 p.m. CT, Monday through Friday.

LEGAL RIGHTS

You are not waiving any of your legal rights by signing this consent form.

WHAT WILL HAPPEN TOYOUR SAMPLES?
De-identified small samples of your blood, urine, and DNA will be stored for future research studies of Polycystic Kidney Disease. The DNA sample may be stored for a long time, even after your death. These samples will be given a code (rather than your name). This code will allow your sample to be used without anyone knowing that it is your sample just by looking at the label. These samples will be stored in central repositories controlled by the NIH (Fisher BioServices and NIDDK Center for Genetics Studies, Rutgers University Cell and DNA Repository).

BENEFITS

There are no direct benefits to you for participating in this study. Information regarding your level of kidney involvement may help to determine how fast your PKD is progressing. This information will be made available to your treating physician. You will continue to receive your usual treatment by your primary physician. No changes to your usual care will be instituted by this study.

ALTERNATIVES

The alternative to participating in this study is not to participate at all. If you decide not to participate, there will not be changes in your treatment and you will continue to receive your usual medical care.

CONFIDENTIALITY

The information gathered during this study will be kept confidential to the extent permitted by law, However, your doctor, representatives of National Institutes of Health, and UAB's Institutional Review Board (lRB) will be able to inspect your medical records and have access to confidential information that identifies you by name. The results of the study, including laboratory tests and X-rays may be published for scientific purposes; however, your identity will not be revealed.

If you receive services at the University of Alabama at Birmingham Hospital as part of this trial, this informed consent document will be placed in and made part of your permanent medical record at these facilities.

Information related to this study, including your name, medical record number, date of birth and social security number maybe shared with the billing offices of UAB and UAB Health System-affiliated entities so that claims may be appropriately subjected to the study sponsor or to your insurance company for clinical services and procedures provided to you during the course of this study.

WITHDRAWAL WITHOUT PREJUDICE

You are free to withdraw your consent and to discontinue participation in this project at any time without Prejudice against further care that you may receive at this institution.

SIGNIFICANT NEW FINDINGS

Any significant new findings that develop during the course of the study that may affect you or your willingness to continue in the research will be provided to you by Dr. Guay-Woodford or her staff.

COST OF PARTICIPATION

There will be no cost to you from participation in the research. The Costs of your standard medical care will be billed to you and/or your insurance company in the usual manner.

STORAGE OF SPECIMENS

Biosamples (blood and urine). Please initial your choice(s) below:

__I agree to allow my blood and urine samples stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

__I do not agree to allow my blood and urine samples stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

Genetic Samples (DNA) [if collected]. Please initial your choice (s) below:

__I agree to allow my DNA sample to be stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

__I do not agree to allow my DNA sample to be stored in the NJDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

If you agree to give your sample, it will be the property of UAB and may be used for research by Dr. Guay-Woodford and CRISP investigators. Other researchers may also ask for part of your sample for future studies.

SIGNATURES

You will receive copy of this signed informed consent and a copy will be placed in your medical records.

_____

Signature of Participant Date

_____

Signature of Witness Date

_____

Signature of Person Obtaining Consent (if Other Than Principal Investigator) Date

UAB-IRB
Consent Form Approval 05-29-07
Expiration Date 05-09-08

University of Alabama at Birmingham
AUTHORIZATION FORUSEIDISCLOSURE OF HEALTH INFORMATION
FOR RESEARCH

What is the purpose of this form? You are being asked to sign this form so that UAB may use and release your health information for research. Participation in research is voluntary. If you choose to participate in
The research, you must sign this form so that your health information may be used for the research.

Participant name: _____
UAB IRB Protocol Number: F070226008
Research Protocol: (Renal Imaging to Assess Progressing in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP II)
Principal Investigator: Lisa M. Guay-Woodford, MD Sponsor: National Institute of Health
Mark Lockhart, MD.

What health information do the researchers want to use? All medical information and personal identifiers including past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of whatever kind related to or collected for use in the research protocol.
Why do the researchers want my health information? The researchers want to use your health information as part of the research protocol listed above and described to you in the Informed Consent document.
Who will disclose, use and/or receive my health information? The physicians, nurses and staff working on the research protocol (whether at UAB or elsewhere); other operating units of UAB, HSF, The Children's Hospital of Alabama, Callahan Eye Foundation Hospital and the Jefferson County Department of Public Health as necessary for their operations; the IRB and its staff; the sponsor of the research and its employees; and outside regulatory agencies, such as the Food and Drug Administration.
How will my health information be protected once it is given to others? Your health information that is
given to the study sponsor will remain private to the extent possible, even though the study sponsor is not required to follow the federal privacy laws. However, once your Information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.
How long will this Authorization last? Your authorization for the uses and disclosures described in this
Authorization does not have an expiration date.
Call I cancel the Authorization? You may cancel this Authorization at any time by notifying the Director of the IRB, in writing, referencing the Research Protocol and IRB Protocol Number. If you cancel this
Authorization, the study doctor and staff will not use any new health information for research. However, researchers may continue to use the health iDfunn8tion that was provided before you cancelled your authorization.
Can I see my health information? You have a right to request to see your health information. However, to ensure the scientific integrity of the research, you will not be able to review the research information until after the research protocol has been completed.

Signature of participant: _____ Date:_____
Or participants' legally authorized representative

Printed Name of participant's representative: _____

Relationship to the participant: _____

Consent Form for Family Member to Participate In Research at UAB

TITLE OF RESEARCH: "Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP II)"

INVESTIGATOR: Lisa M. Guay-Woodford, M.D.
Mark Lockhart, M.D.

SPONSOR: National Institutes of Health

PURPOSE OF THE STUDY

You are being asked to take part in this research project funded by the National Institutes of Health because you have polycystic kidney disease (PKD) and you are a relative of a participant in the original Consortium for Radiologic Imaging Studies of Polycystic kidney disease (CRISP) study. The purpose of this study is to collect more complete family histories of all CRISP patients, to draw a family tree (pedigree) of each family, and to identify genetic factors that may influence the severity of the cystic disease.

If you decide to volunteer and participate in this study, a number of tests will be done that are outlined below. Eligible subjects are being enrolled at other sites in the U.S., including the Mayo Foundation, University of Kansas Medical Center, and Emory University. The data coordinating and imaging analysis center (DCIAC) is located at the University of Pittsburgh.

EXPLANATION OF PROCEDURES

A. What Will Happen To You While You Are In This Research Study?

If you agree to participate in this study a blood sample (30 ml or approximately two tablespoons) will be obtained from a vein for measurement of serum creatinine and DNA.

If you agree to participate in this study you will be asked to allow us to obtain clinical information and reports of imaging studies from your medical record (after a Medical Records Release form is signed by you). You will also be asked to complete a lifestyle questionnaire to assess your smoking history, caffeine exposure, estrogen exposure and levels of physical activity and a family history questionnaire to further extend your family tree.

When possible, the most recent of your Computer Tomography (CT) or Magnetic Resonance Imaging (MRI) examination of the abdomen will be reviewed. If these studies are not available, the most recent ultrasound images will be reviewed to assess renal disease severity. All of this clinical and lifestyle information, plus the available genetic information on your family, will be stored in the CRISP database that is maintained by the DCIAC (The Data Coordinating and Imaging Analysis Center) located at the University of Pittsburgh.

B. How Long Will You Be In This Research Study?

Your participation in this study will be limited to the time necessary to provide the blood sample and information described above.

C. Genetic Testing

The doctors involved in this study would like to isolate genetic material (DNA) from your de-identified (identified by CRISP ID number only) blood sample in order to study the family factors, or genes, that are inherited and cause Autosomal Dominant Polycystic Kidney Disease (ADPKD). In addition, if you agree, your blood cells will be put through a process called immortalization to enable the researchers to have DNA for future research studies related to this project. This DNA will be stored in a central repository at the NIH (NIDDK Center for Genetic Studies, Rutgers University Cell and DNA Repository). Because the genetic tests in this study are not used for regular medical care, you will not be told the results of the test(s). The results will also not be put in your medical record. In case either the DNA isolation or the immortalization process fails, you may be asked to provide an additional blood sample to repeat the procedure.

De-identified (identified by CRISP ID number only) DNA samples will be shared with other CRISP site investigators. When these studies are completed, the researchers may wish to perform additional tests on these samples related to this disease.

If you agree to have your sample(s) stored in the Repository, you can change your mind up until the end of the CRISP II study. When study researchers receive written instructions from you, they will destroy your sample and all information that identifies you. After the CRISP II study ends, you will not be able to withdraw your sample because the Repository will not know which one is yours. The sample will stay in the Repository indefinitely.
You may request the destruction of your DNA sample before the end of the CRISP II study, to do so you can contact Teresa Chacana at 205-934-7649 (Monday through Friday, between the hours of 8:00 a.m. and 5:00 p.m. CT).

Should you not wish to participate in the genetic part of the study, you will not be held back from participating in the rest of the study. The genetic information obtained in this study will not be shared directly with you and will be kept anonymous.

Please initial the options with which you agree.

(A) _____I give my permission to have my DNA isolated and my blood cells immortalized. I understand that if the process is successful, additional blood for DNA studies will not be required. However, if the process is not successful, an additional blood sample may be requested.

(B) _____I do not give my permission for my DNA to be isolated.

(C) _____I do not give my permission for the immortalization process but you may isolate my DNA.

RISKS AND DISCOMFORTS

There are risks related to blood drawing that include pain, bruising and infection.
There is a risk to you of breaches in confidentiality. To minimize this risk, we did not contact you directly, but rather provided your relative who is a CRISP II Study participant with an informational letter to share with you. After reviewing the information, you initiated the contact with Ms. Chacana, the Research Nurse Coordinator.

BENEFITS

There are no direct benefits to you for participating in this study. Findings from this study could potentially help others in the future.

ALTERNATIVES

The alternative to participating in this study is not to participate at all.

CONFIDENTIALITY

The information gathered during this study will be kept confidential to the extent permitted by law. However, your doctor, representatives of National Institute of Health, and UAB's Institutional Review Board (IRB) will be able to inspect your records and have access to confidential information that identifies you by name. The results of the study, including laboratory tests and X-rays may be published for scientific purposes; however, your identity will not be revealed.
If you receive services in University of Alabama at Birmingham Hospital as part of this trial, this informed consent document will be placed in and made part of your permanent medical record at these facilities.

Information relating to this study, including your name, medical record number, date of birth and social security number may be shared with the billing offices of UAB and UAB Health System-affiliated entities so that claims may be appropriately submitted to the study sponsor or to your insurance company for clinical services and procedures provided to you during the course of this study.

WITHDRAWAL WITHOUT PREJUDICE

You are free to withdraw your consent and to discontinue participation in this project at any time without prejudice against further care that you may receive at this institution.

SIGNIFICANT NEW FINDINGS

Any significant new findings that develop during the course of the study that may affect your willingness to continue in the research will be provided to you by Dr. Guay-Woodford or her staff.

COST OF PARTICIPATION

There will be no cost to you from participation in the research. You will not need to pay for test and procedures which are done just for this research study. These tests and procedures include venipuncture, measurement of serum creatinine and extraction of blood DNA for genetic testing. The costs of your standard medical care will be billed to you and/or your insurance company in the usual manner.

PAYMENT FOR PARTICIPATION IN RESEARCH

You will not be paid for taking part in this study.

PAYMENT FOR RESEARCH RELATED INJURIES

UAB and the NIH have made no provision for monetary compensation in the event of injury resulting from the research and in the event of such injury, treatment is provided, but is not provided free of charge.

QUESTIONS

If you have any questions about the research or a research related injury, Dr. Guay-Woodford or Teresa Chacana, her Research Nurse Coordinator will be glad to answer them. Dr. Guay-Woodford's number is 205-934-7308 and Teresa Chacana's number is 205-934-7649. Ms. Chacana may be reached Monday through Friday, between the hours of 8:00 a.m. and 5:00 p.m. CT.

If you have questions about your rights as a research participant, you may contact Ms. Sheila Moore, Director of the Office of the Institutional Review Board for Human Use (IRB). Ms. Moore may be reached at (205) 934-3789 or 1-800-822-8816, press the option for an operator/attendant and ask for extension 4-3789 between the hours of 8:00 a.m. and 5:00 p.m. CT, Monday through Friday.

LEGAL RIGHTS

You are not waiving any of your legal rights by signing this consent form.

WHAT WILL HAPPEN TO YOUR SAMPLES?

A sample of your blood DNA will be stored for future research studies of Polycystic Kidney Disease. The DNA sample may be stored for a long time, even after your death. These samples will be given a code (rather than your name). This code will allow your sample to be used without anyone knowing that it is your sample just by looking at the label. These samples will be stored in central repositories controlled by the NIH (Fisher BioServices and NIDDK Center for Genetics Studies, Rutgers University Cell and DNA Repository).

STORAGE OF SPECIMENS

Biosamples (blood). Please initial your choice(s) below:

___ I agree to allow my blood sample stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

___ I do not agree to allow my blood sample stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

Genetics Samples (DNA) [if collected]. Please initial your choice(s) below:

___ I agree to allow my DNA sample to be stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

___ I do not agree to allow my DNA sample to be stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

If you agree to give your sample, it will be the property of UAB and may be used for research by Dr. Guay-Woodford and CRISP investigators. Other researchers may also ask for part of your sample for future studies.

SIGNATURES

You will receive a copy of this signed informed consent and a copy will be placed in your medical records.

_____ Date
Signature of Participant

_____ Date
Signature of Witness

_____ Date
Signature of Person Obtaining Consent
(if Other Than Principal Investigator)

University of Alabama at Birmingham

AUTHORIZATION FOR USE/DISCLOSURE OF HEALTH INFORMATION FOR RESEARCH

What is the purpose of this form? You are being asked to sign this form so that UAB may use and release your health information for research. Participation in research is voluntary. If you choose to participate in the research, you must sign this form so that your health information may be used for the research.

Participant name:_____

UAB IRB Protocol Number: F070226008

Research Protocol: "Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP II)"

Principal Investigator: Lisa M. Guay-Woodford, MD Mark Lockhart, MD. **Sponsor:** National Institute of Health

What health information do the researchers want to use? All medical information and personal identifiers including past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of whatever kind related to or collected for use in the research protocol.

Why do the researchers want my health information? The researchers want to use your health information as part of the research protocol listed above and described to you in the Informed Consent document.

Who will disclose, use and/or receive my health information? The physicians, nurses and staff working on the research protocol (whether at UAB or elsewhere); other operating units of UAB, HSF, The Children's Hospital of Alabama, Callahan Eye Foundation Hospital and the Jefferson County Department of Public Health, as necessary for their operations; the IRB and its staff; the sponsor of the research and its employees; and outside regulatory agencies, such as the Food and Drug Administration.

How will my health information be protected once it is given to others? Your health information that is given to the study sponsor will remain private to the extent possible, even though the study sponsor is not required to follow the federal privacy laws. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.

How long will this Authorization last? Your authorization for the uses and disclosures described in this Authorization does not have an expiration date.

Can I cancel the Authorization? You may cancel this Authorization at any time by notifying the Director of the IRB, in writing, referencing the Research Protocol and IRB Protocol Number. If you cancel this Authorization, the study doctor and staff will not use any new health information for research. However, researchers may continue to use the health information that was provided before you cancelled your authorization.

Can I see my health information? You have a right to request to see your health information. However, to ensure the scientific integrity of the research, you will not be able to review the research information until after the research protocol has been completed.

Signature of participant;_____ Date:_____
Or participants' legally authorized representative

Printed Name of participant's representative:_____

Relationship to the participant:_____

Created: 02/01/07
Revised: 05/21/07

University of Kansas Consent Form

CONSENT FORM

CONSORTIUM FOR RADIOLOGIC IMAGING STUDIES OF POLYCYSTIC KIDNEY DISEASE (CRISP II)
(participant)

Protocol # QG816940

Investigators:
Jared J. Grantham M.D.
Franz Winklhofer M.D.
Connie Wang M.D.
Louis Wetzel M.D.

Sponsor: National Institutes of Health

INTRODUCTION

You are being asked to take part in this research study because you have polycystic kidney disease (PKD) and you participated in the original Consortium for Radiologic Imaging studies of Polycystic Kidney Disease (CRISP) Study.

Approximately 210 subjects will be enrolled at four centers across the United States. These four centers include the University of Kansas Medical Center (KUMC), Mayo Foundation, The University of Alabama at Birmingham Hospital and Emory University. Jared J. Grantham, M.D., the principal investigator at KUMC will enroll approximately 60 subjects. The Data Coordination and Imaging Analysis Center (DCIAC) for the study is located at the University of Pittsburgh.

The CRISP II protocol does not exclude participants that enroll in other interventional treatment trials. If CRISP II participants are recruited into an interventional treatment trial (e.g. HALT clinical trial) that also requires imaging studies the visits for CRISP II and for the interventional trial will be coordinated to avoid duplication of tests and undue burden on the participant. They will, however, complete the necessary studies of CRISP II that are not included in HALT.

You do not have to participate in this research study. It is important that before you make a decision to participate, you read the rest of this form. You should ask as many questions as needed to understand what will happen to you if you participate in this study

BACKGROUND

You are being asked to take part in this research study because you have polycystic kidney disease (PKD) and you participated in the original Consortium for Radiologic Imaging studies of Polycystic Kidney Disease (CRISP) Study. In this study the research doctors will continue following you for an additional four years (48 Months) to determine

HSC Submission Date:

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

if pictures of your kidneys using Magnetic Resonance Imaging (MRI) can detect changes in kidney size.

PURPOSE

The purpose of this study is to continue following you for another four years to determine if pictures of your kidney using magnetic resonance imaging (MRI) can detect additional changes in kidney size over this period of time. If you enroll, you will participate for 48 months (4 years).

ELIGIBILITY DETERMINATION

You are eligible if you participated in the original CRISP cohort study. Initially, a medical history and a complete physical exam will be done to determine your overall health. The physical exam will include height, weight, and blood pressure measurements. If you have serious heart, liver, lung or other medical conditions, you may not participate in this extended CRISP II study. Included in your medical history, a family tree (pedigree) will be done. Since this is a disease that runs in families we are interested in determining the extent to which polycystic kidney disease shows up in your family. We also want to determine if PKD presents the same in all effected members of your family. We would like to gather the history of PKD from as many generations of your family tree as possible. This will help us understand how the PKD genes affect your family members. We may request information about your family and ask for your help in getting this information.

Once the needed pieces of information are obtained, and if you are eligible, you will be enrolled into the study and admitted to the General Clinical Research Center (GCRC) at University of Kansas Medical Center for testing.

PROCEDURES

If you are eligible and decide to participate in this study, your participation will last approximately four years.

If you are also a participant in the National Institutes of Health (NIH) sponsored HALT clinical trial, or an Otsuka sponsored trials, please read the following statements and make your choice:

1. I permit the deidentified information (identified by CRISP ID number only) collected for the CRISP study to be provided to the HALT or Otsuka investigators

☐ Yes ☐ No Please initial here: _____ Date: _____

2. I permit deidentified information (identified by HALT ID or Otsuka ID number only) collected for the HALT or Otsuka study to be provided to the CRISP investigators

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

☐ Yes ☐ No Please initial here: _____Date: _____

If you agree to participate in the study, you will be scheduled for GCRC visits, at baseline (Year 1) and Year 3, Year 2 and Year 4 will be scheduled for lab draws at the GCRC or your local lab if you live over 1 hour from KUMC. In addition, you will be contacted by telephone every six months.

Baseline (Year 1) and Year 3 visits

For these visits you will be admitted to the General Clinical Research Center (GCRC) at University of Kansas Medical Center. You will spend one full day in the GCRC.

Prior to the visit to the GCRC visit, participants will be mailed a family history questionnaire. During the GCRC visit, the study coordinator will review the completed questionnaire and the information regarding the family history of ADPKD will be updated. The study coordinator will ask the participants permission to contact their relatives and to sign a separate informed consent for this purpose.

A medical history, medication history, and complete physical exam will be done to determine your overall health. The physical exam will include height, weight, and blood pressure measurements. You will have blood pressure measured at least nine times in the same arm that was used in CRISP I.

A urine test to determine pregnancy will be performed on women with child-bearing potential prior to undergoing any test. You will be told if you are pregnant.

Blood and urine samples will be obtained during your visit to determine your chemistry and cholesterol profile, and other markers that may identify risk for renal failure in PKD. About 50 ml or 4 tablespoons of blood will be taken for these tests.

A specialized test of your kidney function with blood and urine collections will be performed at baseline Year 1 and year 3. Your kidney function will be measured using a special test called GFR Test (Glomerular Filtration Rate). This test measures the kidney's ability to filter and clean the blood. Before and during this test you will not be allowed to eat food. However, you will be asked to drink water several times because it is important for the accuracy of the test. A substance called Iothalamate will be injected under your skin in the upper arm. This substance is absorbed from the injection site into the blood and it is carried to the kidneys for filtrations. You will be asked to void three times in the course of the test to collect urine. A small machine, called a Bladder Monitor, will be used to be sure that your bladder empties completely when you void. For this examination, jelly will be placed on the skin and a probe that measures bladder volume will be moved over the skin. Two small blood samples (1 teaspoon [5ml] each) will be obtained by placing a needle in the vein in your arm. This test will take approximately two hours to complete

A Magnetic Resonance Imaging (MRI) study will be done to determine the size of your kidneys. An MRI involves lying still in a hollow tube or scanner for short periods of time. The total duration of the MRI will be approximately 45 minutes. You are moved slowly through the scanner while images of your kidneys are made by measuring the magnetic spin of the kidney. There is no radiation exposure associated with this procedure.

At the baseline visit only, if you have not already done so, you will be asked to provide a blood sample for genetic testing. This testing requires obtaining approximately 2 tablespoons (30 ml) of blood from your arm. The doctors involved in this study will isolate genetic material (DNA) from the blood sample identified by your CRISP ID number only in order to study the family factors, or genes, that are inherited and cause Autosomal Dominant Polycystic Kidney Disease (ADPKD).

Small samples of your blood, urine and DNA will be stored for future research studies of PKD. These samples will be given a code rather than your name. This code will allow your sample to be used withour anyone knowing that it is your ample by just looking at the lable. These samples will be stored in central labscontrolled by the National Institutes of Health (Fisher BioServices and NIDDK Center for Genetics Studies, Rutgers University Cell and DNA Repository). The DNA samples may be stored for a ling time, even after your death.

Recruitment of Family Members

A major part of CRISP II is to collect more complete family histories of all CRISP I patients and create an family tree (pedigree) for each family You will be asked to provide contact information and permission to contact family members who might be at risk of having Polycystic Kidney Disease. With your permission,, we will contact the family members that are known to have PKD to determine whether they are interested in participating in this study.. Affected family members who agree to participate will sign a consent form and provide a blood sample for serum creatinine and DNA extraction. Affected relatives will also be asked to complete a lifestyle questionnaire (smoking history, caffeine use, estrogen use, and levels of physical activity) and a family history questionnaire. Permission to review the most recent imagining study of the kidneys (preferably Computer Tomography [CT] or Magnetic Resonance Imaging [MRI]; ultrasound if CT or MRI is not available) will be requested.

RISKS

Pregnancy Related Risk - Due to the investigational nature of the study, there is not enough medical information to know what the risks might be to a breast-fed infant or to an unborn child in a woman who takes part in this study. Therefore, pregnant or lactating (nursing) women cannot participate in the study. If you are a woman of childbearing potential you will undergo a urinary pregnancy test prior to being accepted into the study. If the pregnancy test is positive, your involvement in the study must be postponed. If you know you are pregnant you must inform the principal investigator and not participate in this study. One of the following birth control

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

measures must be used by all women who can become pregnant and are sexually active or by their sexual partners while in this study: tubal ligation, birth control pill or vasectomy. At each visit women who can become pregnant must have a pregnancy test (blood test) before taking part in this study. You will be told the results of the pregnancy test. If the pregnancy test is positive, the studies will need to be postponed. If you become pregnant after completion of the first visit of this study, you need to inform to Dr. Jared Grantham and he will determine if and when you should be studied again.

There are risks related to blood drawing that include pain, bruising and infection. Risks related to intravenous catheter placements are also present and include pain, bruising and infection. Given that the intravenous line is in place for an extended amount of time (between 2 and 6 hours), mild discomfort may be present for a few days after the test.

There are no known risks from the magnetic resonance imaging. However, the hollow tube is narrow and some people have anxiety related to being closed in or claustrophobia. This occurs in approximately 12% of people. If you have any pacemakers or metal objects that are not compatible with a magnetic resonance image you may not participate in this study.

There may be other risks that have not yet been identified and unexpected side effects that have not been previously observed may occur.

NEW FINDINGS STATEMENT

You will be informed if any significant new findings develop during the course of the study that may affect your willingness to participate in this study.

BENEFITS

There are no direct benefits to you for participating in this study. Information regarding your level of kidney involvement may help to determine how fast you are progressing with PKD. This information will be made available to your treating physician. You will continue to receive your usual treatment by your primary physician. No changes to your usual care will occur in this study. If you are thinking about participating in another clinical study or trial, you need to discuss this with the Study Coordinator and the Principal Investigator before you can participate.

ALTERNATIVES

The alternative to consenting to participate in this study is not to participate at all. If this is the case and you decide not to participate, there will not be changes in your treatment and you will continue to receive your usual medical care.

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

COSTS

There will be no cost to you for participation in this research study. The costs of your standard medical care will be billed to you and/or your insurance company in the usual manner.

PAYMENT TO SUBJECTS

You will not be paid for taking part in this study, however reimbursement for travel expenses will be offered. Standard business mileage rate for travel expenses up to $300.00 will be offered to all participants.

IN THE EVENT OF INJURY

In the event you experience a serious side effect during this study, you should immediately contact Beth Stafford R.N. at 913-588-7609. If it is after 5:00 p.m., a holiday or a weekend, you should call the University of Kansas Medical Center operator and ask to speak to the Nephrology doctor on call.

If any injury or illness should occur to you as a direct result of being in this study, the investigator will be able to tell you what treatment options are available. Payment for lost wages, disability or discomfort is not available. You do not give up any of your rights by signing this form.

INSTITUTIONAL DISCLAIMER STATEMENT

If you believe you have been injured as a result of participating in research at Kansas University Medical Center (KUMC), you should contact the Director, Human Research Protection Program, Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160. Compensation to persons who are injured as a result of participating in research at KUMC may be available, under certain conditions, as determined by state law or the Kansas Tort Claims Act.

CONFIDENTIALITY AND PRIVACY AUTHORIZATION

Study records that identify you will be kept confidential as required by law. Researchers cannot guarantee absolute confidentiality. If the results of this study are published or presented in public, information that identifies you will be removed.

The privacy of your health information is protected by a federal law known as the Health Insurance Portability and Accountability Act (HIPAA). By signing this consent form, you are giving permission ("authorization") for KUMC to use and share your health information for purposes of this research study. If you decide not to sign the form, you cannot be in the study.

To do this research, the research team needs to collect health information that identifies you. They will collect information from study activities described in the Procedures section of this form and information from your medical record that relates to

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

study participation. Your health information will be used at KUMC by Dr. Jared J. Grantham M.D. and members of the research team, The University of Kansas Hospital Medical Record Department, the KUMC Research Institute and officials at KUMC who oversee research, including members of the KUMC Human Subjects Committee and other committees and offices that review and monitor research studies.

By signing this form, you are giving Dr. Grantham and the research team permission to share information about you with persons or groups outside KUMC. Your information will be shared with representatives of the National Institutes of Health, the laboratory that processes study lab samples, the Data Coordinating Center (DCIAC), the Data and Safety Monitoring Board and U.S. agencies that oversee human research (if a study audit is performed). The purpose for using and sharing your information is to make sure the study is done properly.

Some of the persons or groups who receive your health information, including the sponsor, may not be required by law to protect it. Once your information has been shared outside of KUMC, it might be disclosed by others and no longer protected by the federal privacy laws or this authorization.

There is a small risk that if people other than the researchers were given my genetic facts, they could misuse them. If genetic information was given to employers or insurers it could affect my ability to get a job or be insured. Misuse could cause problems for family members. In order to minimize these risks, my genetic information will be kept confidential as noted in this form.

Your permission to use and share your health information will not expire unless you cancel it. Any research information that is placed in your medical record will be kept indefinitely.

While you are participating in this study, you will have access to any study information that is placed in your KUMC medical record. However, genetic information will not be placed in your medical record and will not be made available to you. The genetic information will be shared with the researcher for the purpose of analysis, but will not be shared with you.

QUESTIONS

You have read the information in this form. Dr. Grantham or his associates have answered your question(s) to your satisfaction. You know if you have any more questions after signing this you may contact Dr. Grantham or one of his associates at (913) 588-7609. If you have any questions about your rights as a research subject, you may call the Human Subjects Committe (913) 588-1240 or write them at Mail Stop #1032, University of Kansas Medical Center, 3901 Painbow Blvd., Kansas City, KS 66160.

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

SUBJECT RIGHTS AND WITHDRAWAL FROM THE STUDY

You understand that your participation in this study is voluntary. The choice not to participate or to quit at any time can be made without penalty or loss of benefits. You understand that not participating or quitting will have no effect upon the medical care or treatment you receive now or in the future at the University of Kansas Medical center. The study may be discontinued for any reason without your consent by the investigator conducting the study, by the sponsor of the study, or the FDA. Your participation can be discontinued by the investigator or by the sponsor if it is felt to be in your best interest or if you do not follow the study requirements. You may be asked to return to the clinic for a final visit.

You have a right to change your mind about allowing the research team to have access to your health information. To cancel your permission you must send a written request to Dr. Jared J. Grantham M.D. at KU Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160.

If you cancel permission to use your health information, you will be withdrawn from the study. The researchers and the sponsor may continue to use and share information that was gathered before your cancellation.

CONSENT

Dr. Jared J. Grantham or his associates have given you information about this research study. They have explained what will be done and how long it will take. They explained any inconvenience, discomfort or risks that may be experienced during this study.

You freely and voluntarily consent to participate in this research study. You have read and understand the information in this form and have had an opportunity to ask questions and have them answered. ***You will be given a signed copy of the consent form to keep for your records.***

_____
Type/Print Subject's Name

_____ _____ _____
Signature of Subject Time Date

_____
Type/Print Name of Witness

_____ _____
Signature of Witness Date

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

_____
Type/Print Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date

OPTIONAL SUB-STUDY
You may choose not to donate your blood samples for immortalization and future research studies while still participating in the main study.

In addition, if you agree, your blood cells will be put through a process called immortalization to enable the researchers to have DNA for future research studies related to this project. This DNA will be stored in a central repository at the NIH (NIDDK Center for Genetic Studies, Rutgers University Cell and DNA Repository). Because the genetic tests in this study are not used for regular medical care, you will not be told the results of the test(s). The results will also not be put in your medical record. Should you not wish to participate in this part of the study, you will not be held back from participating in the rest of the study. Given that the identity of these samples will be kept anonymous, the risk of DNA testing with regard to your good name, insurability, employability and paternity are minimal. The genetic information obtained in this study will not be shared directly with you and will be kept anonymous. The information about uses and disclosures of your health information for the main study also applies to your blood samples.

In case either the DNA isolation or the immortalization process fails, you may be asked to provide an additional blood sample to repeat the procedure. When these studies are completed, the researcher may wish to perform additional tests on these samples related to this disease. De-identified (identified by CRISP ID number only) DNA samples will be shared with other CRISP site investigators.

You may request that your DNA sample be destroyed and to do so you can contact the Principal Investigator, Dr. Jared J. Grantham M.D. at 913 588 7609. In case that either the DNA isolation or the immortalization process fails, we may ask you for an additional blood sample to repeat the procedure.

Please initial the options with which you agree.

(A)_____I give my permission to have my DNA isolated and my blood cells immortalized. I understand that if the process is successful, additional blood for DNA studies will not be required. However, if the process is not successful, an additional blood sample may be requested.

(B)_____I do not give my permission for my DNA to be isolated.

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

(C)_____ I do not give my permission for the immortalization process but you may isolate my DNA.

b. Year 2 and Year 4 Visits

On Year 2 and 4 you will be ask to provide a blood sample for measurement of serum creatinine in a central laboratory. The blood sample can be obtained either at the GCRC/KUMC laboratory or at your local physician's office/laboratory. If the blood sample is obtained at a local laboratory, we will provide you with the appropriate tube labeled with the CRISP identification number, a mailing container and instructions.

c. Semi-annual telephone interviews
Every six months, the CRISP study coordinator will contact you to obtain information regarding any medication changes, hospitalizations, doctor visits and outpatient procedures. We will ask your permission to contact and obtain information regarding your health from any physician who has examined or treated you since your last visit or telephone interview. By signing this informed consent form, you are giving us permission to obtain these records.

WHAT WILL HAPPEN TO YOUR SAMPLES?

De-identified small samples of your blood, urine, and DNA will be stored for future research studies of Polycystic Kidney Disease. The DNA sample may be stored for a long time, even after your death. These samples will be given a code (rather than your name). This code will allow your sample to be used without anyone knowing that it is your sample just by looking at the label. These samples will be stored in central repositories controlled by the NIH (Fisher BioServices and NIDDK Center for Genetics Studies, Rutgers University Cell and DNA Repository).

There is a small risk that if people other than the researchers were given my genetic facts, they could misuse them. If genetic information was given to employers or insurers it could affect my ability to get a job or be insured. Misuse could cause problems for family members. In order to minimize these risks, my genetic information will be kept confidential as noted in this form.

STORAGE OF SPECIMENS

Biosamples (blood and urine): Please initial your choice(s) below:

_____I agree to allow my blood and urine samples stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

_____ I do not agree to allow my blood and urine samples stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

_____I wish to be notified if my blood and urine samples are going to be used for research on Polycystic Kidney Disease.

Genetics Samples (DNA) [if collected] Please initial your choice(s) below:

_____I agree to allow my DNA sample to be stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

_____ I do not agree to allow my DNA sample to be stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

_____ I wish to be notified if my DNA sample is going to be used for research on Polycystic Kidney Disease.

If you agree to have your sample(s) stored in the Repository, you can change your mind up until the end of the CRISP study. When study researchers receive written instructions from you, they will destroy your sample and all information that identifies you. After the CRISP study ends, you will not be able to withdraw your sample because the Repository will not know which one is yours. The sample will stay in the Repository indefinitely. If you agree to give your sample, it will be the property of UAB and may be used for research by Dr. Grantham and CRISP investigators. Other researchers may also ask for part of your sample for future studies.

_____
Type/Print Subject's Name

_____ _____ _____
Signature of Subject Time Date

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

CONSENT FORM

Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP II) (relatives)

Protocol # QG816940

Investigators:
Jared J. Grantham M.D.
Franz Winklhofer M.D.
Connie Wang M.D.
Louis Wetzel M.D.

Sponsor: National Institutes of Health

INTRODUCTION

You are being asked to take part in this research study because you have polycystic kidney disease (PKD) and you are a relative of a participant in the original Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP Study). This research study will be conducted at the University of Kansas Medical Center with Jared J. Grantham M.D. as the principal investigator. Approximately 300 affected relatives of CRISP I participants will be enrolled in the study at the University of Kansas Medical Center (approximately five affected relatives for each of the 60 CRISP I participants studied at KUMC). Additional affected relatives will be enrolled at the other CRISP I sites including Emory University, Atlanta, GA, University of Alabama, Birmingham, and the Mayo Clinic, Rochester, MN.

You do not have to participate in this research study. It is important that before you make a decision to participate, you read the rest of this form. You should ask as many questions as needed to understand what will happen to you if you participate in this study.

BACKGROUND

You are being asked to take part in this research study because you have polycystic kidney disease (PKD) and you have a relative who participated in the original Consortium for Radiologic Imaging studies of polycystic kidney disease (CRISP) Study. In the current study the research doctors will continue following your relative for another four years to determine if pictures of the kidney using magnetic resonance imaging (MRI) can detect change in kidney size over a short period of time. If you enroll, you will participate for a single visit with KUMC where a blood sample and complete medical history will be obtained in order to determine the extent to which the PKD is being expressed in your family.

As you read this form describing the study, ask any questions you have. Take your time to decide. Feel free to discuss the study with your family, friends, and healthcare

HSC Submission Date:

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

provider before you decide. You may stop participating at any time during the study. You may decide not to participate. If so, none of your current benefits or normal health care will be affected in any way. When you feel comfortable that all your questions have been answered, and you wish to take part in this study, sign this form in order to begin your participation. Your signature means you have been told about the study and what the risks are. Your signature on this form also means that you want yourself to take part in this study.

PURPOSE

The purpose of this study is to collect more exhaustive family histories of all CRISP I patients to draw an electronic family tree of each family and to identify genetic factors that influence the severity of the cystic disease.

PROCEDURES

If you agree to participate in this study a blood sample (30 ml or approximately two tablespoons) will be obtained from a vein, for measurement of serum creatinine and extraction of DNA.

If you agree to participate in this study your clinical and imaging data will be obtained from your clinical records. Participants will also be asked to complete a lifestyle questionnaire (to assess smoking history, caffeine exposure, estrogen exposure and levels of physical activity) and a family history questionnaire to further extend the traceable family.

When possible, the most recent of your Computer Tomography (CT) or Magnetic Resonance Imaging (MRI) examination of the abdomen will be reviewed. If these studies are not available, the most recent ultrasound images will be reviewed to assess renal disease severity. All of this clinical and lifestyle information, plus the available genetic information on the family, will be stored in the CRISP database that is maintained by the DCIAC (The Data Coordinating and Imaging Analysis Center) located at the University of Pittsburgh.

Participation in this study will be limited to the time necessary to provide the blood sample and information described above.

The doctors involved in this study will isolate genetic material (DNA) from the blood samples, identified by CRISP ID number only, in order to study the family factors, or genes, that are inherited and cause Autosomal Dominant Polycystic Kidney Disease (ADPKD).

RISKS

There are risks related to blood drawing that include pain, bruising and infection.

There are no pregnancy-related risks.

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

NEW FINDINGS STATEMENT

You will be informed if any significant new findings develop during the course of the study that may affect your willingness to participate in this study.

BENEFITS

There are no direct benefits to you for participating in this study. Information regarding your level of kidney involvement may help to determine how fast you are progressing with PKD. This information will be made available to your treating physician. You will continue to receive your usual treatment by your primary physician. No changes to your usual care will occur in this study. If you are thinking about participating in another clinical study or trial, you need to discuss this with the Study Coordinator and the Principal Investigator before you can participate.

ALTERNATIVES

The alternative to consenting to participate in this study is not to participate at all. If this is the case and you decide not to participate, there will not be changes in your treatment and you will continue to receive your usual medical care.

COSTS

There will be no cost to you for participation in the research. You will not need to pay for tests and procedures which are done just for this research study. These tests and procedures include venipuncture, measurement of serum creatinine and extraction of blood DNA for genetic testing. The costs of your standard medical care will be billed to you and/or your insurance company in the usual manner.

PAYMENT TO SUBJECTS

You will not be paid for taking part in this study.

IN THE EVENT OF INJURY

In the event you experience a serious side effect during this study, you should immediately contact Beth Stafford R.N at 913-588-7609. If it is after 5:00 p.m., a holiday or a weekend, you should call 913-588-5000 and ask for the Nephrology doctor on call.

If any injury or illness should occur to you as a direct result of being in this study, the investigator will be able to tell you what treatment options are available. Payment for lost wages, disability or discomfort is not available. You do not give up any of your rights by signing this form.

INSTITUTIONAL DISCLAIMER STATEMENT

If you believe you have been injured as a result of participating in research at Kansas University Medical Center (KUMC), you should contact the Director, Human Research

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

Protection Program, Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160. Compensation to persons who are injured as a result of participating in research at KUMC may be available, under certain conditions, as determined by state law or the Kansas Tort Claims Act.

CONFIDENTIALITY AND PRIVACY AUTHORIZATION

Study records that identify you will be kept confidential as required by law. Researchers cannot guarantee absolute confidentiality. Efforts will be made to keep your personal information confidential. If the results of this study are published or presented in public, information that identifies you will be removed.

The privacy of your health information is protected by a federal law known as the Health Insurance Portability and Accountability Act (HIPAA). By signing this consent form, you are giving permission ("authorization") for KUMC to use and share your health information for purposes of this research study. If you decide not to sign the form, you cannot be in the study.

To do this research, the research team needs to collect health information that identifies you. They will collect information from study activities described in the Procedures section of this form. Your health information will be used at KUMC by Dr. Grantham, members of the research team, the University of Kansas Medical Center Research Institute and officials at KUMC who oversee research, including members of the KUMC Human Subjects Committee and other committees and offices that review and monitor research studies.

By signing this form, you are giving Dr. Grantham and the research team permission to share information about you with persons or groups outside KUMC. Your information will be shared with representatives of the National Institutes of Health (the sponsor of the study), the laboratory that processes study lab samples, the Data Coordinating Center, the Data and Safety Monitoring Board, the U.S. Food and Drug Administration (FDA) and U.S. agencies that oversee human research (if a study audit is performed). The purpose for using and sharing your information is to make sure the study is done properly and to evaluate the safety and effectiveness of the study.

Some of the persons or groups who receive your health information, including the sponsor, may not be required by law to protect it. Once your information has been shared outside of KUMC, it might be disclosed by others and no longer protected by the federal privacy laws or this authorization.

Your permission to use and share your health information will not expire unless you cancel it.
While you are participating in this study, you will have access to your study related information. However, genetic information will not be available to you and will only be

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

shared with the researcher for the purpose of analysis. You may not have access to any of your information after the end of the study.

QUESTIONS

You have read the information in this form. Dr. Grantham or his associates have answered your question(s) to your satisfaction. You know if you have any more questions after signing this you may contact Dr. Grantham or one of their associates at (913) 588-7609. If you have any questions about your rights as a research subject, you may call (913) 588-1240or write the Human Subjects Committee at Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160.

SUBJECT RIGHTS AND WITHDRAWAL FROM THE STUDY

You understand that your participation in this study is voluntary. The choice not to participate or to quit at any time can be made without penalty or loss of benefits. You understand that not participating or quitting will have no effect upon the medical care or treatment you receive now or in the future at the University of Kansas Medical center. The study may be discontinued for any reason without your consent by the investigator conducting the study, by the sponsor of the study, or the FDA. Your participation can be discontinued by the investigator or by the sponsor if it is felt to be in your best interest or if you do not follow the study requirements. You may be asked to return to the clinic for a final visit.

You have a right to change your mind about allowing the research team to have access to your health information. To cancel your permission you must send a written request to Dr. Jared J. Grantham at KU Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160.

If you cancel permission to use your health information, you will be withdrawn from the study. The researchers and the sponsor may continue to use and share information that was gathered before your cancellation. They will stop collecting any additional information about you.

CONSENT

Dr. Grantham or his associates have given you information about this research study. They have explained what will be done and how long it will take. They explained any inconvenience, discomfort or risks that may be experienced during this study.

You freely and voluntarily consent to participate in this research study. You have read and understand the information in this form and have had an opportunity to ask questions and have them answered. ***You will be given a signed copy of the consent form to keep for your records.***

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

Type/Print Subject's Name

Signature of Subject | Time | Date

Type/Print Name of Witness

Signature of Witness | Date

Type/Print Name of Person Obtaining Consent

Signature of Person Obtaining Consent | Date

OPTIONAL SUB-STUDY

You may choose not to donate your blood samples for immortalization and future research studies while still participating in the main study.

In addition, if you agree, your blood cells will be put through a process called immortalization to enable the researchers to have DNA for future research studies related to this project. This DNA will be stored in a central repository at the NIH (NIDDK Center for Genetic Studies, Rutgers University Cell and DNA Repository). Because the genetic tests in this study are not used for regular medical care, you will not be told the results of the test(s). The results will also not be put in your medical record. Should you not wish to participate in this part of the study, you will not be held back from participating in the rest of the study. Given that the identity of these samples will be kept anonymous. The information about uses and disclosures of your health information for the main study also applies to your blood samples.

The genetic information obtained in this study will not be shared directly with you and will be kept anonymous. If you agree to this part of the study, you will give up ownership of this blood sample.

In case either the DNA isolation or the immortalization process fails, you may be asked to provide an additional blood sample to repeat the procedure. When these studies are completed, the researcher may wish to perform additional tests on these samples related to this disease.
De-identified (identified by CRISP ID number only) DNA samples will be shared with other CRISP site investigators.

HSC #: 10824
Approval Date: 5/8/07 to 5/7/08
Assurance #: FWA00003411

You may request that your DNA sample be destroyed and to do so you can contact the Principal Investigator, Dr. Jared Grantham at 913-588-7609. In case that either the DNA isolation or the immortalization process fails, we may ask you for an additional blood sample to repeat the procedure.

Please initial the option with which you agree.

(A)_____I give my permission to have my DNA isolated and my blood cells immortalized. I understand that if the process is successful, additional blood for DNA studies will not be required. However, if the process is not successful, an additional blood sample may be requested.

(B)_____I do not give my permission for my DNA to be isolated.

(C)_____I do not give my permission for the immortalization process but you may isolate my DNA.

WHAT WILL HAPPEN TO YOUR SAMPLES?

A sample of your blood DNA will be stored for future research studies of Polycystic Kidney Disease. The DNA sample may be stored for a long time, even after your death. These samples will be given a code (rather than your name). This code will allow your sample to be used without anyone knowing that it is your sample just by looking at the label. These samples will be stored in central repositories controlled by the NIH (Fisher BioServices and NIDDK Center for Genetics Studies, Rutgers University Cell and DNA Repository).

There is a small risk that if people other than the researchers were given my genetic facts, they could misuse them. If genetic information was given to employers or insurers it could affect my ability to get a job or be insured. Misuse could cause problems for family members. In order to minimize these risks, my genetic information will be kept confidential as noted in this form.

STORAGE OF SPECIMENS

Biosamples (blood): Please initial your choice(s) below:

___ I agree to allow my blood sample stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

___ I do not agree to allow my blood sample stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

___ I wish to be notified if my blood sample is going to be used for research on Polycystic Kidney Disease.

Genetics Samples (DNA) [if collected] Please initial your choice(s) below:

___ I agree to allow my DNA sample to be stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

___ I do not agree to allow my DNA sample to be stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

___ I wish to be notified if my DNA sample is going to be used for research on Polycystic Kidney Disease.

If you agree to have your sample(s) stored in the Repository, you can change your mind up until the end of the CRISP study. When study researchers receive written instructions from you, they will destroy your sample and all information that identifies you. After the CRISP study ends, you will not be able to withdraw your sample because the Repository will not know which one is yours. The sample will stay in the Repository indefinitely. If you agree to give your sample, it will be the property of KUMC and may be used for research by Dr. Grantham and CRISP investigators. Other researchers may also ask for part of your sample for future studies.

_____
Type/Print Subject's Name

_____ _____ _____
Signature of Subject Time Date

HSC #: 10824
Approval Date: 5/9/07 to 5/7/08
Assurance #: FWA00003411

CRISP II Study Flowsheets

Emory University Flow-Sheets

GENERAL CLINICAL RESEARCH CENTER (GCRC) DAY TO DAY ORDERS
EMORY UNIVERSITY SCHOOL OF MEDICINE

TITLE: CRISP II (CONSORTIUM FOR RADIOLOGIC IMAGING STUDIES OF POLYCYSTIC KIDNEY DISEASE) STUDY
INPATIENT STAY (at year 1 and 3)
Study 7005 (version date: 09/17/07)

Admission Date:
Patient Name:
Medical Record No:
Investigators: Arlene Chapman, M.D. (PIC # 10162, home # 404-373-6085); Frederic Rahbari Oskoui, MD (PIC#17680)
Diego Martin, MD, PhD (Radiology: 404-778-3800)
Coordinators: Yoosun Han (PIC# 13695); Beth Wilkening, PA-C (PIC# 11443); Diane Watkins, MA (PIC# 10627); Rivka Elbein, RN (#10945)

Day 0:_____; Date: _____

Initials

_____ 1. Admit to GCRC

_____ 2. Activity ad lib (on Ward)

_____ 3. Vital Signs: BP_____; P _____; R_____; T _____

_____ 4.Height without shoes in cm (to 0.1 cm) _____ cm;

_____ 5. Weight without shoes in kg (to 0.1 kg) _____ kg

_____6. Notify admitting M.D. Dr. Chapman (PIC 10162) or Dr. Rahbari (PIC#17680). Notify coordinator, Yoosun Han (PIC# 13695).

_____ 7. **Place the copies of** informed consent **and** history and physical exam **form in** chart. **Also, have the** patient **fill out** quality of life (SF-36v2) **and** pain questionnaires.

Variances & Actions: **RN Signature:**

Day 0:_____; Date: _____ (continued)

_____ 8. Check **medication list.** Call **Yoosun Han,** if **followings** are included.

- altering renal hemodynamics or with potential nephrotoxicity **(NSAIDs, antibiotics)**
- altering serum creatinine independent of GFR **(trimethoprim [Bactrim], cimetidine)**

* However, participants taking low dose aspirin (81 or 325 mg once daily) will be allowed continue on this dose throughout the study as effects on renal hemodynamics are minimal.

* For a visit in which MR imaging will be done, all morning dose of antihypertensive medications will be held until the imaging exam has been completed. If a participant is on any second-line antihypertensive medications that require twice daily dosing, those medications should be also held the night prior to the MR visit. The purpose of holding the antihypertensive medications prior to the imaging exam is to reduce the hemodynamic effects of medications on renal blood flow measurement.

_____ 9. Regular diet for dinner.

_____10. Subject to take **own medications** during in-patient stay**. Hold antihypertensive** medications for the **evening dose**, if any, **until MRI and MRA completed.** ***Subjects not to take medication in the mornings until after GFR and MR complete.***

_____11. Between 9 p.m. and 10 p.m., **give subject** 3 x 8 oz glasses of **water** (may have more if desire).

_____12. Have the patient in bed. **NPO except liquid after 10pm. *****The subject not to have meals until after GFR test and MR complete in the morning.***

Variances & Actions: **RN Signature:**

Day 1: _____ Date:_____

Initials

_____1. **Wake subject at 7: 00 am. Have the** patient empty bladder. **Have the** patient ring a bell **at the** completion **of the** urination.

Urine voiding times _____am or pm (circle one)

Record urine volume _____mL (* Urine volume must be at least 50 mL.)

_____ 2. Send fresh void urine as soon as possible: *Processing times should be **no longer than 20-30minutes** from the time of acquisition at **Emory GCRC lab.**

1) **to Emory GCRC lab** for □future RNA/ DNA retrieval, and □six 5 mL urine aliquots. The rest of urine remains at Emory GCRC lab as a back-up for 5 days.
2) to Emory University Hospital **(EUH) Lab** for □**urine albumin,** and □**urine creatinine.**

***Send urine** to **EUH Lab** for □**qualitative pregnancy test for all women.**
- Have results on the chart before the end of the day. The patient needs to be rescheduled if she is pregnant.

_____ 3. **Using the same scale as admission**, weight without shoes **in kg (to 0.1 kg)** _____ . __ kg

_____ 4. Place **heplock** in **forearm;** use **0.9% saline** for **flushes.**

_____ 5. Blood will be **collected** as follows**. Time _____am/pm (circle one)**

Send 1 x 3 ml Green top tube (□CP Comprehensive & **□Lipid panel),**
and 1x 5 ml Lavender top tube (□CBC with diff) to Emory University Hospital **(EUH)Lab.** (Check each box after placing order)

Send 3 x 10ml Red/Gray top tubes to the **GCRC Core Lab:** (1 tube for Cleveland Clinic and 2 tubes for NIDDK repository)
and 2 x 8 ml Green/Gray top tubes to the **GCRC Core Lab** for NIDDK repository.

****Send the blood samples IMMEDIATELY to the Core Lab for processing. Core Lab will notify nursing staff if any of the samples are hemolyzed and need to be re-drawn before patient goes to Radiology for MRI/MRA. *****

Variances & Actions: **RN Signature:**

_____

_____

Start of GFR test:

_____6. Have the **patient drink** 6 x 8 oz glasses of **water** in preparation for the iothalamate clearance determination.
Time: _____am/pm @ the end of drinking water.

_____7. Instruct the patient that she or he can urinate, if the patient cannot hold the urine for 60 minutes. Collect all urine over the next 60 min. During the 60 min, save all urine and total @ the end of 60 min, to add 60 minute urine void. If the patient needs to urinate in 55 minutes, use it as 60 minute urine void.

_____8. Prepare iothalamate Injection.
NOTE: Patients > 40 kg all receive the same dose of Iothalamate.
Dose: **0.5 ml Iothalamate** (300 mg) mixed with **0.5 ml sterile Bacteriostatic Water**.

_____9. **One hour after** drinking water, have the **patient urinate** completely. Instruct the **patient** to **ring a bell** at the completion of urination. Record the exact **time** _____am/pm (circle one). Record total **volume** of urine void _____ml

_____10. **Inject Iothalamate meglumine subcutaneously immediately,** after completing **urine void,** by the **deltoid** in the arm **opposite** where the **heplock** is placed. Record exact **time** of injection. _____am/pm

_____11. Send the urine to Emory GCRC lab to **aliquot 5 ml** of **urine** into tubes and label **UO**.

_____12. Have the **patient** drink 2 x 8 oz glasses of water.

_____13. Page **Nephrology fellow, Dr. _____ (PIC# _____),** after injection, to meet the patient and start the bladder ultrasound to mark X for the bladder. Also, let Nephrology fellow have GFR testing flow chart.

_____14. **60 minutes** after iothalamate **injection**, have the **patient** to **urinate completely** again, and collect entire urine specimen as **UE**. Instruct the **patient** to **ring a bell** when finished voiding. Record the exact **time** _____am/pm (circle one), and **volume** _____ ml **Flow rate** _____ml/min (volume/time) (*Time between UO &UE _____min) (*Urine void flow rate **must** be ≥ **3 ml/min**. (equal to or greater than 3 ml/min))

Variances & Actions: **RN Signature:**

_____15. **Bladder ultrasound** is to assess the completion of bladder emptying. This needs to be done **within 10 minutes.** Do ultrasound reading of bladder x 1, and record. **Bladder volume** _____ml (*Bladder volume **must** be < **20 ml**)

*If the bladder volume is > 20 ml, have the patient urinate again. Time _____am/pm (circle one) Volume _____ ml
Repeat ultrasound reading of bladder x 1, and record. Bladder volume _____ml (*Bladder volume must be < 20 ml)

**If the bladder volume is still > 20 ml, extend the test for 10 minutes, and have the patient urinate again.
Have the patient to ring a bell when finished voiding. Record the exact time _____am/pm (circle one), and volume _____ ml
Repeat ultrasound reading of bladder x 1, and record. Bladder volume _____ml (*Bladder volume must be < 20 ml)

***Save all urine of UE, and add all together for accurate **total volume** _____ml. **Time** between UO &UE _____min
Flow rate _____ml/min (volume/time) (*Urine void flow rate **must** be ≥ **3 ml/min**. (equal to or greater than 3 ml/min))

_____16. **Within 5 minutes** of UE voiding, **(*DO NOT DRAW the blood, if the bladder volume is > 20 ml.)**
Draw **4 ml** of **blood (P1)** in sodium heparin **green top** plasma tube **(*DO NOT use light green top tube!)** from the **heplock** placed.
Time of blood draw _____am/pm (circle one)

_____17. Send 4 ml of blood (P1) plasma tube to **Emory GCRC Lab** to (1) **Centrifuge** for 10 min at 3,000 rpm and
(2) **Aliquot** plasma into clear top tube **(P1)**
(3) Store the specimen in the refrigerator until the specimen is shipped.

_____ 18. Discard UE (equilibration urine) urine specimen, after making sure that the bladder volume was < 20 ml.

_____ 19. Have the **patient** drink 1-2 x 8 oz glasses of **water**.

_____ 20. Instruct the patient that she or he can urinate, if the patient cannot hold the urine for 45 minutes. In that case, save the urine that was voided in between, to add 45 minute urine void. If the patient needs to urinate in 40 minutes, use it as 45 minute urine void.

_____21. **45 minutes** after UE, have the **patient urinate** completely, and collect entire urine specimen as **U1**. Instruct the **patient** to **ring a bell** when finished voiding. Record the exact **time** _____am/pm (circle one), and **volume** _____ ml (**must** be **at least 150 ml**)
Flow rate _____ml/min (volume/time) (*Time between UE &U1 _____min) (*Urine void flow rate **must** be ≥ **3 ml/min.**
(equal to or greater than 3 ml/min))

Variances & Actions: **RN Signature:**

_____ 22. Bladder ultrasound is to assess the completion of bladder emptying. This needs to be done **within 10 minutes.** Do ultrasound reading of bladder x 1, and record. **Bladder volume** _____ml (*Bladder volume **must** be < **20 ml**)

*If average the residual bladder volume is > 20 ml, or patient has voided < 150 ml, have the patient void again.
Time _____am/pm (circle one) **Volume** _____ ml
Repeat ultrasound reading of bladder x 1, and record. Bladder volume _____ml (*Bladder volume must be < 20 ml)

**If the bladder volume is still > 20 ml or patient has voided < 150 ml, extend the test for 30 minutes and have the patient urinate again.
Have the patient to ring a bell when finished voiding. Record the exact time _____am/pm (circle one), and volume _____ ml
Repeat ultrasound reading of bladder x 1, and record. Bladder volume _____ml (*Bladder volume must be < 20 ml)

***Save all urine of U1, and add all together for accurate **total volume** _____ml **Time** between UE&U1 _____min
Flow rate _____ml/min (volume/time) (*Urine void flow rate **must** be ≥ **3 ml/min**. (equal to or greater than 3 ml/min))

_____23. **Within 5 minutes** of U1 voiding, **(*DO NOT DRAW the blood, if the bladder volume is > 20 ml or total U1 urination <150ml) Draw 4 ml** of **blood (P2)** in sodium heparin **green top** plasma tube **(*DO NOT use light green top tube!)** from the **heplock** placed. Time of blood draw _____am/pm (circle one)

_____24. After P2 blood draw, remove the heplock.

_____25. **Send** 4 ml of blood **(P2)** plasma tube to **Emory GCRC** to
(1) **Centrifuge** for 10 min at 3,000 rpm and
(2) **Aliquot** plasma into clear top tube **(P2)**
(3) Store the specimen in the refrigerator until the specimen is shipped.

_____26. **Send** the U1 **urine specimen** to **Emory GCRC** to **aliquot 5 ml** of U1 into **tube** and **label U1.**

_____27. Store the specimens in the refrigerator until the specimens are shipped.
(*GFR kit is to be shipped to Mayo Medical Laboratories, for measurement from Emory GCRC Laboratory. From Emory GCRC lab, Sharon at 2-1181 will be called to ship the specimens on working business day.)

Variances & Actions: **RN Signature:**

MR exam:

_____28. Coordinator will escort the patient to **MRI/MRA** at the scheduled time. **_____am**. This should take approximately 30 minutes.

Start of BP measurement:

_____**29.** During the last 30 minutes, has the patient smoked or consumed caffeine? (Circle One) **Yes** **No**
(*If yes, please wait 30 minutes since last cigarette or caffeine consumption.)

_____**30.** **Non-dominant** arm (in terms of handedness) (circle one). **Right** **Left**

_____**31.** Cuff size (Circle one.) **C**hild (17-22 cm) **A**dult (22-32 cm) **L**arge (33-42 cm)

_____**32.**1) Measure the **non-dominant** arm circumference (the opposite side of the writing hand) at half way between acromial process and the tip of the elbow to determine blood pressure cuff size.

Arm circumference:_____cm
Sitting blood pressure: _____mmHg

2) Repeat Step (1) for the **dominant** arm:

Arm circumference:_____cm
Sitting blood pressure:_____mmHg

_____**33.** Is there a difference in **systolic BP** of **20 mm Hg or more** between **both arms**? (circle one) **Yes** **No**
(* If **Yes**, use the **arm** that had **20 mmHg higher** in **systolic BP** reading, instead of non-dominant arm.**)**

Study reference arm is _____
Serial number of the Dinamap monitor_____ □**Automated** □PCC monitor (**non-automated**) **(Mark one)**
Brand name of BP monitor _____

_____**34.** Take **Blood pressure** on **non-dominant arm, (unless dominant arm** has **higher systolic BP** of **20 mm Hg or more),** three times with appropriate size cuff after **seated quietly** for **5 minutes** with the arm resting at heart level, taken 3 times **at least 30 seconds**

Variances & Actions: **RN Signature:**

intervals.

Time_____:_____BP#1_____ HR#1_____ bpm

Time_____:_____BP#2_____ HR#2_____ bpm

Time_____:_____BP#3_____ HR#3_____ bpm

_____**35.** Is there a **difference** of **more than 10 mm Hg** (systolic or diastolic) between the **second** and **third** readings in one sitting? (Circle one)
Yes **No** (If **Yes**, a **fourth** and **fifth** reading will be recorded for that sitting.)

Time_____:_____BP#4_____ HR#4_____ bpm

Time_____:_____BP#5_____ HR#5_____ bpm

_____ 36. Patient is to stand for 3 minutes. Ask patient if he/she feels lightheaded. Take one blood pressure measurement in the study reference arm.

Time_____:_____ BP_____ HR _____bpm

_____37. Patient can have breakfast and medications after GFR test and MR exam.

_____38. Patient can be discharged with instructions to follow up with primary care physician.

_____39. Make copies of completed day to day order and H&P and put in basket.

Physician's Signature: _____ **Date: _____**
Arlene Chapman, M.D. (PIC # 10162)

Variances & Actions: **RN Signature:**

Mayo Clinic Flow-Sheets

This printout is current as of 7/23/2007, 9:13:15AM

Lab Flowsheet Verification for protocol 06-009502, Study Plan IPRC

Flowsheet Revision Number: 0 **Is this template marked as complete and in production: YES**

Blood Volume For Day 2 is 53.50 mL
Total Blood Volume For This Study Plan = 53.50 mL
NOTE: This blood volume will NOT include HMSR bloods that are not built into this template

High level processing instructions:

The study coordinator will provide the 5 mL screw-top tubes, 1.5 mL orange-top tubes, and labels. Do not use the aliquot labels from the CRU Scheduling System, except for the label for the 50 mL conical tube for centrifuging the RNA/DNA urine.

Note: You will not use all of the labels on the label sheets.

********** *Short Renal Clearance* **********
Order under the UO specimen as 81476. Enough labels will print from Lab 3 for all of the required specimens. When labels print from Lab3, write the following on the labels, one for each specimen. U0, U1, P1, and P2.

*****NOTE: Specimens must be shipped on the day of collection.*****

You will receive 4 Shipping Manifest forms from the study coordinator:
* *Repository - Serum/Plasma Samples*
* *Central Lab - CCF (2 forms - one for the first specimen collected ("A" and "B" together on the same form and one for the second specimen.)*
* *Repository - Urine Samples (Specimens labeled MCP-1)*

Each set of the creatinine aliquots should have its own manifest sheet, "Central Lab - CCF" (The A and B aliquots both go on one sheet).

On the Manifest forms enter the number of tubes and double check to make sure the accession numbers on the forms match the accession numbers on the tubes.

Before sending to the SSA, check to make sure all of the CRU labels have been taken off of the tubes and that only the drug company labels are on the tubes.

Once all urine and blood specimens have been processed, put into a 5 lb. styro on wet ice and send to the SSA with the Shipping Manifest forms. The specimens need to reach the SSA by 1:30 in order to be shipped on the day of collection, which is a requirement of the drug company.

Shipping forms:

Day: *2*	**6:00**	**Tmpt:**	**Desc:**	**HMSR BLOOD**
Urine	Sarstedt 6	5.00 ml	Tube label: ''	**results will go to medical record**
Instructions:	*Aliquot from random urine collection and send to CCL.*			

No Aliquots	Temperature	Destination Lab
	Ambient	CCL

Test Code	Mnemonic	Description
81260	RMA	Mircoalbumin-Random, U

Day: *2*	**6:00**	**Tmpt:**	**Desc:**	No test orders
Urine	Urine, Hat	60.00 ml	Tube label: *'Random Urine'*	**KIT**
Instructions:	*Aliquot.*			

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Pt ID?	Instructions	
Nbr 1	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 2	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 3	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 4	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 5	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 6	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				

Nbr 7	30.00	Frozen (store at -70C)	SSA	*'FNA/DNA Urine Centrifuge Tube'*	No	*KEEP TUBE ON ICE THROUGHOUT THIS ENTIRE PROCESS.* *Document the urine volume, processing times, and voiding time on the provided requisition form.* *Within 20 - 30 mins. of collection perform the following:* *1. Centrifuge at 1600 rpms for 5 mins.* *2. Using a sterile pipette, decant the supernatant and discard.* *3. Using a sterile pipette, transfer the bottom 250 uL pellet (sometimes barely- or nonvisible). to a 1.5 mL eppendorf tube previously prepared with 750 uL of TriReagent.* *4. Invert several times to mix and freeze.*	**KIT**

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Nbr 8	0.30	Frozen (store at -70C)	SSA	*'FNA/DNA'*	No	*Freeze at -70 C and send to SSA with pink card.*	**KIT**

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *2*	**7:00**	**Tmpt:**	**Desc:**	No test orders
Blood	Green/black	8.00 ml	Tube label: *'Stored Plasma'*	**KIT**

Instructions: *Centrifuge at 3K for 15 mins. Remove the CRU label from the tube. Refrigerate and send to SSA on cold pack on the day of collection with pink card.*

No Aliquots	Temperature	Destination Lab
	Refrigerated	SSA

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *2*	**7:00**	**Tmpt:**	**Desc:**	No test orders
Blood	Green/black	8.00 ml	Tube label: *'Stored Plasma'*	**KIT**

Instructions: *Centrifuge at 3K for 15 mins. Remove the CRU label from the tube. Refrigerate and send to SSA on cold pack on the day of collection with pink card.*

No Aliquots	Temperature	Destination Lab
	Refrigerated	SSA

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *2* **7:00** **Tmpt:** **Desc:** No test orders

Blood SST/Gld 3.5 3.00 ml Tube label: *'Creatinine'* **KIT**

Instructions: *Allow to clot. Centrifuge at 3 K for 15 minutes. Aliquot serum equally between the two orange-top tubes labeled "Serum C-1."*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	0.50	Frozen (store at -70C)	SSA	*'Serum C-1'*	No	*Freeze at - 20 C. Send to SSA with pink card.*

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Nbr 2	0.50	Frozen (store at -70C)	SSA	*'Serum C-1'*	No	*Freeze at - 20 C. Send to SSA with pink card.*

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *2* **7:00** **Tmpt:** **Desc:** **HMSR BLOOD results will go to medical record**

Blood SST/R&B 8.5 8.50 ml Tube label: *''*

Instructions: *Do not process, send to CCL.*

No Aliquots	Temperature	Destination Lab
	Ambient	CCL

Test Code	Mnemonic	Description
8053	LPSC	Lipid Panel
87972	ELPN	Electrolyte Panel, Serum

Day: *2* **7:00** **Tmpt:** **Desc:** No test orders

Blood SST/Red 10 10.00 ml Tube label: *'Stored Serum'* **KIT**

Instructions: *Allow to clot for 30 mins. Centrifuge at 3K for 15 mins. Remove the CRU label from the tube. Refrigerate and send to SSA on cold pack on the day of collection with pink card.*

No Aliquots	Temperature	Destination Lab
	Refrigerated	SSA

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *2* **7:00** **Tmpt:** **Desc:** No test orders

Blood SST/Red 10 10.00 ml Tube label: *'Stored Serum'* **KIT**

Instructions: *Allow to clot for 30 mins. Centrifuge at 3K for 15 mins. Remove the CRU label from the tube. Refrigerate and send to SSA on cold pack on the day of collection with pink card.*

No Aliquots	Temperature	Destination Lab
	Refrigerated	SSA

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *2* **7:55** **Tmpt:** **Desc: *U0*** **HMSR BLOOD results will go to medical record**

Urine | Urine, Hat | 5.00 ml | Tube label: *'U0'*

Instructions: *Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	5.00	Refrigerated	Renal	*'U0'*	No	*Place in the refrigerator and send all renal clearance specimens together at the end of the visit.*

Test Code	Mnemonic	Description
81476	NSRC	Renal Clearance, Short, Iothalmate

Day: *2* **9:00** **Tmpt:** **Desc:** No test orders

Urine | Urine, Hat | 60.00 ml | Tube label: *'UE'*

Instructions: *Participant to void at this time and RN to record time and TV. Do not save urine*

No Aliquots	Temperature	Destination Lab
	Ambient	NONE

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *2* **9:05** **Tmpt:** **Desc: *P1*** No test orders

Blood | NaHep/Grn 4 | 3.00 ml | Tube label: *'P1'*

Instructions: *Centrifuge at 3K for 10 mins. Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	1.50	Refrigerated	Renal	*'P1'*	No	*Send to the Renal Lab on wet ice via General Service.*

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *2* **9:45** **Tmpt:** **Desc: *U1*** **HMSR BLOOD results will go to medical record**

Urine | Urine, Hat | 5.00 ml | Tube label: *'U1'*

Instructions: *Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	5.00	Refrigerated	CCL	*'U1'*	No	*Place in the refrigerator and send all renal clearance specimens together at the end of the visit.*

Test Code	Mnemonic	Description
81476	NSRC	Renal Clearance, Short, Iothalmate

Day: *2*	**9:50**	**Tmpt:**	**Desc: *P2***	No test orders

Blood NaHep/Grn 4 3.00 ml Tube label: *'P2'*

Instructions: *Centrifuge at 3K for 10 mins. Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	1.50	Refrigerated	CCL	*'P2'*	No	*Send to the Renal Lab on wet ice via General Service.*

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

CRISP II

IRB #06-009502

Study Plan: IPRC - Inpatient Renal Clearance yr 1 and 3

DOB:

Clinic #:

Name:

Pt. emergency contact informatio

Name _____

Number _____

Relationship _____

Documentation Form: Low Sodium Diet Menu, VAPP, MD Orders

Role	Name	Pager #	(W)Phone #	(H)Phone #	(C)Phone #
PI	**Torres, Vicente E. MD, PhD**	**4-7527**	**(507) 284-3744**	**507-282-5096**	_____
Co-I	Abdalla, Adil A. M.D.	8-9377	266-1963	_____	_____
Co-I	King, Bernard F M.D.	4-6313	(507) 284-1728	_____	_____
Coord	**Kubly, Vickie J.**	**8-2356**	**(507) 266-9207**	_____	_____
Coord	**Spencer, Dorothy**	**6-8774**	**507-266-3868**	_____	_____
Dietetics Coord	O'connor, Helen M. RD	127-06605	255-5703	_____	_____
Lab Coord	Hare, Jennifer R. RST	127-10522	5-6905	_____	_____
Nurse Coord	Broten, LouAnn	_____	(507) 255-5701	_____	_____
Pharmacy Coord	Miller, Debbie D. PH	_____	5-7928	_____	_____
Unit Coord	Henkel, Mary RN	_____	507-255-5701	_____	_____

Send flowsheet to: Dorothy Spencer / vickie Kubly @ EiSL 33 Nephrology

PFH Date _____ **CVI Date** _____

Consent signed: _____ / _____ **PG Test:** _____ / _____ / _____

DATE INITIALS RESULTS DATE INITIALS

Additional Comments

Revision 3 completed by Broten, LouAnn on 9/10/2007

Day 1

1500

Admission In-pt.

Ht. _____cm Wt. _____ kg

VS: T_____; P_____; BP_____; R_____

_____Verify consent

_____Review CVI/PFH if appropriate

_____Baseline RN assessment

_____Check Creatinine fom MICs or Docs Browser note: ____.____mg/dL - the result may be from several years out and that is what we are to use.

_____**Patients are to take their evening dose of HTN medication** but are to **hol all meds tomorrow until after the MRI**.

1530

Criteria

Note allergies to Iodine of any kind & document severity
Severe_____ Mild_____ Moderate_____
If patient has had a previous severe reaction to contrast, notify Dr. Torres in regard to canceling the test.

CRITERIA FOR IMMEDIATE NOTIFICATIONOF INVESTIGATOR
1. Iothalamate allergic reaction
2. Incomplete bladder emptying
3. Continuously low urine output (< 3ml/min.)
4. Headache, nausea, diarrhea, other physical complaints

1700

VS

For use with BP assessment in AM please do the following BP check:

The participant is to have obstained from smoking and caffeine for at least 30 min prior to BP measurements

Use the Dinemap or Phillips monitors

Measure the upper arm circumference to determine cuff size
Right_____cm Left_____cm Cuff size_____
Adult cuff [24->33 cm]
Large cuff [33-41 cm]
Child cuff [<24 cm]
Thigh cuff [>41 cm]

*******Record cuff size, dominate arm, & BP readings on MICS**

The patricipant is to sit for 5 minutes with feet uncrossed and the BP's are to be taken 3 times in each arm 3min apart.

The **non-dominent** arm will be used to obtain the BP's

If on 3 consecutive measurements there is a difference in the systolic BP of 20 mm Hg or more between arms the non-dominant arm will be determined as being the arm with the lowest total Mean Arterial Preassures (MAPS) instead of which hand is non-dominate. To determine this do the following:

Right arm -

Time	Systolic / Diastolic	Mean
_____	_____/_____	_____
_____	_____/_____	_____
_____	_____/_____	_____

Left arm -

Time	Systolic / Diastolic	Mean
_____	_____/_____	_____
_____	_____/_____	_____
_____	_____/_____	_____

TOTAL MAP _____

1730

SMH - low sodium meal Have participant order a 90 mEq low sodium general diet meal from St. Marys dietary or participant may go out on pass until 9pm after being seen by Dr. Torres and / or Nurse practitioner.

1900

Blood draw - STAT [HCL] - Pg Draw Pg test when applicable and send to STAT lab if not done in the last 48 hrs.
RESULTS _____

2000

Renal Clearance room set-up Place the following in patient room:
Set up syringes per protocol
Heating pad
Scale for RC [place on solid counter and plug in]
Have bladder scanner with gel bottle
Clock or stopwatch
Urinal /hat

2100

Oral fluid Load Participant to drink 3 - 8oz. glasses of water between 9-10 PM

2200

Bed time Patient to be in bed with lights out by 10 pm.

Fasting Patient to be fasting until after RC study & MRI except for water

Day 2

0600

Awaken patient Awaken patient

Patient is NOT to take any medications until after MRI completed.

Urine collection - clean catch Obtain a clean catch urine sample per standard procedure. Aliquot per instruction on lab flowsheet. **TIME**_____

A urinary catheter is not approved for this study

Assessment - BID Do RN assessment

0605

WT Weight _____kg to be done after bladder has been emptied.

0630

VS For BP assessment:

Obtain after patient awake for 30 min.

The participant is to have obstained from smoking and caffeine for at least 30 min prior to BP measurements

Use the Dinemap or Phillips monitors

Use the non- dominent arm and cuff size that was determined last evening.
ARM_____ CUFF_____

The patricipant is to sit for 5 minutes with feet uncrossed and the BP's are to be taken 3 times at least 30 seconds apart.

Blood Pressure Measurement Procedural Steps:

1. Have participant bare arm, removing restrictive clothing

2. Position Cuff:

   a. Center of cuff placed over brachial artery

   b. Bottom edge of cuff is positioned 1 to 1.5 inches above antecubital space

   c. Cuff is wrapped smoothly & snuggly on arm so that only 2 fingertips can fi under the edge of the cuff.

   d. Straighten BP cuff tubing so that it is parallel to patients arm.

4. Verify that participant is relaxed and properly positioned:

   a. Sitting upright (no slouching), back supported

   b. Both feet on the floor (legs/ ankles not crossed)

   c. Arm is supported at heart level

   d. BP device display screen is not visible to the participant

   e. Participant not to talk, eat or drink during BP measurements

Record:

Time _____ P_____ BP_____ T_____
_____ P_____ BP_____
_____ BP_____

Average P_____ Average BP_____

0645

Oral fluid Load Patient to begin drinking six 8oz [240mL ea] glasses of water (may include 1 cu of decaf coffee) to be completed by **0800**.
# of glasses taken _____

Void Patient may void between now and 0700. Do not need to save urine.

Patient not to void after 0710 untill 0755, if possible. If pt. needs to void betwee 0710 and 0730 - Do not save, **but pt. must void at 0755.**

0700

Start - NS lock Start IV saline lock for blood draws - Draw HMSR bloods at this time

Blood draw Draw baseline bloods at this time (total 47.5ml)
8.5ml SST. for HMSR tests (Creatinine, Electrolyte pannel, Lipid panel)
8ml Green/black - **X2** - Kit
3ml in 3.5ml SST - Kit
10ml SST - **X2** - Kit

May do with IV start

Iothalimate - SQ Notify pharmacy to send Iothalamate for 8am injection

0730

Questionnaires Review and complete GFR checklist and continue throughout study. See attachment. The GFR test MUST BE RESCHEDULED if the answer to any of the statements in the checklist is "No" - notify study coordinator.

0755 **UO**

Urine - UO UO (baseline): Have subject empty bladder as completely as possible
Time void ended_____
Total Vol_____ Aliquot 5ml into appropriate tube. Discard remainder.

Record all urines and bloods on Short renal clearance form (attached)

0800

Med-Iothalamate SQ *Note: Blood draw is from opposite arm, so use best arm for veni-puncture.

Use POSTERIOR aspect of UPPER ARM. Gently pinch skin, insert needle, release skin, (draw back to make certain not in vessel), and inject Iothalamate.

Time: _____ Injection Site: _____ Right; _____ Left

Record in MICS & on Short renal clearance form

Oral fluid Load Have participant drink (1-2) 8oz glasses of water to maintain output. # of glasses_____

0850

FYI study **Renal Lab Guidelines:** Be sure bladder is empty. Average residual bladder

Information

volume should be < 20 mls. (Note: In some situations, <10% of voided volume, [PROVIDED residual volume is <50mls], is acceptable.

Urine Flow Rate **Must be <u>equal to or greater than 3ml per min</u>.**
If the flow rate does not meet this criteria at any time THE TEST MUST BE RESCHEDULED. See GFR checklist

0900 **UE**

Urine - UE

UE (60 minutes from Iothalamate injection): [+or - 5 min]
Have subject empty bladder as completely as possible
Time void ended_____ TV_____**No aliquot at this void**
Discard urine.

UE

Bladder Ultrasound Instructions

VOID # 1: Obtain 5 bladder ultrasound readings within 1-2 minutes of voiding and record
1. _____ **2.** _____ **3.** _____ **4.** _____ **5.** _____

If bladder has an average of > 20mls of urine, have pt. revoid immediately after firs void & ultrasound again.

VOID # 2 [IF NEEDED]:
1. _____ **2.** _____ **3.** _____ **4.** _____ **5.** _____

If Average of residual bladder volume is > 20 mls, extend Equilibration Period for 5 min. and have participant void again.

VOID # 3 [IF NEEDED]:
1. _____ **2.** _____ **3.** _____ **4.** _____ **5.** _____

Record urine vol. _____, duration _____, and flow [ml/min] _____[Urine vol. Divided by duration = flow]
*Flow is figured to 3 places behind the decimal then rounded to 2 places on *Short Renal Clearance* form.

0905 **P1**

Blood draw - P1

P1 (60 minute): TIME_____ (record on Short Renal Clearance form)
3mL into a 4mL Green
Do within 5 min. maximum of UE by venipuncture in oposite arm of injection
Tourniquet time MUST be LESS than 1 min
tourniquet used: _____yes _____no Time left on: _____seconds

0940

FYI study Information

Of primary concern is the differentiation recorded on the GFR from the UE to U1. It is **EXTREMELY IMPORTANT** that the time of urine collection duration is

absolutely accurate from end of UE to end of U1.

0945 **U1**

Urine - U1

U1 = All urine collected for at least 45 minutes after UE
Have subject empty bladder as completely as possible, If more than one void, pool and save all urine for accurate TV.
Time void ended_____ TV_____
Aliquot 5ml into appropriate tube and discard remainder.

U1

Bladder Ultrasound Instructions

VOID # 1: Obtain 5 bladder ultrasound readings within 1-2 minutes of voiding an record
1. _____ 2. _____ 3. _____ 4. _____ 5. _____

If bladder has an average of > 20mls of urine, have pt. revoid immediately after fir void & ultrasound again.

VOID # 2 [IF NEEDED]:
1. _____ 2. _____ 3. _____ 4. _____ 5. _____

If Average of residual bladder volume is > 20 mls, extend Equilibration Period for **15 - 30 min., [but less than 90 min from UE]** and have participant void again.

VOID # 3 [IF NEEDED]:
1. _____ 2. _____ 3. _____ 4. _____ 5. _____

Record urine vol. _____, duration _____, and flow [ml/min] _____[Urine vol. Divided by duration = flow]
*Flow is figured to 3 places behind the decimal then rounded to 2 places on *Short Renal Clearance* form.

0950 **P2**

Blood draw - P2

P2 = Plasma collected immediately after U1 TIME _____ (record on Short Renal Clearance form)

3mL into a 4mL Green

Do within 5 min. maximum of U1 by venipuncture in oposite arm of injection
Tourniquet time MUST be LESS than 1 min
tourniquet used: _____yes _____no Time left on: _____seconds

1000

Fasting

Have patient remain fasting until after MRI

Remind patient not to take any medication until after MRI

1100

MRI Await escort/study coordinator to take patient to MRI Confirm appointment time at MRI_____ (5-8755)

1200

SMH - low sodium meal Have participant order meal from St. Marys dietary for _____ time. (low sodium meal)

1300

VS Upon return from MRI
VS: T_____; P_____; BP_____; R_____

Dc IV Dc IV

Dismissal Dismiss patient if stable

Participant will have appointment with Dr. Torres in the afternoon.

FYI study Information Make 2 copies of the Short renal clearance form and give
1. One to the lab to send with the samples
2. Attach one to the flowsheet
3. Fax copy of GFR checklist and a copy of the short renal clearance form to Dorothy Spencer @ 5-0770

RC bloods and urines

Time	Setup	Green/black	NaHep/Grn 4	SST/Gld 3.5	SST/Red 10	SST/R&B 8.5	Urine, Hat	Sarstedt 6	Comments
Day 2									
0600	all to lab						60	5	Urine collection - clean catch
0645									Oral fluid Load 6 glasses
0700	11.5, 8,8,10,10	8, 8		3	10, 10	8.5			
0755	5						5		Urine - UO
0800									Med-Iothalamate SQ
0800									Oral fluid Load 1-2 glasses
0900	none						60		Urine - UE discard after TV **-No aliquot needed**
0905	3		3						Blood draw - P1
0945	5						5		Urine - U1
0950	3		3						Blood draw - P2

06-009502 IPRC | Patient Name (x-xxx-xxx) mm/dd/yyyy | Printed 10/10/2007 4:08 PM

DO NOT ALTER DOCUMENT
IRB # 06-009502 Nurse Information

Title: Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP II)

Objective: This study seeks to draw unequivocal linkage between the rate of kidney/cyst enlargement and qualitative and quantitative (declining renal function reflected in iothalamate clearance and albuminuria) end-points, provide a marker of disease progression and develop and test other biomarkers of disease progression.

Study Design: This is a four year prospective, observational study of up to 58 subjects conducted at the CRU-SMH. Subjects come to the CRU for two visits year 1 and year 3. Subjects receive iothalamate 300 mg SQ at each visit to determine glomerular filtration rate.

Study Drug Administration: (preferred injection site = non blood draw arm)

- For subjects 40 kg or greater administer 300 mg/mL iothalamate SQ into the posterior upper arm.

Pharmacology: Iothalamate is a radiological iodinated contrast media used for renal function tests.

Concomitant Medications: No restrictions are listed in the protocol. Per Investigator hold AM dose of hypertension medications on the day of the study until completion of iothalamate clearance test and MRI.

Side Effects/Warnings:

- Injection site reaction
- Allergic reaction

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

APPENDIX 1 GFR CHECKLIST

THIS FORM MUST BE COMPLETED AND RETURNED to address below

- **Participant's Initials: ____ ____ ____; MML CONTROL No.: M-_____**
  from Short Renal Clearance Form
- **Participant's CRISP ID: _____**
- **SITE: (Circle One) Alabama Emory Kansas MAYO**
- **Date of Collection:_____/_____/2007**
  Month Day Year

Check In

1. **CLINICAL STABILITY: ⟶ No ☐ Yes ☐**
   (NOTE: Clinical Stability is defined as the ABSENCE of: Viral Syndrome; Fever; Acute Pain; Diarrhea; etc.).**
2. **Compliance with non-allowed medications: ⟶ No ☐ Yes ☐**

DAY 1

1. **Fasting (> 8 hours) ⟶ No ☐ Yes ☐**
2. **Hydration as per Protocol ⟶ No ☐ Yes ☐**
3. **Equilibration time 60 ± 5 minutes ⟶ No ☐ Yes ☐**
4. **Urine Flow rate ≥ 3 ml/minute for UE ⟶ No ☐ Yes ☐**
5. **P1 within 5 minutes of UE ⟶ No ☐ Yes ☐**
6. **Residual bladder volume < 20 ml OR ⟶ No ☐ Yes ☐**
   10% of voided urine (but NOT > 50 ml) @ UE
7. **Collection time for U1 is 45 – 90 minutes. ⟶ No ☐ Yes ☐**
8. **P2 is within 5 minutes of U1 ⟶ No ☐ Yes ☐**
9. **Residual bladder volume < 20 ml OR**
   10% of voided urine (NOT > 50 ml) @ U1 ⟶ No ☐ Yes ☐
10. **Urine Flow rate ≥ 3 ml/minute for U1 ⟶ No ☐ Yes ☐**

NOTE: If the answer is "No" to any of the above, THE TEST MUST BE RESCHEDULED.! **Please page Dr. Torres Vickie, or Dorothy, PRIOR to canceling test.

NOTE: Please send this form and Original GCRC Flowsheet to:
Vickie Kubly, Dorothy Spencer, Study Coordinators
Eisenberg S-33
Nephrology PKD Research
Thank you! 6-9207 / 6-3868)

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

SHORT RENAL CLEARANCE SHEET

DOCTOR: DR. IRB:

NAME:_____
CLINIC NO:_____ DATE:_____

DIAGNOSIS:_____

AGE:_____ SEX_____ WT: _____kgs. Ht:_____cm BP _____

Allergies:_____ Iothalmate Injection Time:_____

MEDICATIONS:_____

FASTING:_____ WATER LOAD GIVEN:_____

ESTIMATED FUNCTION: GFR _X_ SERUM CREATININE_____

Total Intake: Oral Water _____
Total Output: Urine output_____

COLLECTION OF SAMPLES

BLOOD	**URINE**			
Time	**Time**	**VOL ÷ DURATION**	**= FLOW RATE**	**Water**
	Pre_____			_____
P0_____ (baseline)	**U0**_____;	_____ ÷ _____	= _____	
BP cuff used: ___yes, __no, ___mmHg				
P1____	**UE**_____; ultrasound____ ____ ____ ____ ____;			
BP cuff used: ___yes, __no, ___ mmHg				
	VOL / DURATION	*= FLOW RATE*		*Water*
	_____ ÷ _____	= _____		_____
P2____	**U1**_____; ultrasound____ ____ ____ ____ ____;			
BP cuff used: ___yes, __no, ___ mmHg				
	VOL / DURATION	*= FLOW RATE*		
	_____ ÷ _____	= _____		

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

This printout is current as of 7/23/2007, 9:12:16AM

Lab Flowsheet Verification for protocol 06-009502, Study Plan IPRCH

Flowsheet Revision Number: 0 **Is this template marked as complete and in production: YES**

Blood Volume For Day 2 is 14.50 mL
Total Blood Volume For This Study Plan = 14.50 mL
NOTE: This blood volume will NOT include HMSR bloods that are not built into this template

High level processing instructions:

******Attention******
This patient is also participating in the 1715-05 (HALT) study. In order to eliminate the chance for duplicate specimens being collected, this flow sheet contains specimens that need to be collected in addition to those needed for the HALT study.

The study coordinator will provide the 5 mL screw-top tubes, 1.5 mL orange-top tubes, and labels. Do not use the aliquot labels from the CRU Scheduling System, except for the label for the 50 mL conical tube for centrifuging the RNA/DNA urine.

Note: You will not use all of the labels on the label sheets.

********** Short Renal Clearance **********
Order under the UO specimen as 81476. Enough labels will print from Lab 3 for all of the required specimens. When labels print from Lab3, write the following on the labels, one for each specimen. U0, U1, P1, and P2.

*****NOTE: Specimens must be shipped on the day of collection.*****

You will receive 4 Shipping Manifest forms from the study coordinator:
* *Repository - Serum/Plasma Samples*
* *Central Lab - CCF (2 forms - one for the first specimen collected ("A" and "B" together on the same form and one for the second specimen.)*
* *Repository - Urine Samples (Specimens labeled MCP-1)*

Each set of the creatinine aliquots should have its own manifest sheet, "Central Lab - CCF" (The A and B aliquots both go on one sheet).

On the Manifest forms enter the number of tubes and double check to make sure the accession numbers on the forms match the accession numbers on the tubes.

Before sending to the SSA, check to make sure all of the CRU labels have been taken off of the tubes and that only the drug company labels are on the tubes.

Once all urine and blood specimens have been processed, put into a 5 lb. styro on wet ice and send to the SSA with the Shipping Manifest forms. The specimens need to reach the SSA by 1:30 in order to be shipped on the day of collection, which is a requirement of the drug company.

Shipping forms:

Day: *2*	**6:00**	**Tmpt:**	**Desc:**	**HMSR BLOOD**
Urine	Sarstedt 6	5.00 ml	Tube label: "	**results will go to medical record**

Instructions: *Aliquot from random urine collection and send to CCL.*

No Aliquots	Temperature	Destination Lab
	Ambient	CCL

Test Code	Mnemonic	Description
81260	RMA	Mircoalbumin-Random, U

Day: *2*	**6:00**	**Tmpt:**	**Desc:**	No test orders
Urine	Urine, UA	60.00 ml	Tube label: *'Random Urine'*	**KIT**

Instructions: *Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions	
Nbr 1	4.50	Frozen (store at -70C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 2	4.50	Frozen (store at -70C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 3	30.00	Frozen (store at -70C)	SSA	*'FNA/DNA Urine Centrifuge Tube'*	No	*KEEP TUBE ON ICE THROUGHOUT THIS ENTIRE PROCESS.* *Document the urine volume, processing times, and voiding time on the provided requisition form.* *Within 20 - 30 mins. of collection perform the following:* *1. Centrifuge at 1600 rpms for 5 mins.* *2. Using a sterile pipette, decant the supernatant and discard.* *3. Using a sterile pipette, transfer the bottom 250 uL pellet (sometimes barely- or nonvisible). to a 1.5 mL eppendorf tube previously prepared with 750 uL of TriReagent.* *4. Invert several times to mix and freeze.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 4	0.30	Frozen (store at -70C)	SSA	*'FNA/DNA'*	No	*Freeze at -70 C and send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				

Day: *2* **7:00** **Tmpt:** **Desc:** **HMSR BLOOD results will go to medical record**

Blood SST/R&B 8.5 8.50 ml Tube label: ''

Instructions: *Do not process, send to CCL.*

No Aliquots	Temperature	Destination Lab
	Ambient	CCL

Test Code	Mnemonic	Description
8053	LPSC	Lipid Panel
87972	ELPN	Electrolyte Panel, Serum

Day: *2* **7:55** **Tmpt:** **Desc: *U0*** **HMSR BLOOD results will go to medical record**

Urine Urine, Hat 5.00 ml Tube label: *'U0'*

Instructions: *Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	5.00	Refrigerated	Renal	*'U0'*	No	*Place in the refrigerator and send all renal clearance specimens together at the end of the visit.*

Test Code	Mnemonic	Description
81476	NSRC	Renal Clearance, Short, Iothalmate

Day: *2* **9:00** **Tmpt:** **Desc:** No test orders

Urine Urine, Hat 60.00 ml Tube label: *'UE'*

Instructions: *Participant to void at this time and RN to record time and TV. Do not save urine*

No Aliquots	Temperature	Destination Lab
	Ambient	NONE

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *2* **9:05** **Tmpt:** **Desc: *P1*** No test orders

Blood NaHep/Grn 4 3.00 ml Tube label: *'P1'*

Instructions: *Centrifuge at 3K for 10 mins. Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	1.50	Refrigerated	Renal	*'P1'*	No	*Send to the Renal Lab on wet ice via General Service.*

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *2* **9:45** **Tmpt:** **Desc: *U1*** **HMSR BLOOD results will go to medical record**

Urine Urine, Hat 5.00 ml Tube label: *'U1'*

Instructions: *Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	5.00	Refrigerated	CCL	*'U1'*	No	*Place in the refrigerator and send all renal clearance specimens together at the end of the visit.*

Test Code	Mnemonic	Description
81476	NSRC	Renal Clearance, Short, Iothalmate

Day: *2* **9:50** **Tmpt:** **Desc: *P2*** No test orders

Blood NaHep/Grn 4 3.00 ml Tube label: *'P2'*

Instructions: *Centrifuge at 3K for 10 mins. Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	1.50	Refrigerated	CCL	*'P2'*	No	*Send to the Renal Lab on wet ice via General Service.*

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

06-009502 IPRCH | Patient Name (x-xxx-xxx) mm/dd/yyyy | Printed 10/10/2007 4:31 PM

CRISP II

IRB #06-009502
Study Plan: IPRCH - Inpatient Renal Clearance w/HALT yr1&3

DOB:
Clinic #:
Name:

Pt. emergency contact information
Name _____
Number _____
Relationship _____

Documentation Form: Low Sodium Diet Menu, VAPP, MD Orders

Role	Name	Pager #	(W)Phone #	(H)Phone #	(C)Phone #
PI	**Torres, Vicente E. MD, PhD**	**4-7527**	**(507) 284-3744**	**507-282-5096**	_____
Co-I	Abdalla, Adil A. M.D.	8-9377	266-1963	_____	_____
Co-I	King, Bernard F M.D.	4-6313	(507) 284-1728	_____	_____
Coord	**Kubly, Vickie J.**	**8-2356**	**(507) 266-9207**	_____	_____
Coord	**Spencer, Dorothy**	**6-8774**	**507-266-3868**	_____	_____
Dietetics Coord	O'connor, Helen M. RD	127-06605	255-5703	_____	_____
Lab Coord	Hare, Jennifer R. RST	127-10522	5-6905	_____	_____
Nurse Coord	Broten, LouAnn	_____	(507) 255-5701	_____	_____
Pharmacy Coord	Miller, Debbie D. PH	_____	5-7928	_____	_____
Unit Coord	Henkel, Mary RN	_____	507-255-5701	_____	_____

Send flowsheet to: Dorothy Spencer / vickie Kubly @ EiSL 33 Nephrology

PFH Date _____ **CVI Date** _____

Consent signed: _____ / _____ **PG Test:** _____ / _____ / _____
DATE INITIALS RESULTS DATE INITIALS

Additional Comments

Revision 2 completed by Broten, LouAnn on 9/10/2007 - 1 -

Day 1

1500

Admission In-pt.

Ht. _____cm Wt. _____ kg

VS: T_____; P_____; BP_____; R_____

_____Verify consent

_____Review CVI/PFH if appropriate

_____Baseline RN assessment

_____Check Creatinine fom MICs or Docs Browser note: ____.____mg/dL - the result may be from several years out and that is what we are to use.

_____**Patients are to take their evening dose of HTN medication** but are to **hold all meds tomorrow until after the MRI.**

1530

Criteria

Note allergies to Iodine of any kind & document severity
Severe_____ Mild_____ Moderate_____
If patient has had a previous severe reaction to contrast, notify Dr. Torres in regards to canceling the test.

CRITERIA FOR IMMEDIATE NOTIFICATIONOF INVESTIGATOR
1. Iothalamate allergic reaction
2. Incomplete bladder emptying
3. Continuously low urine output (< 3ml/min.)
4. Headache, nausea, diarrhea, other physical complaints

1730

SMH - low sodium meal

Have participant order a 90 mEq low sodium general diet meal from St. Marys dietary or participant may go out on pass until 9pm after being seen by Dr. Torres and / or Nurse practitioner.

1900

Blood draw - STAT [HCL] - Pg

Draw Pg test when applicable and send to STAT lab if not done in the last 48 hrs. RESULTS _____

2000

Renal Clearance room set-up

Place the following in patient room:
Set up syringes per protocol
Heating pad
Scale for RC [place on solid counter and plug in]

Have bladder scanner with gel bottle
Clock or stopwatch
Urinal /hat

2100

Oral fluid Load Participant to drink 3 - 8oz. glasses of water between 9-10 PM

2200

Bed time Patient to be in bed with lights out by 10 pm.

Fasting Patient to be fasting until after RC study & MRI except for water

Day 2

0600

Awaken patient Awaken patient

Patient is NOT to take any medications until after MRI completed.

Urine collection - clean catch Obtain a clean catch urine sample per standard procedure. Aliquot per instructions on lab flowsheet. **TIME**_____

A urinary catheter is not approved for this study

Assessment - BID Do RN assessment

0605

WT Weight _____kg to be done after bladder has been emptied.

0630

VS For BP assessment:

Obtain after patient awake for 30 min

The participant is to have obstained from smoking and caffeine for at least 30 min prior to BP measurements

Use the HALT monitors

Use the non- dominent arm and cuff size that was determined on the HALT study.

ARM_____ CUFF_____

If on HALT study - Check their machine with the CTM calibrater machine prior to registering the measurements. See attachment : the Readings must be within 2 points of each other to be OK.

The patricipant is to sit for 5 minutes with feet uncrossed and the BP's are to be taken 3 times at least 30 seconds apart.

Blood Pressure Measurement Procedural Steps:

Follow these steps when assessing patients technique and observe use of home monitor . Patient to position and place cuff.

Serial # _____of pts home monitor located on the back upper right corner.

1. Verify proper arm and cuff size for BP measurement (ask the participant which arm they were instructed to use by the study coordinator).

2. Have participant bare arm, removing restrictive clothing

3. Position Cuff:

   a. Center of cuff placed over brachial artery

   b. Bottom edge of cuff is positioned 1 to 1.5 inches above antecubital space

   c. Cuff is wrapped smoothly & snuggly on arm so that only 2 fingertips can fit under the edge of the cuff.

   d. Straighten BP cuff tubing so that it is parallel to patients arm.

4. Verify that participant is relaxed and properly positioned:

   a. Sitting upright (no slouching), back supported

   b. Both feet on the floor (legs/ ankles not crossed)

   c. Arm is supported at heart level

   d. BP device display screen is not visible to the participant

   e. Participant not to talk, eat or drink during BP measurements

Record:

Time _____ P_____ BP_____ T_____

_____ P_____ BP_____
_____ BP_____

Average P_____ Average BP_____

0645

Oral fluid Load Patient to begin drinking six 8oz [240mL ea] glasses of water (may include 1 cup of decaf coffee) to be completed by **0800**.
# of glasses taken _____

Void Patient may void between now and 0700. Do not need to save urine.

Patient not to void after 0710 untill 0755, if possible. If pt. needs to void between 0710 and 0730 - Do not save, **but pt. must void at 0755.**

0700

Start - NS lock Start IV saline lock for blood draws - Draw HMSR bloods at this time

Blood draw Draw baseline bloods at this time **8.5ml SST x1, 8ml PST x 2. 10 ml SST x2**.
Creatinine
Electrolyte pannel
Lipid panel

HALT bloods

May do with IV start

Iothalimate - SQ Notify pharmacy to send Iothalamate for 8am injection

0730

Questionnaires Review and complete GFR checklist and continue throughout study. See attachment. The GFR test MUST BE RESCHEDULED if the answer to any of the statements in the checklist is "No" - notify study coordinator.

0755 **UO**

Urine - UO UO (baseline): Have subject empty bladder as completely as possible
Time void ended_____
Total Vol_____ Aliquot 5ml into appropriate tube. Discard remainder.

Record all urines and bloods on Short renal clearance form (attached)

0800

Med-Iothalamate SQ

*Note: Blood draw is from opposite arm, so use best arm for veni-puncture.

Use POSTERIOR aspect of UPPER ARM. Gently pinch skin, insert needle, release skin, (draw back to make certain not in vessel), and inject Iothalamate.

Time: _____ Injection Site: _____ Right; _____ Left

Record in MICS & on Short renal clearance form

Oral fluid Load

Have participant drink (1-2) 8oz glasses of water to maintain output. # of glasses_____

0850

FYI study Information

Renal Lab Guidelines: Be sure bladder is empty. Average residual bladder volume should be < 20 mls. (Note: In some situations, <10% of voided volume, [PROVIDED residual volume is <50mls], is acceptable.

Urine Flow Rate **Must be <u>equal to or greater than 3ml per min</u>.**
If the flow rate does not meet this criteria at any time THE TEST MUST BE RESCHEDULED. See GFR checklist

0900

UE

Urine - UE

UE (60 minutes from Iothalamate injection): [+or - 5 min]
Have subject empty bladder as completely as possible
Time void ended_____ TV_____No aliquot at this void
Discard urine.

UE

Bladder Ultrasound Instructions

VOID # 1: Obtain 5 bladder ultrasound readings within 1-2 minutes of voiding and record
1. _____ **2.** _____ **3.** _____ **4.** _____ **5.** _____

If bladder has an average of > 20mls of urine, have pt. revoid immediately after first void & ultrasound again.

VOID # 2 [IF NEEDED]:
1. _____ **2.** _____ **3.** _____ **4.** _____ **5.** _____

If Average of residual bladder volume is > 20 mls, extend Equilibration Period for **5** min. and have participant void again.

VOID # 3 [IF NEEDED]:
1. _____ **2.** _____ **3.** _____ **4.** _____ **5.** _____

Record urine vol. _____, duration _____, and flow [ml/min] _____[Urine vol. Divided by duration = flow]
*Flow is figured to 3 places behind the decimal then rounded to 2 places on *Short Renal Clearance* form.

0905 **P1**

Blood draw - P1

P1 (60 minute): TIME_____ (record on Short Renal Clearance form)
3mL into a 4mL Green
Do within 5 min. maximum of UE by venipuncture in oposite arm of injection
Tourniquet time MUST be LESS than 1 min
tourniquet used: _____yes _____no Time left on: _____seconds

0940

FYI study Information

Of primary concern is the differentiation recorded on the GFR from the UE to U1. It is **EXTREMELY IMPORTANT** that the time of urine collection duration is absolutely accurate from end of UE to end of U1.

0945 **P1**

Urine - U1

U1 = All urine collected for at least 45 minutes after UE
Have subject empty bladder as completely as possible, If more than one void, pool and save all urine for accurate TV.
Time void ended_____ TV_____
Aliquot 5ml into appropriate tube and discard remainder.

U1

Bladder Ultrasound Instructions

VOID # 1: Obtain 5 bladder ultrasound readings within 1-2 minutes of voiding and record
1. _____ 2. _____ 3. _____ 4. _____ 5. _____

If bladder has an average of > 20mls of urine, have pt. revoid immediately after first void & ultrasound again.

VOID # 2 [IF NEEDED]:
1. _____ 2. _____ 3. _____ 4. _____ 5. _____

If Average of residual bladder volume is > 20 mls, extend Equilibration Period for **15 - 30 min., [but less than 90 min from UE]** and have participant void again.

VOID # 3 [IF NEEDED]:
1. _____ 2. _____ 3. _____ 4. _____ 5. _____

		Record urine vol. _____, duration _____, and flow [ml/min] _____[Urine vol. Divided by duration = flow] *Flow is figured to 3 places behind the decimal then rounded to 2 places on *Short Renal Clearance* form.
0950		**P2**
	Blood draw - P2	**P2** = Plasma collected immediately after U1 TIME _____ (record on Short Renal Clearance form) **3mL** into a 4mL Green Do within 5 min. maximum of U1 by venipuncture in oposite arm of injection **Tourniquet time MUST be LESS than 1 min** tourniquet used: _____yes _____no Time left on: _____seconds
1000		
	Fasting	Have patient remain fasting until after MRI Remind patient not to take any medication until after MRI
1100		
	MRI	Await escort/study coordinator to take patient to MRI Confirm appointment time at MRI_____ (5-8755)
1200		
	SMH - low sodium meal	Have participant order meal from St. Marys dietary for _____ time. (low sodium meal)
1300		
	VS	Upon return from MRI VS: T_____; P_____; BP_____; R_____
	Dc IV	Dc IV
	Dismissal	Dismiss patient if stable Participant to be seen by Dr. Torres in afternoon
	FYI study Information	Make 2 copies of the Short renal clearance form and give **1.** One to the lab to send with the samples **2.** Attach one to the flowsheet

3. Fax copy of GFR checklist and a copy of the short renal clearance form to Dorothy Spencer @ 5-0770

RC bloods and urines

Time	Setup	NaHep/Grn 4	SST/R&B 8.5	Urine, Hat	Urine, UA	Sarstedt 6	Comments
Day 2							
0600	all to lab				60	5	Urine collection -clean catch
0645							Oral fluid Load - 6 glasses
0645							Void
0700	8.5		8.5				Blood draw HMSR
0755	5			5			Urine - UO
0800							Med-Iothalamate SQ
0800							Oral fluid Load 1-2 glasses
0900	none			60			Urine - UE discard after TV - **No aliquot**
0905	3	3					Blood draw - P1
0945	5			5			Urine - U1
0950	3	3					Blood draw - P2

06-009502 IPRCH | Patient Name (x-xxx-xxx) mm/dd/yyyy | Printed 10/10/2007 4:31 PM

DO NOT ALTER DOCUMENT
IRB # 06-009502 Nurse Information

Title: Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP II)

Objective: This study seeks to draw unequivocal linkage between the rate of kidney/cyst enlargement and qualitative and quantitative (declining renal function reflected in iothalamate clearance and albuminuria) end-points, provide a marker of disease progression and develop and test other biomarkers of disease progression.

Study Design: This is a four year prospective, observational study of up to 58 subjects conducted at the CRU-SMH. Subjects come to the CRU for two visits year 1 and year 3. Subjects receive iothalamate 300 mg SQ at each visit to determine glomerular filtration rate.

Study Drug Administration: (preferred injection site = non blood draw arm)

- For subjects 40 kg or greater administer 300 mg/mL iothalamate SQ into the posterior upper arm.

Pharmacology: Iothalamate is a radiological iodinated contrast media used for renal function tests.

Concomitant Medications: No restrictions are listed in the protocol. Per Investigator hold AM dose of hypertension medications on the day of the study until completion of iothalamate clearance test and MRI.

Side Effects/Warnings:

- Injection site reaction
- Allergic reaction

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

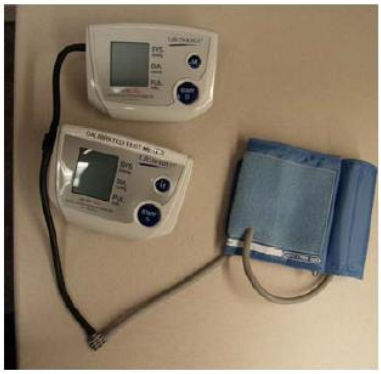
06-009502 IPRCH | Patient Name (x-xxx-xxx) mm/dd/yyyy | Printed 10/10/2007 4:31 PM

Calibration Test Meter Procedure

1. Participant will have home monitor cuff attached to their arm after demonstrating proper use of the home BP monitor.
2. Keep the BP cuff on the participants arm.
3. Turn patient's home monitor off (press start button).
4. Obtain Calibration Test Meter (CTM) from the medication room at SMH or the storage area with equipment between chemo rooms at Charlton.
5. Verify the CTM has the black tubing attached to it.
6. Remove the BP tubing from the participant's home monitor and place the end of the home monitor BP tubing into the 'female' end of the black tubing attached to the CTM.
7. Place the 'male' end of the black tubing into the participant's home BP monitor.
8. Verify cuff still in proper position and that participant is seated properly.
9. Press the [Start] button on the CTM.
10. Wait for the CTM monitor screen to display '0'.
11. Press [Start] button on participant's home monitor.
12. Observe both monitor screens as they 'count down' – numbers should be within 2 points of each other.
13. If an [error] message is displayed, turn off both machines (to turn off, press [Start] button). Wait 30 seconds and repeat steps starting at #9 above.
14. Record blood pressure reading and pulse on flowsheet.
15. When calibration procedure completed, reconnect BP cuff tubing to participant's home monitor to proceed with sequential BP measurements.

Patient's home monitor

CTM meter



Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

APPENDIX 1 GFR CHECKLIST

THIS FORM MUST BE COMPLETED AND RETURNED to address below

- **Participant's Initials: ____ ____ ____; MML CONTROL No.: M-_____**
  from Short Renal Clearance Form
- **Participant's CRISP ID: _____**
- **SITE: (Circle One) Alabama Emory Kansas MAYO**
- **Date of Collection:_____/_____/2007**
  Month Day Year

Check In

1. **CLINICAL STABILITY: ⟶ No ☐ Yes ☐**
   (NOTE: Clinical Stability is defined as the ABSENCE of: Viral Syndrome; Fever; Acute Pain; Diarrhea; etc.).**
2. **Compliance with non-allowed medications: ⟶ No ☐ Yes ☐**

DAY 1

1. **Fasting (> 8 hours) ⟶ No ☐ Yes ☐**
2. **Hydration as per Protocol ⟶ No ☐ Yes ☐**
3. **Equilibration time 60 ± 5 minutes ⟶ No ☐ Yes ☐**
4. **Urine Flow rate ≥ 3 ml/minute for UE ⟶ No ☐ Yes ☐**
5. **P1 within 5 minutes of UE ⟶ No ☐ Yes ☐**
6. **Residual bladder volume < 20 ml OR ⟶ No ☐ Yes ☐**
   10% of voided urine (but NOT > 50 ml) @ UE
7. **Collection time for U1 is 45 – 90 minutes. ⟶ No ☐ Yes ☐**
8. **P2 is within 5 minutes of U1 ⟶ No ☐ Yes ☐**
9. **Residual bladder volume < 20 ml OR**
   10% of voided urine (NOT > 50 ml) @ U1 ⟶ No ☐ Yes ☐
10. **Urine Flow rate ≥ 3 ml/minute for U1 ⟶ No ☐ Yes ☐**

NOTE: If the answer is "No" to any of the above, THE TEST MUST BE RESCHEDULED.! **Please page Dr. Torres Vickie, or Dorothy, PRIOR to canceling test.

NOTE: Please send this form and Original GCRC Flowsheet to:
Vickie Kubly, Dorothy Spencer, Study Coordinators
Eisenberg S-33
Nephrology PKD Research
Thank you! 6-9207 / 6-3868)

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

SHORT RENAL CLEARANCE SHEET

DOCTOR: DR. IRB:

NAME:_____
CLINIC NO:_____ DATE:_____

DIAGNOSIS:_____

AGE:_____ SEX_____ WT: _____kgs. Ht:_____cm BP _____

Allergies:_____ Iothalmate Injection Time:_____

MEDICATIONS:_____

FASTING:_____ WATER LOAD GIVEN:_____

ESTIMATED FUNCTION: GFR _X_ SERUM CREATININE_____

Total Intake: Oral Water _____
Total Output: Urine output_____

COLLECTION OF SAMPLES

BLOOD Time	**URINE Time**	**VOL ÷ DURATION = FLOW RATE**	**Water**
	Pre_____		_____
P0_____ (baseline)	**U0**_____;	_____ ÷ _____ = _____	
BP cuff used: ___yes, __no, ___mmHg			
P1____	**UE**_____; ultrasound____ ____ ____ ____ ____;		
BP cuff used: ___yes, __no, ___ mmHg			
	VOL / DURATION	*= FLOW RATE*	*Water*
	_____ ÷ _____	= _____	_____
P2____	**U1**_____; ultrasound____ ____ ____ ____ ____;		
BP cuff used: ___yes, __no, ___ mmHg			
	VOL / DURATION	*= FLOW RATE*	
	_____ ÷ _____	= _____	

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

This printout is current as of 7/23/2007, 9:14:33AM

Lab Flowsheet Verification for protocol 06-009502, Study Plan OPRC

Flowsheet Revision Number: 0 **Is this template marked as complete and in production: YES**

Blood Volume For Day 1 is 53.50 mL
Total Blood Volume For This Study Plan = 53.50 mL
NOTE: This blood volume will NOT include HMSR bloods that are not built into this template

High level processing instructions:

The study coordinator will provide the 5 mL screw-top tubes, 1.5 mL orange-top tubes, and labels. Do not use the aliquot labels from the CRU Scheduling System, except for the label for the 50 mL conical tube for centrifuging the RNA/DNA urine.

Note: You will not use all of the labels on the label sheets.

********** *Short Renal Clearance* **********
Order under the UO specimen as 81476. Enough labels will print from Lab 3 for all of the required specimens. When labels print from Lab3, write the following on the labels, one for each specimen. U0, U1, P1, and P2.

*****NOTE: Specimens must be shipped on the day of collection.*****

You will receive 4 Shipping Manifest forms from the study coordinator:
* *Repository - Serum/Plasma Samples*
* *Central Lab - CCF (2 forms - one for the first specimen collected ("A" and "B" together on the same form and one for the second specimen.)*
* *Repository - Urine Samples (Specimens labeled MCP-1)*

Each set of the creatinine aliquots should have its own manifest sheet, "Central Lab - CCF" (The A and B aliquots both go on one sheet).

On the Manifest forms enter the number of tubes and double check to make sure the accession numbers on the forms match the accession numbers on the tubes.

Before sending to the SSA, check to make sure all of the CRU labels have been taken off of the tubes and that only the drug company labels are on the tubes.

Once all urine and blood specimens have been processed, put into a 5 lb. styro on wet ice and send to the SSA with the Shipping Manifest forms. The specimens need to reach the SSA by 1:30 in order to be shipped on the day of collection, which is a requirement of the drug company.

Shipping forms:

Day: *1*	**6:30**	**Tmpt:**	**Desc:**	**HMSR BLOOD**
Urine	Sarstedt 6	5.00 ml	Tube label: ''	**results will go to medical record**
Instructions:	*Aliquot from random urine collection and send to CCL.*			

No Aliquots	Temperature	Destination Lab
	Ambient	CCL

Test Code	Mnemonic	Description
81260	RMA	Mircoalbumin-Random, U

Day: *1*	**6:30**	**Tmpt:**	**Desc:**	No test orders
Urine	Urine, Hat	60.00 ml	Tube label: *'Random Urine'*	**KIT**
Instructions:	*Aliquot.*			

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions	
Nbr 1	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 2	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 3	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 4	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 5	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				
Nbr 6	4.50	Frozen (store at -20C)	SSA	*'MCP-1'*	No	*Freeze at -20C. Send to SSA with pink card.*	**KIT**
	Test Code	Mnemonic	Description				
		!NONE	No Test Order Type				

Nbr 7	30.00	Frozen (store at -70C)	SSA	*'FNA/DNA Urine Centrifuge Tube'*	No	*KEEP TUBE ON ICE THROUGHOUT THIS ENTIRE PROCESS.* *Document the urine volume, processing times, and voiding time on the provided requisition form.* *Within 20 - 30 mins. of collection perform the following:* *1. Centrifuge at 1600 rpms for 5 mins.* *2. Using a sterile pipette, decant the supernatant and discard.* *3. Using a sterile pipette, transfer the bottom 250 uL pellet (sometimes barely- or nonvisible). to a 1.5 mL eppendorf tube previously prepared with 750 uL of TriReagent.* *4. Invert several times to mix and freeze.* *1.*	**KIT**

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Nbr 8	0.30	Frozen (store at -70C)	SSA	*'FNA/DNA'*	No	*Freeze at -70 C and send to SSA with pink card.*	**KIT**

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *1*	**7:15**	**Tmpt:**	**Desc:**	No test orders
Blood	Green/black	8.00 ml	Tube label: *'Stored Plasma'*	**KIT**

Instructions: *Centrifuge at 3K for 15 mins. Remove the CRU label from the tube. Refrigerate and send to SSA on cold pack on the day of collection.*

No Aliquots	Temperature	Destination Lab
	Refrigerated	SSA

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *1*	**7:15**	**Tmpt:**	**Desc:**	No test orders

Blood Green/black 8.00 ml Tube label: *'Stored Plasma'* **KIT**

Instructions: *Centrifuge at 3K for 15 mins. Remove the CRU label from the tube. Refrigerate and send to SSA on cold pack on the day of collection.*

No Aliquots	Temperature	Destination Lab
	Refrigerated	SSA

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *1*	**7:15**	**Tmpt:**	**Desc:**	No test orders

Blood SST/Gld 3.5 3.00 ml Tube label: *'Creatinine'* **KIT**

Instructions: *Allow to clot. Centrifuge at 3 K for 15 minutes. Aliquot serum equally between the two orange-top tubes labeled "Serum C-1."*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	0.50	Frozen (store at -20C)	SSA	*'Serum C-1'*	No	*Freeze at - 20 C. Send to SSA with pink card.*

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 2	0.50	Frozen (store at -20C)	SSA	*'Serum C-1'*	No	*Freeze at - 20 C. Send to SSA with pink card.*

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *1*	**7:15**	**Tmpt:**	**Desc:**	**HMSR BLOOD results will go to medical record**

Blood SST/R&B 8.5 8.50 ml Tube label: *''*

Instructions: *Do not process, send to CCL.*

No Aliquots	Temperature	Destination Lab
	Ambient	CCL

Test Code	Mnemonic	Description
8053	LPSC	Lipid Panel
87972	ELPN	Electrolyte Panel, Serum

Day: *1*	**7:15**	**Tmpt:**	**Desc:**	No test orders

Blood SST/Red 10 10.00 ml Tube label: *'Stored Serum'* **KIT**

Instructions: *Allow to clot for 30 mins. Centrifuge at 3K for 15 mins. Remove the CRU label from the tube. Refrigerate and send to SSA on cold pack on the day of collection with pink card.*

No Aliquots	Temperature	Destination Lab
	Refrigerated	SSA

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *1*	**7:15**	**Tmpt:**	**Desc:**	No test orders
Blood	SST/Red 10	10.00 ml	Tube label: *'Stored Serum'*	**KIT**

Instructions: *Allow to clot for 30 mins. Centrifuge at 3K for 15 mins. Remove the CRU label from the tube. Refrigerate and send to SSA on cold pack on the day of collection.*

No Aliquots	Temperature	Destination Lab
	Refrigerated	SSA

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *1*	**8:25**	**Tmpt:**	**Desc: *U0***	**HMSR BLOOD results will go to medical record**
Urine	Urine, Hat	5.00 ml	Tube label: *'U0'*	

Instructions: *Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	5.00	Refrigerated	Renal	*'U0'*	No	*Place in the refrigerator and send all renal clearance specimens together at the end of the visit.*

Test Code	Mnemonic	Description
81476	NSRC	Renal Clearance, Short, Iothalmate

Day: *1*	**9:30**	**Tmpt:**	**Desc:**	No test orders
Urine	Urine, Hat	60.00 ml	Tube label: *'UE'*	No Clock Time

Instructions: *Participant to void at this time and RN to record time and TV. Do not save urine*

No Aliquots	Temperature	Destination Lab
	Ambient	NONE

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *1*	**9:35**	**Tmpt:**	**Desc: *P1***	No test orders
Blood	NaHep/Grn 4	3.00 ml	Tube label: *'P1'*	

Instructions: *Centrifuge at 3K for 10 mins. Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	1.50	Refrigerated	Renal	*'P1'*	No	*Send to the Renal Lab on wet ice via General Service.*

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

Day: *1*	**10:15**	**Tmpt:**	**Desc: *U1***	**HMSR BLOOD results will go to medical record**
Urine	Urine, Hat	5.00 ml	Tube label: *'U1'*	

Instructions: *Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	5.00	Refrigerated	CCL	*'U1'*	No	*Place in the refrigerator and send all renal clearance specimens together at the end of the visit.*

Test Code	Mnemonic	Description
81476	NSRC	Renal Clearance, Short, Iothalmate

Day: *1* **10:20** **Tmpt:** **Desc: *P2*** No test orders

Blood NaHep/Grn 4 3.00 ml Tube label: *'P2'*

Instructions: *Centrifuge at 3K for 10 mins. Aliquot.*

Aliquot	Vol (ml)	Temperature	Destination Lab	Label on tube	Print Pt ID?	Instructions
Nbr 1	1.50	Refrigerated	CCL	*'P2'*	No	*Send to the Renal Lab on wet ice via General Service.*

Test Code	Mnemonic	Description
	!NONE	No Test Order Type

06-009502 OPRC | Patient Name (x-xxx-xxx) mm/dd/yyyy | Printed 10/10/2007 4:42 PM

CRISP II

IRB #06-009502
Study Plan: OPRC - Outpatient Renal Clearance yr 1 & 3

DOB:
Clinic #:
Name:

Pt. emergency contact information
Name _____
Number _____
Relationship _____

Documentation Form: Low Sodium Diet Menu, VAPP, MD Orders

Role	Name	Pager #	(W)Phone #	(H)Phone #	(C)Phone #
PI	**Torres, Vicente E. MD, PhD**	**4-7527**	**(507) 284-3744**	**507-282-5096**	_____
Co-I	Abdalla, Adil A. M.D.	8-9377	266-1963	_____	_____
Co-I	King, Bernard F M.D.	4-6313	(507) 284-1728	_____	_____
Coord	**Kubly, Vickie J.**	**8-2356**	**(507) 266-9207**	_____	_____
Coord	**Spencer, Dorothy**	**6-8774**	**507-266-3868**	_____	_____
Dietetics Coord	O'connor, Helen M. RD	127-06605	255-5703	_____	_____
Lab Coord	Hare, Jennifer R. RST	127-10522	5-6905	_____	_____
Nurse Coord	Broten, LouAnn	_____	(507) 255-5701	_____	_____
Pharmacy Coord	Miller, Debbie D. PH	_____	5-7928	_____	_____
Unit Coord	Henkel, Mary RN	_____	507-255-5701	_____	_____

Send flowsheet to: Dorothy Spencer / vickie Kubly @ EiSL 33 Nephrology

PFH Date _____ **CVI Date** _____

Consent signed: _____ / _____ (DATE / INITIALS)

PG Test: _____ / _____ / _____ (RESULTS / DATE / INITIALS)

Additional Comments
US please activate Revolving Account

Revision 2 completed by Broten, LouAnn on 9/10/2007

Day 1

Renal Clearance room set-up

Place the following in patient room:
Set up syringes per protocol
Heating pad
Scale for RC [place on solid counter and plug in]
Have bladder scanner with gel bottle
Clock or stopwatch
Urinal /hat

Basic room set-up

Place the following in patient room:
Set up syringes per protocol
Heating pad
Scale for RC [place on solid counter and plug in]
Have bladder scanner with gel bottle
Clock or stopwatch
Urinal /hat

0600

Admission Out Patient

Ht. _____cm Wt. _____ kg

VS: T_____; P_____; BP_____; R_____

_____Verify consent

_____Review CVI/PFH if appropriate

_____Baseline RN assessment

_____Participant should have drank 3 - 8oz. glasses of water between 9-10 PM last evening

_____Patients are to have taken their evening dose of HTN medication. Patient is NOT to take any medications until after MRI completed.

_____Check Creatinine fom MICs or Docs Browser note: ____.____mg/dL - the result may be from several years out and that is what we are to use.

Fasting

Patient to be fasting until after RC study & MRI except for water

0615

Criteria

Note allergies to Iodine of any kind & document severity

Severe_____ Mild_____ Moderate_____
If patient has had a previous severe reaction to contrast, notify Dr. Torres in regards to canceling the test.

CRITERIA FOR IMMEDIATE NOTIFICATIONOF INVESTIGATOR
1. Iothalamate allergic reaction
2. Incomplete bladder emptying
3. Continuously low urine output (< 3ml/min.)
4. Headache, nausea, diarrhea, other physical complaints

Blood draw - STAT [HCL] - Pg

Draw Pg test when applicable and send to STAT lab if not done in the last 48 hrs.
RESULTS _____

0630

Urine collection - clean catch

Obtain a clean catch urine sample per standard procedure. Aliquot per instructions on lab flowsheet. **TIME**_____

A urinary catheter is not approved for this study

0645

VS

The participant is to have obstained from smoking and caffeine for at least 30 min prior to BP measurements

Use the Dinemap or Phillips monitors

Measure the upper arm circumference to determine cuff size
Right_____cm Left_____cm Cuff size_____
Adult cuff [24->33 cm]
Large cuff [33-41 cm]
Child cuff [<24 cm]
Thigh cuff [>41 cm]
*****Record cuff size, dominate arm, & BP readings on MICS**

The patricipant is to sit for 5 minutes with feet uncrossed and the BP's are to be taken 3 times in each arm 3min apart.

The **non-dominent** arm will be used to obtain the BP's

Blood Pressure Measurement Procedural Steps:

1. Have participant bare arm, removing restrictive clothing

2. Position Cuff:

a. Center of cuff placed over brachial artery

b. Bottom edge of cuff is positioned 1 to 1.5 inches above antecubital space

c. Cuff is wrapped smoothly & snuggly on arm so that only 2 fingertips can fi under the edge of the cuff.

d. Straighten BP cuff tubing so that it is parallel to patients arm.

4. Verify that participant is relaxed and properly positioned:

a. Sitting upright (no slouching), back supported

b. Both feet on the floor (legs/ ankles not crossed)

c. Arm is supported at heart level

d. BP device display screen is not visible to the participant

e. Participant not to talk, eat or drink during BP measurements

If on 3 consecutive measurements there is a difference in the systolic BP of 20 mm Hg or more between arms. The non-dominant arm will be determined as being th arm with the lowest total Mean Arterial Preassures (MAPS) instead of which hanc is non-dominate. To determine this do the following:

Right arm -

Time	Systolic / Diastolic	Mean	Pulse
_____	_____/_____	_____	_____
_____	_____/_____	_____	_____
_____	_____/_____	_____	

Left arm -

Time	Systolic / Diastolic	Mean	Pulse
_____	_____/_____	_____	_____
_____	_____/_____	_____	_____
_____	_____/_____	_____	

TOTAL MAP _____

Average BP and pulse values from above with non-dominate arm =_____

Average P_____ Average BP_____

0700

Oral fluid Load Patient to begin drinking six 8oz [240mL ea] glasses of water (may include 1 cup of decaf coffee) to be completed by **0800**.
# of glasses taken _____

Void Patient may void between now and 0700. Do not need to save urine.

Patient not to void after 0710 untill 0755, if possible. If pt. needs to void between 0710 and 0730 - Do not save, **but pt. must void at 0755.**

0715

Start - NS lock Start IV saline lock for blood draws - Draw HMSR bloods at this time

Blood draw Draw baseline bloods at this time (total 47.5ml)
8.5ml SST. for HMSR tests (Creatinine, Electrolyte pannel, Lipid panel)
8ml Green/black - **X2** - Kit
3ml in 3.5ml SST - Kit
10ml SST - **X2** - Kit

May do with IV start

0730

Questionnaires Review and complete GFR checklist and continue throughout study. See attachment. The GFR test MUST BE RESCHEDULED if the answer to any of the statements in the checklist is "No" - notify study coordinator.

Iothalimate - SQ Notify pharmacy to send Iothalamate for 0830 injection

0825 **UO**

Urine - UO UO (baseline): Have subject empty bladder as completely as possible
Time void ended_____
Total Vol_____ Aliquot 5ml into appropriate tube. Discard remainder.

Record all urines and bloods on Short renal clearance form (attached)

0830

Med-Iothalamate SQ *Note: Blood draw is from opposite arm, so use best arm for veni-puncture.

Use POSTERIOR aspect of UPPER ARM. Gently pinch skin, insert needle, release skin, (draw back to make certain not in vessel), and inject Iothalamate.

Time: _____ Injection Site: _____ Right; _____ Left

Record in MICS & on Short renal clearance form

Oral fluid Load Have participant drink (1-2) 8oz glasses of water to maintain output. # of glasses_____

0920

FYI study Information **Renal Lab Guidelines:** Be sure bladder is empty. Average residual bladder volume should be < 20 mls. (Note: In some situations, <10% of voided volume, [PROVIDED residual volume is <50mls], is acceptable.

Urine Flow Rate **Must be equal to or greater than 3ml per min.**
If the flow rate does not meet this criteria at any time THE TEST MUST BE RESCHEDULED. See GFR checklist

0930 **UE**

Urine - UE UE (60 minutes from Iothalamate injection): [+or - 5 min]
Have subject empty bladder as completely as possible
Time void ended_____ TV_____No aliquot at this void
Discard urine.

UE

Bladder Ultrasound Instructions **VOID # 1:**Obtain 5 bladder ultrasound readings within 1-2 minutes of voiding an record
1. _____ **2.** _____ **3.** _____ **4.** _____ **5.** _____

If bladder has an average of > 20mls of urine, have pt. revoid immediately after first void & ultrasound again.

VOID # 2 [IF NEEDED]:
1. _____ **2.** _____ **3.** _____ **4.** _____ **5.** _____

If Average of residual bladder volume is > 20 mls, extend Equilibration Period for **5** min. and have participant void again.

VOID # 3 [IF NEEDED]:
1. _____ **2.** _____ **3.** _____ **4.** _____ **5.** _____

Record urine vol. _____, duration _____, and flow [ml/min] _____[Urine vol. Divided by duration = flow]
*Flow is figured to 3 places behind the decimal then rounded to 2 places on *Short Renal Clearance* form.

0935 **P1**

Blood draw - P1

P1 (60 minute): TIME_____ (record on Short Renal Clearance form)
3mL into a 4mL Green
Do within 5 min. maximum of UE by venipuncture in oposite arm of injection
Tourniquet time MUST be LESS than 1 min
tourniquet used: _____yes _____no Time left on: _____seconds

1010

FYI study Information

Of primary concern is the differentiation recorded on the GFR from the UE to U1.
It is **EXTREMELY IMPORTANT** that the time of urine collection duration is absolutely accurate from end of UE to end of U1.

1015 **U1**

Urine - U1

U1 = All urine collected for at least 45 minutes after UE
Have subject empty bladder as completely as possible, If more than one void, poo
and save all urine for accurate TV.
Time void ended_____ TV_____
Aliquot Aliquot 5ml into appropriate tube and discard remainder.

U1

Bladder Ultrasound Instructions

VOID # 1: Obtain 5 bladder ultrasound readings within 1-2 minutes of voiding ar
record
1. _____ 2. _____ 3. _____ 4. _____ 5. _____

If bladder has an average of > 20mls of urine, have pt. revoid immediately after first void & ultrasound again.

VOID # 2 [IF NEEDED]:
1. _____ 2. _____ 3. _____ 4. _____ 5. _____

If Average of residual bladder volume is > 20 mls, extend Equilibration Period for
15 - 30 min., [but less than 90 min from UE] and have participant void again.

VOID # 3 [IF NEEDED]:
1. _____ 2. _____ 3. _____ 4. _____ 5. _____

Record urine vol. _____, duration _____, and flow [ml/min] _____[Urine vol. Divided by duration = flow]
*Flow is figured to 3 places behind the decimal then rounded to 2 places on *Short Renal Clearance* form.

1020 **P2**

Blood draw - P2

P2 = Plasma collected immediately after U1 TIME _____ (record on Short Renal Clearance form)

		3mL into a 4mL Green
		Do within 5 min. maximum of U1 by venipuncture in oposite arm of injection **Tourniquet time MUST be LESS than 1 min** tourniquet used: _____yes _____no Time left on: _____seconds
1030		
	Fasting	Have patient remain fasting until after MRI Remind patient not to take any medication until after MRI
	SMH - low sodium meal	Have participant order meal from St. Marys dietary for _1230_ time. (low sodiu meal)
1100		
	MRI	Await escort/study coordinator to take patient to MRI Confirm appointment time MRI_____ (5-8755)
1300		
	VS	Upon return from MRI VS: T_____; P_____; BP_____; R_____
	Dc IV	Dc IV
	Dismissal	Dismiss patient if stable Participant will have afternoon appointment with Dr. Torres.
	FYI study Information	Make 2 copies of the Short renal clearance form and give **1.** One to the lab to send with the samples **2.** Attach one to the flowsheet **3.** Fax copy of GFR checklist and a copy of the short renal clearance form to Dorothy Spencer @ 5-0770

RC bloods and Urines

Time	Setup	Green/black	NaHep/Grn 4	SST/Gld 3.5	SST/Red 10	SST/R&B 8.5	Urine, Hat	Sarstedt 6	Comments
Day 1									
0630	all to lab						60	5	Urine collection - clean catch
0700									Oral fluid Load - 6 glasses
0715	11.5, 8,8,10,10	8, 8		3	10, 10	8.5			Blood draw
0825	5						5		Urine - UO
0830									Med-Iothalamate SQ
0830									Oral fluid Load 1-2 glasses
0930	none						60		Urine - UE discard after TV **NO Aliquot - Discard**
0935	3		3						Blood draw - P1
1015	5						5		Urine - U1
1020	3		3						Blood draw - P2

06-009502 OPRC | Patient Name (x-xxx-xxx) mm/dd/yyyy | Printed 10/10/2007 4:42 F

DO NOT ALTER DOCUMENT
IRB # 06-009502 Nurse Information

Title: Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP II)

Objective: This study seeks to draw unequivocal linkage between the rate of kidney/cyst enlargement and qualitative and quantitative (declining renal function reflected in iothalamate clearance and albuminuria) end-points, provide a marker of disease progression and develop and test other biomarkers of disease progression.

Study Design: This is a four year prospective, observational study of up to 58 subjects conducted at the CRU SMH. Subjects come to the CRU for two visits year 1 and year 3. Subjects receive iothalamate 300 mg SQ at each visit to determine glomerular filtration rate.

Study Drug Administration: (preferred injection site = non blood draw arm)

- For subjects 40 kg or greater administer 300 mg/mL iothalamate SQ into the posterior upper arm.

Pharmacology: Iothalamate is a radiological iodinated contrast media used for renal function tests.

Concomitant Medications: No restrictions are listed in the protocol. Per Investigator hold AM dose of hypertension medications on the day of the study until completion of iothalamate clearance test and MRI.

Side Effects/Warnings:

- Injection site reaction
- Allergic reaction

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

APPENDIX 1 GFR CHECKLIST

THIS FORM MUST BE COMPLETED AND RETURNED to address below

- **Participant's Initials: ____ ____ ____; MML CONTROL No.: M-_____**
  from Short Renal Clearance Form
- **Participant's CRISP ID: _____**
- **SITE: (Circle One) Alabama Emory Kansas MAYO**
- **Date of Collection:_____/_____/2007**
  Month Day Year

Check In

1. **CLINICAL STABILITY: → No ☐ Yes ☐**
   (NOTE: Clinical Stability is defined as the ABSENCE of: Viral Syndrome; Fever; Acute Pain; Diarrhea; etc.).**
2. **Compliance with non-allowed medications: → No ☐ Yes ☐**

DAY 1

1. **Fasting (> 8 hours) → No ☐ Yes ☐**
2. **Hydration as per Protocol → No ☐ Yes ☐**
3. **Equilibration time 60 ± 5 minutes → No ☐ Yes ☐**
4. **Urine Flow rate ≥ 3 ml/minute for UE → No ☐ Yes ☐**
5. **P1 within 5 minutes of UE → No ☐ Yes ☐**
6. **Residual bladder volume < 20 ml OR → No ☐ Yes ☐**
   10% of voided urine (but NOT > 50 ml) @ UE
7. **Collection time for U1 is 45 – 90 minutes. → No ☐ Yes ☐**
8. **P2 is within 5 minutes of U1 → No ☐ Yes ☐**
9. **Residual bladder volume < 20 ml OR**
   10% of voided urine (NOT > 50 ml) @ U1 → No ☐ Yes ☐
10. **Urine Flow rate ≥ 3 ml/minute for U1 → No ☐ Yes ☐**

NOTE: If the answer is "No" to any of the above, THE TEST MUST BE RESCHEDULED.! **Please page Dr. Torres Vickie, or Dorothy, PRIOR to canceling test.

NOTE: Please send this form and Original GCRC Flowsheet to:
Vickie Kubly, Dorothy Spencer, Study Coordinators
Eisenberg S-33
Nephrology PKD Research
Thank you! 6-9207 / 6-3868)

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

SHORT RENAL CLEARANCE SHEET

DOCTOR: DR. IRB:

NAME:_____
CLINIC NO:_____ DATE:_____

DIAGNOSIS:_____

AGE:_____ SEX_____ WT: _____kgs. Ht:_____cm BP _____

Allergies:_____ Iothalmate Injection Time:_____

MEDICATIONS:_____

FASTING:_____ WATER LOAD GIVEN:_____

ESTIMATED FUNCTION: GFR _X_ SERUM CREATININE_____

Total Intake: Oral Water _____
Total Output: Urine output_____

COLLECTION OF SAMPLES

BLOOD	**URINE**			
Time	**Time**	**VOL ÷ DURATION**	**= FLOW RATE**	**Water**
	Pre_____			_____
P0_____ (baseline)	**U0**_____;	_____ ÷ _____	= _____	
BP cuff used: ___yes, __no, ___mmHg				
P1____	**UE**_____; ultrasound____ ____ ____ ____ ____;			
BP cuff used: ___yes, __no, ___ mmHg				
	VOL / DURATION	*= FLOW RATE*		*Water*
	_____ ÷ _____	= _____		_____
P2____	**U1**_____; ultrasound____ ____ ____ ____ ____;			
BP cuff used: ___yes, __no, ___ mmHg				
	VOL / DURATION	*= FLOW RATE*		
	_____ ÷ _____	= _____		

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

Prepared by Research Support
Hospital Pharmacy Services 10/10/2007ddm

University of Alabama-Birmingham Flow-Sheets

GCRC Protocol #: 1311
IRB #: F070226008

Title: "RENAL IMAGING TO ASSESS PROGRESSION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): EXTENSION (CRISP II)"

Inpatient Study plan: CRISP II Year 1 (FV-06), and Year 3 (FV-08)

PATIENT:_____	VISIT YEAR: FV06 or FV08 **(circle one)**
PATIENT CRISP ID:_____	UAB-Medical Records #: _____

INVESTIGATORS:

Dr. Lisa M. Guay-Woodford, MD	Pager: 7302	Phone: 934-7308	
Dr. Mark Lockhart, MD	Pager: 3489	Phone: 934-7130	
RESEARCH NURSE COORDINATOR:			
Teresa Chacana, RN, BSN	Pager: 6193	Phone : 934-7649	Fax: 975-0814
ADMITTING MD:			
Dr. Michal Mrug, MD	Pager: 7739	Phone: 934-7308	

MRI: 934-2796 or 934-3069
GCRC Nursing Station: 934-4857
GCRC Lab: 934-7967 (Gloria Richardson)
Outreach Lab: 975-8100 (Contact Person: 975-8103 (Kathy Hamilton)

STUDY VISIT WORKSHEET

DAY 1: Arrival to GCRC for admission after 3 PM.

RN Initials

_____ 1. Admit to GCRC, MD: Dr. Lisa M. Guay-Woodford.
_____ 2. Page/call Teresa Chacana, RN upon participant's arrival.
_____ 3. Weight without shoes in kg (to 0.1 kg) _____ kg. (1kg = 2.2 lbs)
_____ 4. Height without shoes in cm (to 0.1 cm) _____ cm. (2.54cm = 1 inch)
_____ 5. V/S: B.P. _____/_____; Pulse _____; Respirations _____
_____ 6. Complete initial BP assessment for CRISP II: To determine what arm will be used on sitting and standing BP readings in the morning of DAY 2 (at 5:30 AM).

INITIAL BP ASSESSMENT FOR CRISP II:

-Obtain after patient awake for 30 min.
-The participant is to have abstained from smoking and caffeine for at least 30 min prior to.
-Use the Dinemap / Critikon BP monitor.
-Measure the upper arm circumference (both arms) to determine cuff size.

Adult cuff [24->33 cm]
Large cuff [33-41 cm]
Child cuff [<24 cm]
Thigh cuff [>41 cm]

Right_____cm **Cuff size_____**

Left_____cm **Cuff size_____**

Created: 6-12-07
Revised: 9-10-07

NON DOMINANT ARM (in terms of handedness) RIGHT arm LEFT arm
(Circle one)

PREPARATION AND MEASUREMENTS

CRISP II will use the **non- dominant arm (in terms of handedness)** for sitting BP readings. **BUT**, **IF** on 3 consecutive measurements there is a difference in the systolic BP of 20 mm Hg or more between arms the non-dominant arm will be determined as being the arm with the lowest total Mean Arterial Pressures (MAPS) instead of which hand is non-dominate.

TO DETERMINE THE ARM TO USE ON DAY 2 AM FOR BP READINGS DO THE FOLLOWING:

-The participant is to sit for 5 minutes with both feet on the floor (legs/ ankles not crossed)
-Have participant bare arm, removing restrictive clothing
-**Arm is supported at heart level**
-Center of cuff placed over brachial artery
-Bottom edge of cuff is positioned 1 to 1.5 inches above antecubital space
-Cuff is wrapped smoothly & snuggly on arm so that only 2 fingertips can fit under the edge of the cuff.
-Straighten BP cuff tubing so that it is parallel to patients arm.
-Verify that participant is relaxed and properly positioned:
-Sitting upright (no slouching), back supported
-**BP device display screen is not visible to the participant**
-Participant not to talk, eat or drink during BP measurements
-**BP's are to be taken 3 times at least 30 seconds apart** in both arms.

Right arm (use appropriate cuff)

Time	Systolic / Diastolic	Mean
_____	_____/_____	____
_____	_____/_____	____
_____	_____/_____	____

TOTAL MAP_____

Left arm (use appropriate cuff)

Time	Systolic / Diastolic	Mean
_____	_____/_____	____
_____	_____/_____	____
_____	_____/_____	____

TOTAL MAP _____

Use this non- dominant arm and this cuff size to obtain CRISP II sitting and standing BP readings on DAY 2 at 5:30 AM

NON- DOMINANT ARM is (Circle one) Right arm Left arm CUFF_____

_____ 8. Place copy of informed consent on chart.
Consent signed _____/_____
DATE INITIALS

RN Initials

_____ 9. On admission, (childbearing women)**:** send urine to Outreach Lab for **PREGNANCY TEST**: Use a clean urine cup, minimum sample: 1 ml.

_____ 10. Review pt's medication list and disallowed medications list. Call Teresa if disallowed medications are included.

LIST OF MEDICATIONS THAT SHOULD BE AVOIDED BY CRISP STUDY PARTICIPANTS.

PLEASE NOTE: These medicines should not be taken for at least ONE week prior to Enrollment and each subsequent Visit in the CRISP Study.

**Extra-Strength Tylenol® is acceptable for pain or discomfort.

Names of some of the more-common Non-Steroidals (NSAIDS)

1. **Salicylates (Aspirin, Empirin, Midol)**
2. **Fioricet**
3. **FiorinaL**
4. **Phrenilin Forte**
5. **Ibuprofen/Excedrin/Advil**
6. **Motrin**
7. **Nuprin**
8. **Naproxen Sodium/Naprosyn/Anaprox/Aleve**
9. **Diclofenac**
10. **Indomethacin**
11. **Sulindac**
12. **Tolmetin**
13. **Celecoxib**
14. **Rofecoxib**
15. **Meclofenamate**
16. **Mefanamic Acid**
17. **Nambumetone**
18. **Piroxicam**
19. **Fenoprofen**
20. **Ketaprofen (Extended Release)**
21. **Oxaprozin**
22. **Etodolac**
23. **Ketorolac**
24. **Toradol**
25. **Celebrex**
26. **Viox**
27. **$C0X^2$ Inhibitors**
28. ***NOTE: Hydrochlorothiazide (any Diuretics) should not be started as a NEW antihypertensive treatment < 2 wks prior to Enrollment Visit. (If it is necessary for you to start this medication, Enrollment should be delayed for 2 weeks).**
29. **The following medications also interfere with Creatinine excretion and should not be used for 4 days prior to each Visit:**
    - **Trimethoprim (Bactrim/Septra)**
    - **Cimetidine/Tagamet.**

RN Initials

_____11. Participant to complete quality of life (form 41; it was mailed at home to complete and bring with them to this visit) and pain (form 42) questionnaires.

_____12. Subject to take own medications during inpatient stay. **Hold the evening dose of antihypertensive medications**, if any, until MRI completed. Subjects SHOULD NOT take medication in the morning (of second day admission) until after MRI and GFR are completed.

_____13. Activity ad-lib.

_____14. Diet (2 gm Na, Low Cholesterol, Caffeine-free).

_____15. Medical history, interview, physical, by Dr. Michal Mrug.

_____16. Consent signed by Dr. Guay-Woodford.

_____17. **Note Allergies**: _____
Note allergies to shellfish and Iodine of any kind and document severity
Allergy to Iodine **(circle one)**: Yes No
If Yes, Specify symptoms_____

_____16. Review Categories of Contrast Reactions Appendix (on page 16-17 in this study visit worksheet: **(circle one).**

None Mild Moderate Severe

If the Participant has had a previous severe reaction to Contrast (Iodine), Notify via UAB pager 934-3411 to Dr. Michal Mrug or Teresa Chacana, RN, BSN about Steroid Prep or canceling the test.
STEROID PREP: Medrol 32mg PO & Benadryl 50mg PO twelve (12) hours prior to the test (for GFR), Then Medrol 32mg PO two (2) hours prior to the test.

_____17. GCRC RN to review pregnancy test result **(circle one)** Positive Negative N/A

_____18. If Pregnancy test is positive, notify Dr. Michal Mrug and DO NOT Continue Study/Tests.

_____19. **21:00**:
The participant must drink at least 4 - 6 glasses of water (8 oz. each) between 9 and 10 p.m.
The amount of water may be less if the participant is under physician orders to restrict fluid intake.
The participant must stay NPO except for water after 10:00 p.m.
Participant to go to bed with lights out at 10 PM

_____20. **Hold next AM meds until after BP monitoring, MRI and GFR are completed.**

LABS: To collect at Day 1: Admission

_____ Urine Pregnancy Test (use a clean urine cup, minimum sample: 1 ml). Send to Outreach Lab.

CRITERIA FOR IMMEDIATE NOTIFICATION OF INVESTIGATOR:

1. Positive Pregnancy Test. Participant will not continue visit.
2. History of Iothalamate allergic reaction.
3. Incomplete bladder emptying [residual should be less than 20mL or in some situations (i.e. large bladder, large urine output) less than 10% of voided volume, but not greater than 50 mL is acceptable].
3. Continuously low urine output [urine flow should be equal or greater than 3ml/min}.
4. Headache, nausea, diarrhea, other physical complaints.

DAY 2

RN Initials

_____1. **05:00 AM**
Hold AM meds. Blood and urine samples will be collected in the AM prior to morning hydration or taking medications or food.

_____2. Participant remains fasting, caffeine and smoking free

_____3. Label tubes with: Patient's Initials, UAB MR #, the 6-digit CRISP ID #, date of collection, time of collection, type of sample (i.e. Urine), P.I.: Lisa Guay-Woodford and site: UAB.

_____4. Awaken Participant to void. Save urine for urine samples. Note voiding time _____:_____ a.m.

_____5. Collect urine samples: **Place tubes on ice**.
Note: (processing times should be no longer than 20-30 minutes from the time of acquisition)

Urine will be collected for:

____ URINE ALBUMIN, URINE CREATININE, URINE ALBUMIN/CREATININE RATIO: from random urine, collect at least 10 ml in a no preservative urine cup. Send to Outreach Lab.

____ NIDDK BIOSAMPLE REPOSITORY–URINE: At least 35 ml of freshly voided urine. Sent to GCRC lab for the following processing:

GCRC LAB: Specimens will be centrifuged in a 50 mL PP tubes at 500 g for 5 minutes as soon as possible, with volume, processing times, and voiding times noted **(processing times should be no longer than 20-30 minutes from the time of acquisition).** Tubes will be kept in ice throughout this process. The bottom 250 µL pellet (sometimes barely- or non-visible) will be transferred with a 1.0 mL pipette to a 1.5 mL eppendorf tube previously prepared with 750 µL of TriReagent (Molecular Research Center, Inc. Cincinnati, OH), and inverted several times and put on ice prior to freezing at -80˚C for future RNA/DNA retrieval. The remaining urine sample will then be transferred to 10 ml polypropylene (not polystyrene) Falcon culture tubes, stored in six 5 mL aliquots, place **all samples on ice prior to freezing at -80˚C** before they are sent to the NIDDK Repository at Fisher Bioservices. Samples designated for the NIDDK Repository at Fisher Bioservices are to be stored in specimen boxes provided by the repository. The NIDDK Repository will supply all tubes, labels and shipping materials. Sample shipment will be done by Teresa Chacana, RN.

RN Initials

_____6. **05:30 AM**. **Blood Pressure Assessment**

-Obtain BPs after patient is awake for at least 30 min.
-No caffeine or smoking 30 minutes prior to Blood Pressure readings
-Use the Dinemap / Critikon BP monitor
-Use the non dominant arm and cuff that was determinated last evening

NON- DOMINANT ARM is (Circle one)	Right arm	Left arm	CUFF_____

-Both feet on the floor (legs/ ankles not crossed)
-Arm is supported at heart level
-Participant not to talk, eat or drink during BP measurements
-BP device display screen is not visible to the participant.

Blood Pressure Measurement Procedural Steps:

-Have participant bare arm, removing restrictive clothing.
-Position Cuff: **a)** Center of cuff placed over brachial artery **b)** Bottom edge of cuff is positioned 1 to 1.5 inches above antecubital space **c)** Cuff is wrapped smoothly & snuggly on arm so that only 2 fingertips can fit under the edge of the cuff **d)** Straighten BP cuff tubing so that it is parallel to participant's arm.
-Verify that participant is relaxed and properly positioned: Sitting upright (no slouching), back supported.
-The participant is to sit for 5 minutes with feet uncrossed and the BP's are to be taken 3 times at least 30 seconds apart.
.-Obtain:

-Three SITTING B/Ps readings at least 30 sec. apart on the Non Dominant with arm supported at heart level

Time: ___:___ am pm; (sitting) ____/ ____ (mm Hg); Pulse Rate:_____ ; MAP:_____

Time: ___:___ am pm; (sitting) ____/ ____ (mm Hg); Pulse Rate: _____; MAP: _____

Time: ___:___ am pm; (sitting) ____/ ____ (mm Hg); Pulse Rate: _____; MAP: _____

Is there a difference of more than 10 mm Hg (systolic or diastolic) between the second and third readings in one sitting?
Yes No **(Circle one)** (**If Yes**, a fourth and fifth reading will be recorded for the sitting).

Time: ___:___ am pm; (sitting) ____/ ____ (mm Hg); Pulse Rate: _____; MAP: _____

Time: ___:___ am pm; (sitting) ____/ ____ (mm Hg); Pulse Rate: _____; MAP: _____

RN Initials

-Have participant to stand up for 3 minutes with arm supported at heart level and obtain:

-**One STANDING BP on the Non Dominant** arm with arm held or positioned at heart level:

Time: ___:___ am / pm (standing) ____/ ____ (mm Hg); Pulse Rate: _____; MAP: _____

_____7. Blood Labs: Check label in tubes with the Patient's Initials, UAB MR #, the 6-digit CRISP ID #, date of collection, time of collection, sample (i.e. Blood), P.I.: Lisa Guay-Woodford and site: UAB.

_____8. **Start Saline lock** to be used for blood samples and GFR test samples.

Note: USE arm with BEST venous access for venipuncture. Use 3mls Saline Flush lock after blood draws.

_____9. Collect blood samples

Blood will be collected for:

____ TOTAL ELECTROLYTE PANEL – sodium, potassium, chloride, total CO2 –
____ LIPID PANEL – Total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol –
____ SERUM CREATININE – For "local sample", use one Tiger Top SST or a Gold top SST tube with 3.5 ml minimum blood.

These three labs require a minimum total of 10 mL of blood in a Tiger Top SST. Sent to the Outreach Lab

Serum creatinine – this lab will be obtained in duplicate, one processed at the local lab and the other frozen and batch shipped to the Cleveland Clinic Laboratory annually.

____SERUM CREATININE SAMPLE TO CLEVELAND CLINIC LABORATORY requires 7-**10 mL of blood in a single Tiger top, SST tube. Take tube to GCRC lab.**
_____GCRC LAB: For the above sample, (serum creatinine sample to Cleveland Clinic Laboratory), serum will be obtained, allowing the blood to clot for 30 minutes and centrifuging for at least 10 minutes in the usual manner (spin 10 minutes at 3000 RPM) 1 mL of serum will be transferred to a five-mL tube and labeled with a unique accession number (#1-A). A single QC sample, identical but with a unique accession number (#2-A), will be prepared as back up sample. **Keep both tubes frozen at -20 C.** All excess fluid will be stored at -20 degrees Celcius as a back-up sample (labeled with accession #1-B) until results are available.

____NIDDK BIOSAMPLE REPOSITORY –Blood: Twenty mL will be collected **in two SST tubes (tiger-top, 10 mL each)** and 16 mL **in two PST tubes (green/grey-top, 8 mL each).** Gently invert tubes (but do not shake). Invert SST tubes (tiger top) 6 times and PST tubes (green top) 8-10 times. Take tubes to GCRC lab.
_____GCRC LAB: For the NIDDK biosample repository, serum samples will be obtained from 2 SST tubes (tiger top) and plasma samples will be obtained from 2 PST tubes (green top).

RN nitials

Let SST (tiger top) tubes clot in a vertical position for a minimum of 30 minutes. Note: PSTs contain an anticoagulant (heparin), so there is no need for clotting time. Centrifuge all tubes ideally within one hour of collection, but certainly within two hours. Spin SST tubes (tiger top) at 1300 RCF (g) for 15 minutes. Spin PST tubes (green top) at 1300 RCF (g) for at least 10 minutes. No decanting is necessary. **Place tubes in refrigerator** until shipment. Samples designated for the NIDDK Repository at Fisher Bioservices are to be stored in specimen boxes provided by the repository. The NIDDK Repository will supply all tubes, labels and shipping materials.
Tubes to be shipped refrigerated (on frozen cold packs) to the NIDDK Biosample Repository at Fisher Bioservices on the day of collection, where they will be aliquotted into 1 mL tubes and archived. Sample shipment will be done by Teresa Chacana, RN.

____GENETIC STUDIES**: **Three yellow top tubes with ACD**. Invert each tube gently 8-9 times to mix blood with additives and keep them at room temperature. Take tubes to GCRC lab.

(** Draw them if not obtained previously Pt. must consent for the Genetic Studies

_____GCRC LAB: For the genetic studies no processing is needed. **Keep at room temperature**. Sample shipment will be done by Teresa Chacana, RN.

_____10. **STORAGE of SAMPLES at GCRC LAB**

Long time storage at GCRC freezer:
____Urine samples: 1.5 mL eppendorf tube, Six 5 ml aliquots (obtained before BP readings)
____ Serum creatinine to Cleveland
____ Any extra excess of serum
Long time storage at GCRC refrigerator:
____Two tiger top tubes
____Two green top tubes

_____11. Keep participant NPO (may drink water moderately). Do not give participant cold water at any time due to vasoconstriction.

_____12. **07:00 AM**

Call MRI at 4-2796 to make sure they are ready for the participant. No contrast will be used in this stud
Call Escort Service to ensure that Participant arrives in MRI waiting area @ 07:15 a.m. (Or at least 15 minutes prior to appointment time).**Patient may void between now and 9:00am (Do NOT save this urine). NOTE**: Participant will STILL have to void @ 9:55 a.m. for U0.sample of GFR test.

_____13. **07:30 AM**:

MRI Study appointment time____:____ a.m. (Use 24 hour clock). PLEASE NOTE: MRI of kidneys will be routinely scheduled @ 07:30-8:00 a.m. on the MRI research machine.

_____14. **GFR Procedure**

-Review GFR procedure (Test #81476) and start to complete APPENDIX C GFR CHECKLIST. (P. 9)
-Review GFR glossary (P. 10) and GFR General Collection and Processing Instructions (P.11).
-Review Injection Procedure for 10:00 a.m. See Iothalamate Glomerular Filtration Rate (GFR) Test #81476. (P. 12)
-Review GFR Testing Flowchart (P. 13).
-Explain procedure to participant, confirm fasting and make sure the participant has not participated in other contrast studies within the last 12 hrs.

APPENDIX C GFR CHECKLIST

THIS FORM MUST BE COMPLETED AND RETURNED WITH SPECIMENS!!

- Participant Initials: ___.___.___ Control Number: _____
  (from Short Renal Clearance Green Label)
- SITE: (Circle One) Alabama Emory Kansas Mayo
- Date of Collection:_____/_____/20_____
  Month Day Year

DAY 1

1.	CLINICAL STABILITY: (NOTE: Clinical Stability is defined as the ABSENCE of: Viral Syndrome; Fever; Acute Pain; Diarrhea; etc.)	No ☐ Yes ☐
2.	Compliance with non-allowed medications:	No ☐ Yes ☐

DAY of GFR Test

1.	Fasting (4 hrs or 2 hrs if participant is diabetic)	No ☐ Yes ☐
2.	Hydration as per Protocol	No ☐ Yes ☐
3.	Equilibration time 60 ± 5 minutes	No ☐ Yes ☐
4.	Urine Flow rate ≥ 3 ml/minute for UE	No ☐ Yes ☐
5.	P1 within 5 minutes of UE	No ☐ Yes ☐
6.	Residual bladder volume < 20 ml OR 10% of voided urine (NOT > 50 ml) @ UE	No ☐ Yes ☐
7.	Collection time for U1 is 45 – 90 minutes.	No ☐ Yes ☐
8.	P2 is within 5 minutes of U1	No ☐ Yes ☐
9.	Residual bladder volume < 20 ml OR 10% of voided urine (NOT > 50 ml) @ U1	No ☐ Yes ☐
10.	Urine Flow rate ≥ 3 ml/minute for U1	No ☐ Yes ☐

NOTE: If the answer is "No" to any of the above, PLEASE CALL Teresa Chacana, RN or Dr Michal Mrug via UAB Paging in regard to canceling GFR test.. The GFR test MUST BE RESCHEDULED if the answer to any of the statements in the Checklist is "No". Notify Teresa Chacana if this occurs.

GFR RENAL GUIDELINES:

- Urine Flow Rate must be equal to or greater than 3 ml per minute. If the flow rate does not meet this criterion, THE TEST MUST BE RESCHEDULED. (See GFR checklist).
-Be sure the bladder is empty after each void. Average residual bladder volume should be < 20 ml. (**NOTE:** In some situations (e.g. high urine output, large bladders) a residual < 10% of voided volume [PROVIDED residual volume is < 50 ml], is acceptable).
-Urinary catheter is not approved for this Study.

GFR Glossary

1. **Uo—initial pre-injection urine sample. Aliquot a minimum of 5 mL into one of the urine containers provided. Record the collection time. Write "Uo" on the urine container. Send to GCRC Lab.**

2. **Iothalamate Injection Time—Record the injection time and dose.**

3. **Ue—Equilibration urine collection. Collect this specimen 60 minutes after the iothalamate injection time. Be sure the bladder is completely empty. Record the collection time and discard the urine specimen.**

4. **P1—Collect a sodium heparin plasma within 5 minutes of collecting the UE. Record the collection time. Aliquot the plasma into the green tube provided. Write "P1" on the vial. Send to GCRC lab.**

5. **U1—GFR testing urine collection. Collect specimen 45 minutes after the Ue collection. Be sure the bladder is completely empty: minimum of 100 mLs of urine is optimal. Quantitatively measure the U1 volume and record both the volume and collection time. Aliquot a minimum of 5 mL into the 2nd urine container provided. Write "U1" on the Urine container. Send to GCRC lab.**

6. **P2—Collect a sodium heparin plasma within 5 minutes of collecting the U1. Record the collection time. Aliquot the plasma into the 2nd green tube provided. Write "P2" on the vial. Send to GCRC lab.**

7. **U1 Collection Duration—Record the time difference from the Ue collection time to the U1 collection time.**

8. **Indicate name and phone number of a person that can answer any questions regarding the collection of these specimens.**

GCRC Laboratory:

Teresa will provide the "GFR kit" with tubes for urine and blood samples.
Urine samples (Uo and U1): From each of the urine cups, GCRC RN will aliquot 5 ml of urine in the clear tube labeled Uo or U1 (as correspond). Discard remainder of urine. Keep refrigerated.
Blood samples (P1 and P2): Green top tubes with at least 3 ml plasma centrifuge at 3000 rpm for 10 min. Aliquot 3 ml serum into the clear tube labeled P1 or P2 (as correspond). Keep refrigerated.
Teresa Chacana, RN will ship the samples the same day at refrigerated temperature.

A sheet with the following information will be shipped to Mayo Clinic along with GFR urine and blood samples by Teresa Chacana, RN.
The original form will be completed by Teresa with data from the worksheet. One copy of this original form is placed in the transport bag and one copy is sent back to Mayo Clinic

GFR: General Collection and Processing Instructions:
(To be done by GCRC Nurse and GCRC lab as per worksheet instructions)

CLIENT NUMBER:_____

Collection Date_____ Time:_____a.m. or p.m.

THE FOLLOWING INFORMATION MUST BE PROVIDED BEFORE TESTING CAN BE COMPLETED.

Patient Weight:_____kg (in kilograms)
Patient Height:_____cm (in centimeters)

Initial Urine Collection time (Uo) _____:_____ am pm (circle one)
Iothalamate Injection time _____:_____ am pm (circle one)

Equilibration Urine (Ue) Collection Time: _____:_____am pm
(Specimen discarded) (Circle one)

Plasma (P1) Collection Time: _____:_____ am pm (circle one)
(Must be no longer than 5 minutes after Ue collection)

GFR Testing Urine (U1) Collection Time:_____:_____ am pm
(Circle one)
U1 Collection Volume:_____mLs

Plasma (P2) Collection Time: _____:_____ am pm (circle one)
(Must be no longer than 5 minutes after U1 Collection)

U1 Collection Duration: _____minutes
Time difference from Equilibration Urine (Ue) to GFR testing Urine (U1)

Collection Facility Contact name: _____
Phone Number: _____

Iothalamate Glomerular Filtration Rate (GFR) Test #81476.

GFR Testing Flowchart

RN Initials

_____15. May keep Benadryl (50 mg PO/PRN) at participant's bedside.

-Participant may void now (before 9:00 AM-discard urine) but should not to void after this time.

_____16. **09:00 AM**:

-Participant may void before 9:00 AM but should not to void after this time point until 09:55 a.m. if possible.

-Between 9:00 and 10:00 AM the participant should drink **(4 – 6) 8 oz. glasses of water** (960-1440 ml)

-Participant may have more if desire in preparation for the GFR test (may include 1 cup of decaf. coffee).

-Participant not to void after this time point until 09:55 a.m. if possible.

-The amount of water may be less if the participant is under physician orders to restrict fluid intake. Participant can not void during this time. If the participant can not hold urine and more than one void occur between 9:00 and 10:00 am, pool and save all urine for accurate volume total and to obtain a representative urine sample (U0)

-Do not give participant cold water at any time due to vasoconstriction. Drinking of water to be completed by 10:00 a.m.

Time at the end of drinking water: _____:_____ a.m. Note mls of water taken _____ ml.

_____17. Name of Nurse performing GFR: _____

_____18. **09:55 AM**

-Have Participant empty bladder to begin GFR Test. **Save urine.**

-From this urine will obtain **U0** (initial urine = Urine collected before Iothalamate Injection).

U0 - Time Void ENDED (U0): _____:____ a.m. (record the time participant returns after voiding)
If more than one void and urine is pooled, the collection time will be the time of last void.

_____19. Prepare Injection of Iothalamate (during the time participant is voiding to get Uo)

Note: The arm with the BEST venous access was used for venipuncture. Iothalamate (Conray® 60%), is injected into the OPPOSITE arm.

For participants >40 kg, a dose of 300 mg (0.5 ml) of Iothalamate Meglumine (Conray® 60%), mixed with 0.5 ml Sterile Water is given subcutaneously (SQ).

-With a 1-ml Tuberculin Syringe, **draw up 0.5 ml of Iothalamate**. **Add 0.5 ml of sterile Bacteriostatic Water.**

-This mixture will be **injected SQ** at 10:00 am into the arm OPPOSITE the arm that is selected for blood drawing.

Iothalamate Vials are for single dose use ONLY. Discard unused VIAL portion.

Iothalamate Lot# _____ Exp Date_____

Sterile Water Lot# _____ Exp Date_____

Initials

_____20. **10:00 AM**
Injection of Iothalamate**: Dose:**_____

Time: _____:_____ a.m.: Subcutaneous Injection of Iothalamate Meglumine.

Use POSTERIOR aspect of UPPER ARM. Gently pinch skin, insert needle, release skin, (draw back to make certain not in vessel), and inject Iothalamate.
Deltoid Injection Site: _____ Right; _____ Left

_____21. From the urine just saved, Aliquot 5 ml of urine into screw-top polypropylene tube. Label container U0 with the Participant's initials, 6-digit CRISP Subject ID #, date of collection, time of collection, sample (i.e. U0), Control Number (obtain from short Renal clearance form), Principal Investigator's name (Guay-Woodford) and site (UAB). Discard remainder of urine.
_____GCRC LAB Urine sample (Uo) Keep the above aliquot (5 ml of urine in the clear tube labeled U0) **refrigerated**. Teresa Chacana, RN will ship the sample the same day at refrigerate temperature.

_____22. Instruct participant to drink (**11/4 - 21/2) 8 oz glasses of water** (300-600mls) to maintain urine output. (The amount of water may be less if the participant is under physician orders to restrict fluid intake). Do not give participant cold water at any time due to vasoconstriction. **Do not void until 60 minutes after injection**.
Amount of water taken: _____ ml

_____23. **11:00 AM**
Have Participant empty bladder as completely as possible. Participant may need to go bathroom more than one time to obtain the **Ue: equilibration urine = Urine collected 60 minutes (+ or – 5 min.) after Iothalamate Injection**.

NOTE: please accurately record all urine volumes & times void ended (if urine is pooled from more than one void), as well as each ultrasound reading of residual urine.

_____24. Use the ultrasound monitor /bladder scan to assess bladder and record residual.
If average residual bladder volume is greater than 20 ml, have Participant immediately void again. (SECOND VOID). If the bladder residual volume still is > 20 ml, extend the Equilibration Period for 5 minutes and have participant void again) (THIRD VOID). Measure all urine, add the 2nd & 3rd voids, if done, to ensure that Flow Rate is >3ml/min.

(Bladder Ultrasound should be done within 1 – 2 minutes after voiding).

Time Void	Scan #1	Scan #2	Scan #3	Scan #4		

RN Initials

_____25. **Ue Collection Time_____:_____am (record the time participant returns after voiding)**
If more than one void and urine is pooled, the collection time will be the time of last void. Discard this urine, no aliquot at this time.

_____26. **Total Ue Volume _____ (ml)** **Flow (ml/min) _____.___**
*Flow is rounded to 2 places behind the decimal
Urine flow rate must be equal to or greater than 3 ml per minute. If the flow rate does not meet this criterion, THE TEST MUST BE RESCHEDULED (see GFR checklist, p.9)

_____27. **11:05 AM**
P1 = Plasma collected immediately after collecting Ue
Do P1 within 5 minutes maximum of the time the Ue void ended at (Ue collection time)
Tourniquet time MUST be LESS than 1 min.
Blood draw from opposite arm of Iothalamate Injection.

Tourniquet used ___yes ___no Time left on ____:____ Seconds

Label container P1 with the Participants 6-digit CRISP Subject ID #, date of collection, time of collection, sample (i.e. P1), control number, and Principal Investigator's (PI) name and site (UAB).

_____28. **Plasma (P1) Collection Time: _____:_____a.m. 3 ml - into 5 ml GREEN-top tube**

_____GCRC LAB Blood sample (P1)-Green top tube with at least 3 ml plasma centrifuge at 3000 rpm for10 min. Aliquot 3 ml serum into the clear tube labeled P1. **Keep refrigerated**. Teresa Chacana, RN will ship the sample the same day at refrigerated temperature.

_____ 29. **Instruct participant to drink (11/4 - 21/2) 8 oz glasses of water** (300-600mls) to maintain output. (The amount of water may be less if the participant is under physician orders to restrict fluid intake). Do not give participant cold water at any time due to vasoconstriction. **Do not void until 45 minutes after Ue.**

Amount of water taken: _____ml.

_____30. **11:45 AM**
Have Participant empty bladder as completely as possible. Participant may need to go bathroom more than one time to obtain the **U1 (GFR testing urine) = All urine collected for at least 45 minutes (but no more than 90 minutes) after Ue. It should be at least 100 ml.**

NOTE: please accurately record all urine volumes (first, second & third voids) & times void ended, as well as each ultrasound reading of residual urine.

RN Initials

_____31. Do Ultrasound readings of bladder and record residual.

(Bladder Ultrasound should be done within 1 – 2 minutes after voiding).

Time Void	Scan #1	Scan #2	Scan #3	Scan #4		

(If average residual bladder volume is > than 20 ml, have Participant void again immediately. (2nd Void)) If the bladder volume still is > 20 ml. Extend the collection period for 15-30 minutes (always < 90 min. total) and have Participant void again (3rd Void). It is imperative that the bladder is as empty as possible. If more than one void, pool and save all urine for accurate volume total and to obtain a representative urine sample. Collection time will be the time of last void.

_____32. **U1 Collection time _____:_____ a.m. (record the time participant returns after voiding)**
If more than one void and urine is pooled, the collection time will be the time of last void.

_____33. **U1 Collection Volume: _____ ml**

Duration_____ (min) = Flow (ml/min) _____._____
*Flow is rounded to 2 places behind the decimal.

Urine Flow Rate must be equal to or greater than 3 ml per minute. If the flow rate does not meet this criterion, THE TEST MUST BE RESCHEDULED. (See GFR checklist, p.9)

_____34. From the urine just saved: U1 - Aliquot 5 ml urine into a screw-top polypropylene tube. Discard remainder.
Label container U1 with the Participants 6-digit CRISP Subject ID #, date of collection, time of collection, sample (i.e. U1), Control Number, and Principal Investigator's (PI) name.
_____ **GCRC** LAB Urine sample: (U1) Keep the above aliquot (5 ml of urine in the clear tube labeled U1) **refrigerated.** Teresa Chacana, RN will ship the sample the same day at refrigerate temperature.

RN Initials

_____35. **U1 COLLECTION DURATION= _____minutes. This is the time difference, in minutes, from Ue** (Equilibration Urine) **to U1** (GFR testing Urine)

PLEASE NOTE:
Of primary concern is the time differentiation recorded on the GFR form from UE to U1. (Double-check math for the time difference). It is extremely important that the time of urine collection is absolutely accurate. The collection times recorded for Ue and U1 should exactly reflect the time the participant ENDED the void.

_____36. **11:50 AM**
P2 = Plasma collected immediately after collecting U1
Do within 5 minutes maximum of the time the U1void ended at (U1collection time)
Tourniquet time MUST be LESS than 1 min.
Blood draw from opposite arm of Iothalamate Injection.

Tourniquet used ___yes ___no Time left on _____ Seconds

Label container P2 with the Participants 6-digit CRISP Subject ID #, date of collection, time of collection, Sample (sample i.e P2), Control Number, and Principal Investigator's (PI) name and site (UAB).

_____37. **(P2) Collection Time: _____:_____a.m. 3 ml - into 5- ml GREEN-top tube**

GCRC LAB Blood sample (P2) Green top tube with at least 3 ml plasma centrifuge at 3000 Rpm for 10 min. Aliquot 3 ml serum into the clear tube labeled P2. **Keep refrigerated**. Teresa Chacana, RN will ship the sample the same day at refrigerated temperature.

_____38. **After GFR test complete, discontinue Saline lock.**
END RENAL CLEARANCE TEST.

_____39. Make a copy of the Short Renal Clearance Request Form & place it in the patient's chart.

_____40. **12:00 Noon**
Diet (90 mEq Na, Low Cholesterol) Caffeine allowed

_____41. Page Teresa Chacana, RN, UAB Pager #: 6193 prior to dismissal.

_____42. **12:30 PM**
DISMISSAL FROM GCRC **BEFORE 15:00.**

GCRC Protocol #: 1311
IRB #: F070226008

CATEGORIES OF CONTRAST REACTIONS

PLEASE NOTE: Reactions to contrast at the dose used for determination of GFR are extremely rare.

MILD

Nausea; vomiting	Altered taste	Sweats
Cough	Itching	Rash (hives)
Warmth (heat)	Pallor	Nasal stuffiness
Headache	Flushing	Swelling - eyes; face
Dizziness	Chill	
Anxiety	Shaking	

Treatment: Requires close observation, assurance, but usually no medication.

MODERATE

Moderate degree of mild signs/symptoms* and/or systemic symptoms including:

Pulse change	Hypertension	Bronchospasm
Hypotension	Dyspnea-wheezing	Laryngospasm

*Sufficient to be clinically evident

Treatment: Requires prompt recognition, close, careful observation and often treatment, but usually not hospitalization.

SEVERE

Potentially life-threatening, moderate or severe signs/symptoms, e.g., laryngospasm, seizures, pulmonary edema, persistent hypotension, cardiac arrest.

Treatment: Requires prompt recognition and treatment; almost always requires hospitalization.

Nursing Perspective

PLEASE NOTE: Reactions to contrast at the dose used for determination of GFR are extremely rare.
Acute reactions to iodinated contrast media are classified by their severity and their outcome. Three categories commonly used are:

MILD: Nausea and vomiting, headaches, dizziness, anxiety, chills, shaking, mild urticaria, itching, nasal congestion, swelling -- eyes; face

Treatment: Requires close observation, assurance, but usually no medication.
Notify PI or designee
Follow orders per PI's/designee's instructions

MODERATE: more- pronounced degree of mild signs/symptoms, plus diffuse erythema, diffuse hives, transient hypotension, hypertension, bronchospasm, laryngeal edema.

Early signs and symptoms:

1. Diffuse hives --Patient has several hives on face and torso and often complains of itching and discomfort. Also may be associated with sneezing and watery eyes.

2. Erythema - Patient is generally red all over, and may or may not be uncomfortable.

3. Hypotension --If hypotension is a vasovagal response from ureteral compression, pain, or anxiety, the Patient is usually pale, diaphoretic, lightheaded, and nauseated. Patients with erythema that become hypotensive are usually red and puffy but start to look mottled as fluid is redistributed to the interstitial space. These Patients complain of dizziness and state that their "skin feels tight."

4. Hypertension -- Patients present with flushed face, dizziness, and headache.

5. Bronchospasm -- Patients often complain of tightness in the chest, coughing and wheezing along with restlessness and feel the need to sit up.

6. Laryngeal edema -- Patients experiencing moderate symptoms of laryngeal edema will frequently complain that their "throat feels full" and that they are having difficulty swallowing. You may notice hoarseness, wheezing, stridor, or cyanosis.

7. Angina -- Patients complain of chest pain or chest tightness and sometimes shortness of breath. They typically appear anxious.

Sufficient to be clinically evident
Treatment: Requires prompt recognition, close, careful observation and often treatment, but usually not hospitalization.
Notify PI or designee
Follow orders per PI's/designee's instructions

MAJOR (Severe) -- More pronounced degree of moderate signs and symptoms plus convulsions, arrhythmias, pulmonary edema, and cardiac arrest.

1. Pulmonary edema -- Patients will sometimes complain of immediate shortness of breath and will become terribly agitated, diaphoretic and cough pink, frothy sputum or a patient may complain of a vague sense of discomfort and then progress slowly to the state mentioned above.

2. Cardiac arrest -- Patient becomes unresponsive, breathless, and pulseless.

Treatment: Requires prompt recognition and treatment; almost always requires hospitalization.
Notify PI or designee
Follow orders per PI's/designee's instructions

GCRC Protocol #: 1311
IRB #: F070226008

Mrs. Chacana to complete the following Originals Study Forms and to do the Procedures listed:

_____. Registration form (form 2) only at first visit: FV-06
_____. Identification form (form 51) at first visit: FV-06 and update it at FV-08
_____. Symptoms form (form 12)
_____. Physical Findings form (form 11)
_____. Women's OB-GYN form (form 40)
_____. Family History form (form 44)
_____. Biannual Clinic Visit/Meds and Events form (form 28)
  _____Review and list current medicine (at FV-06)
  _____Update list of medicine (at FV-08)
_____. GCRC samples packing and shipping instruction (To be done by Teresa Chacana, RN)
  ____Insure that all specimens are labeled correctly
  ____Put the plasma and urine aliquots into the "Refrigerated Specimens" transport bag with a frozen cold pack inside of box.
  ____Place a copy of the completed requisition form into the outer pocket of the transport bag.
  ____Mail a copy of the completed requisition form to Vickie Kubly, Mayo Clinic in the postage paid return envelope included.
  ____Ship the specimens at refrigerate temperature.
_____. NIDDK Repository at Fisher Bioservices samples packing and shipping instruction. (To be done by Teresa Chacana, RN)
  ____They are to be stored in specimen boxes provided by the repository.
  ____The NIDDK Repository will supply all tubes, labels and shipping materials
  ____Tubes to be shipped refrigerated (on frozen cold packs) to the NIDDK Biosample Repository at Fisher Bioservices on the day of collection, where they will be aliquotted into 1 mL tubes and archived.
_____. NIDDK GENETIC STUDIES samples packing and shipping instruction: (To be done by Teresa Chacana, RN)
  ____They are to be shipped in specimen boxes provided by the NIDDK Genetic Repository (Rutgers University Cell and DNA repository).
  ____Three yellow top tubes are going to be shipped at room temperature in a Safety Mailer.

Notes and Comments:

University of Kansas Flow-Sheets

PROTOCOL #69 CRISP II

FVO6/BASELINE(Year 1) & GFR WORKSHEET

(This in not an official CRISP form. All data must be transferred to the appropriate study forms)

Date of Visit _____/_____/_____ DOB _____/_____/____ Age _____

Name _____

CRISP Study ID Number _____ KU Study ID Number K- _____

KU MRN Number _____ KU Lab Grant# _____

Lab Billing – Grant – 49453640

Ht (cm) _____ (in) _____ Wt (kg) _____ (lb) _____

Must remove shoes & heavy clothing

Temp (C) _____ P _____ R _____

Sitting BPs x3 ***Wait 30 seconds between BPs***

(1)BP _____ (2)BP _____ (3)BP _____

Standing BP x1 **After *standing 3 minutes***

(1)BP _____

_____

Signature/Title

PROCEDURES

- Get all lab labels from study coordinator upon arrival, Review visit lab needs
- Place copy of signed consent in GCRC chart
- VS – Document on Form 11: Current Physical Findings Form
- GCRC Staff to complete forms provided by Study Coordinator.
- Study Coordinator will review all completed forms.

1

LABS

GFR Lab Kit – 2 Urine vials, label UO & U1
- 2 serum vials, label P1 & P2

1 - Potty Hat/Graduated Cylinder
1 – 4.5ml lt.green-top tube
3 – Tiger top serum tube (SST)
3 – Green/Gray top plasma tube (PST)
1 – Urine cup (minimum 60ml needed for CRISP Study)
(total 90ml needed for CRISP & HALT)
2 – Green top Na Heparin tubes

8– 5ml Cryovials
1-2ml white cryovial
1 – 50ml Falcon tube

1 - TB syringe

Labs drawn @ _____ by _____

with ____ G butterfly or ____G IV Cath @ site _____

Urine collected @ _____ by _____

LAB PROCESSING

KU Lab

1 – 5ml lt.green-top tube (creatinine, Na, K, Cl, CO2, total chol, trigly, HDL, LDL)
1 – Urine cup 10 ml fresh urine minimum (albumin, creatinine)
Keep ambient
Label with: Study ID
Grant-xxxx
Date & Time of collection
Complete Req and take to KU lab

Blood Archive

NIDDK Repository:

2 – Tiger top serum tube (SST)
2 – Green/Gray top plasma tube (PST)
Invert SST tube 5 times, Invert PST tube 10 times
Let stand for 30 minutes (PST contains heparin and will not clot)
Centrifuge all tubes within one hour @ 3400 rpm for 15 minutes.
No decanting
Refrigerate, box labeled *CRISP II NIDDK*

Cleveland Clinic (CCF):
1 –Tiger Top (SST) serum tube
Invert 5 times, Let stand for 30 minutes
Centrifuge within one hour @ 3400 rpm for 15 minutes.
Transfer into 5ml cryovial
Place in -80^{0}C Freezer, box labeled *CRISP II CCF*

Fresh Urine Archive
KU MCP-1
1- PST Green/Gray-top tube
Freshly voided urine – minimum 4ml
2 – 5ml Cryovials

Invert PST tube 10 times
Let stand for 30 minutes (PST contains heparin and will not clot)
Centrifuge within one hour @ 3400 rpm for 15 minutes.
Transfer plasma into 5ml cryovial

Aliquot 4ml urine into 5ml cryovial

Attach appropriate labels
Place in -80^{0}C Freezer, box labeled *CRISP II Grantham*

NIDDK Repository:
1 – 50ml Falcon tube
Aliquot urine into 50ml Falcon tube (minimum 30ml)
Place immediately in ice until centrifuged
Centrifuge within 30 minutes @ 2100 rpm for 5 minutes
Using a 1ml pipette - Pipette the 'pellet' (sometime barely visible or even non- visible) from the cone of the tube into a 2ml white cryovial
Pipette 5ml of the remaining urine into each of 6 – 5ml cryovials
Place cryovials in -80^{0}C Freezer, box labeled *CRISP II NIDDK*
Document:
Urine Collection Time _____ AM PM

Total Volume _____ ml

Processing Time _____ AM PM

ICON Urine Pregnancy Test Neg Pos ***If positive, notify Dr Grantham DO NOT CONTINUE W/TEST***

Lot # _____

NA/male NA/Hyst NA/Tubal

Exp Date _____

Document in GCRC Log

GFR Test Labs

Urine UO & U1

2 – 10 ml urine transfer vials
Document time & total collected volume for each time period on GFR worksheet
Aliquot 10 ml urine into appropriate time labeled transfer vial
Refrigerate

Blood/Serum P1 & P2

2 – Green top Na Heparin tubes
2 – 3ml serum transfer vials
Centrifuge green top tubes @ 3200 for 10 min
May wait and spin both together on table top centrifuge
Transfer serum into appropriate time labeled transfer vial
Document time for each time period on GFR worksheet
Refrigerate

GFR Checklist

Does Subject have an allergy to Iodine Yes No
If YES, Are symptoms mild moderate severe
If YES, Specify symptoms _____
If YES, Notify Dr Grantham (pgr 917-7210) **BEFORE** beginning test

____ Verify Participant has NOT voided within last 45-60 minutes
* ***If participant has voided within previous 60 min, note this on the GFR Checklist and CONTINUE with the test***

____ Verify Participant has had six 8-oz glasses of water since lab draw
* Ready pitcher of water at room temp.
* DO NOT give participant COLD water d/t vasoconstriction

____ Verify Fasting/NPO except for fluids (>8 hours)
* Participant is to remain NPO until MRI exams are completed.

____ Verify NO use of soda or caffeine beverages AM of testing

____ Verify NO use of NSAIDS/ASA, antibiotics, diuretics (hydrochlorothiazide) in past 7 days (If YES, notify Dr Grantham **BEFORE** beginning test)

____ List any AM medication participant has taken (see ConMed Form for dosages)

____ Verify clinical stability for testing:
* Absence of fever, viral syndrome, acute pain, diarrhea, etc...
* May use butterfly needle to draw blood samples individually

GFR TEST (kit)

Criteria for Immediate Notification of Principal Investigator

1. Iothalamate allergic reaction
   see GRF Testing Manual, Appendix D, Mayo Medical Laboratories, November 27, 2000 on file in the Study Coordinator's office and in the GCRC
2. Incomplete bladder emptying
3. Continuously low urine output
4. Headache, nausea, diarrhea, or other physical complaints

NOTE Urinary catheter is not approved for this study No radio-isotope is used for this study

Scan bladder PRE-VOIDING to determine location

(UO = Urine collection before injection)
Void to begin Renal Clearance Test.
Have participant empty bladder as completely as possible, residual must be <20 ml

UO : Time Void ENDED _____AM PM Urine volume _____mls
(record in clock time)

: **Aliquot 10 ml** urine into the white transfer tube and label as **"UO"**
: **Discard remaining urine**
: **Scan bladder x3**
1. _____mls 2. _____mls 3. _____mls
: **UO Avg Residual Bladder Volume _____mls** (**MUST** be <20mls)
If residual bladder volume is >20mls, have participant void again and recheck,
Record both sets of readings on this worksheet.
1. _____mls 2. _____mls 3. _____mls
These measurements are not recorded on the CRF

Have participant drink one to two, 8-oz glasses of water to maintain urine output. Water is to be of room temperature. Cold water may cause vasoconstriction. Provide blankets to prevent chilling and vasoconstriction.

Iothalamate Injection

NOTE ***Inject Iothalamate in the OPPOSITE arm selected for blood draws***

:Time of injection _____
(record in clock time)
:Subcutaneous injection site R L
Use POSTERIOR aspect of UPPER ARM.
Administered by _____
:Dose: 0.5 ml Iothalamate Meglumine (300 mg) mixed with 0.5 ml Sterile Bacteriostatic Water. NOTE: Participants >40 kg all receive the same dose of Iothalamate.
Iothalamate Lot# _____ Exp Date_____
Sterile Water Lot# _____ Exp Date_____
Iothalamate & Sterile Water are found in the locked GCRC Med Cabinet
Vials are for single use ONLY. Discard unused portion

Equilibration time 60 minutes (set timer) after injection

(UE = Urine collected 60 minutes after injection)

Have participant empty bladder as completely as possible.

UE : Time Void Ended _____AM PM Urine volume _____mls
(record in clock time)

: Discard Urine. NO aliquot at this time.

: Scan bladder X3

1. _____ml 2. _____ ml 3. _____ml

: UE Average Residual Bladder Volume _____ml (MUST **be <20 mls)**

If **average** residual bladder volume is >20mls, have participant void again. If the bladder volume is still >20 mls, extend the equilibration period for **10 minutes** and have participant void again. Make a notation on the worksheet and forms.

NOTE Be sure bladder is empty. Average residual bladder volume should be <20 mls. In some situations, <10% of voided volume, but no greater than 50mls, is acceptable

(P1. = Plasma collected immediately after collecting UE)

Blood MUST be drawn within 5 minutes max.

If a tourniquet is used, time **MUST be <1 minute**

P1.: Collection Time _____AM PM Tourniquet time _____ minutes
(record in clock time) (if used record time, if not used NA)

Blood drawn from IV Cath or with _____G butterfly @ site _____

: Collect 5 ml blood in 10 ml green-top tube

: Centrifuge @ 3200 rpm for 10 minutes

: Aliquot serum into white serum transfer tube and label "P1."

Have participant drink one to two, 8-oz glasses of water to maintain urine output. Water is to be of room temperature to prevent vasoconstriction. Keep participant warm.

Continue equilibration time for another 45 minutes after UE.

(U1. = Urine collected for a least 45 minutes after UE)
Have participant empty bladder as completely as possible
Must be at least 45 minutes after UE and no longer than 90 minutes (a minimum of 100mls of urine is required between UE and U1.)

NOTE If more than one void, pool and save all urine for accurate volume total and to obtain a representative urine sample.

U1. : Time Void Ended _____AM PM Urine volume _____mls
(record in clock time)

: **Aliquot 10 ml** urine in white transfer tube and label **"U1."**

: **Scan bladder X3, average and record**

1. _____ml 2. _____ml 3. _____ml

: **U1. Average Residual Bladder Volume: _____ ml**

If **average** residual bladder volume is >20 mls or participant has voided <100 mls, have participant void again. If the residual volume is still >20 mls or participant has voided <100, extend the test for **30 minutes** and have participant void again

NOTE Be sure bladder is empty. Average residual bladder volume should be <20 mls. In some situations, <10% of voided volume, but no greater than 50 mls is acceptable.

(P2. = Plasma collected immediately after collecting U1.)
Blood MUST be drawn within 5 minutes max.
If a tourniquet is used, time **MUST be <1 minute**

P2. : Collection Time _____AM PM **Tourniquet time _____ minutes**
(record in clock time) (If used record time, if not used NA)

Blood drawn from IV Cath or with _____G butterfly @ site _____

: **Collect 5 ml blood in 10 ml green-top tube**
: **Centrifuge @ 3200 for 10 minutes**
: **Aliquotserum into white serum transfer tube and label "P2."**

RECORD ALL DATA ON THE GFR TEST FORM
GFR TEST IS COMPLETED

Keep participant NPO until after MRI. May drink water/juice moderately.

GFR Test completed by _____
Signature/Title

GFR Test Worksheet checked by _____
Study Coordinator Signature/Title

Study Coordinator Information

____ Complete GFR Shipping Container
* Ice Pack wrapped in disposable cloth to prevent freezing specimens

____ * Serum tubes X2, labeled with
* CRISP P1 or P2
* Study ID xxxxxx
* Green label/Control number
* Date of collection
* Site Kansas

____ * Urine containers X2, labeled with
* CRISP U0 or U1
* Study ID# xxxxxx
* Green label/Control number
* Date of collection
* Site Kansas

Place above labs in bag and insert GFR Req Form and GFR Checklist in pocket

_____Fill out and attach **Fed Ex** mailing form

* Mayo Medical Laboratories Ph 800-533-1710
200 First Street SW
Rochester, MN 55905
Payment bill to Mayo's Fed Ex Account # 11303722-9

____ Take GFR shipping container to the shipping dock **BEFORE** 3pm

MRI Exam

Reception x8-1830 Fax x8-1845
Call if going to be late

____ Upon arrival to MR, Check participant in at desk
* Have MR **Req/Form 433** filled out
* Obtain copy of patient signed KUMC HIPAA form & place in study chart

GRANT BILLING # 49453640 *** DO NOT BILL TO PARTICIPANT**

____ Participant should void prior to exam
____ Review breath holding instructions

PARTICIPANT HAS COMPLETED THE CRISP STUDY VISIT

Participant may resume normal diet and activities

Upon return to Office

____ Fax MRI series form to Larry, AFTER the form has been entered in WDES. Fax# 87876

____ Fax Shipment Alert Form to MML Fax# 1-507-284-1790
(fax from KUKI office)

Beth	office x87609 cell 913-634-1771 hm 913-829-3416	Larry	office x8-7869 (no pgr)
		MRI	office x8-1830, Techs x8-1835

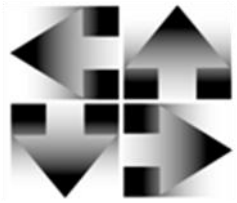
Dr's

Grantham, PI pgr 917-7210
cell 913-486-6058
hm 913-338-3878
office x87605

Winklhofer pgr 917-1734

Wetzel pgr 917-6412

Consortium for Radiologic Imaging Studies of
Polycystic Kidney Disease



CRISP II STUDY
ADDRESS DIRECTORY

October 2007

Prepared by:
Data Coordinating Image Analysis Center
University of Pittsburgh
Pittsburgh, PA 15213
(412) 641-2328

CRISP II Study Address Directory

DIRECTORY TABLE OF CONTENTS

National Institute of Diabetes and Digestive and Kidney Diseases
Bethesda, Maryland

MEYERS, Catherine M., MD
Director, Inflammatory Renal Disease Programs
NIH – NIDDK
2 Democracy Plaza – Room 641
6707 Democracy Boulevard
Bethesda, MD 20892-5458

Telephone: (301) 594-7717
Fax: (301) 480-3510
email: meyersc@extra.niddk.nih.gov

MOEN, Laura K., PhD
Program Official
NIH – NIDDK
2 Democracy Plaza, Room 605
6707 Democracy Blvd.
Bethesda, MD 20892

Telephone: (301) 594-7717
Fax: (301) 480-3510
email: moenl@niddk.nih.gov

External Advisory Committee
Consortium for Radiological Imaging Studies of Polycystic Kidney Disease, Phase II

BLUEMKE, David A., MD, PhD
Clinical Director, MRI
Russel H. Morgan Dept. of Radiology
Johns Hopkins Medical Institutions
Bethesda, MD 21287
Telephone: (410) 955-4062
Fax: (410) 955-9799
email: dbluemke@jhmi.edu

FELDMAN, Harold., MD, MSCE
Director,
Clinical Epidemiology and Biostatistics
Associate Professor of Medicine and Epidemiology
Renal-Electrolyte and Hypertension Division
University of Pennsylvania
720 Blockey Hall
423 Guardian Drive
Telephone: (215) 898-0901
Fax: (215) 898-0643
email:njones@cceb.med.ipenn.edu

FREEMAN, Katherine, PhD (Chairman)
Director, Biostatistics
Montefiore Medical Center
111 East 210th Street
Bronx, NY 10467
Telephone: (718) 231-6704
Fax: (718) 515-8514
email: Kfreeman@montefiore.org

POLLAK, Martin, MD
Brigham & Women's Hospital
Department of Medicine
77 Ave. Louis Pasteur, HIM543
Boston, MA 02115
Telephone: (617) 525-5840
Fax: (617) 525-5841
email: mpollak@rics.bwh.harvard.edu

WATNICK, Terry J., MD
Johns Hopkins Univ. School of Medicine
Nephrology Division
720 Rutland Ave.
Ross 954
Baltimore, MD 21205
Telephone: (410) 614-1650
Fax:
email: twatnick@jhmi.edu

Steering Committee

	Phone	Fax
Chairman William M. Bennett, MD	(503) 413-7349	(503) 413-6563
K. Ty Bae, MD, PhD	(412) 383-1980	(412) 383-2306
James E. Bost, MS, PhD	(412) 246-6932	(412) 246-6954
Arlene B. Chapman, MD	(404) 686-8280	(404) 686-8299
Jared J. Grantham, MD	(913) 588-7605	(913) 588-9251
Peter C. Harris, PhD	(507) 266-0541	(507) 266-3774
Catherine M. Meyers, MD	(301) 594-7717	(301) 480-3510
Laura K. Moen, PhD	(301) 594-7717	(301) 480-3510
Michal Mrug, MD	(205) 975-6129	(205) 975-5689
Vicente E. Torres, MD, PhD	(507) 284-0944	(507) 266-7891

Chairman William M. Bennett, MD	bennettw@lhs.org
K. Ty Bae, MD, PhD	baek@upmc.edu
James E. Bost, MS, PhD	bostje@upmc.edu
Arlene B. Chapman, MD	arlene.chapman@emoryhealthcare.org
Jared J. Grantham, MD	jgrantha@kumc.edu
Peter C. Harris, PhD	harris.peter@mayo.edu
Catherine M. Meyers, MD	meyersc@extra.niddk.nih.gov
Laura K. Moen, PhD	moenl@niddk.nih.gov
Michal Mrug, MD	mmrug@uab.edu
Vicente E. Torres, MD, PhD	torres.vicente@mayo.edu

Ancillary Studies Committee

	Phone	Fax
Chairman Jared J. Grantham, MD	(913) 588-7605	(913) 588-9251
K. Ty Bae, MD, PhD	(412) 383-1980	(412) 383-2306
James E. Bost, MS, PhD	(412) 246-6932	(412) 246-6954
Arlene B. Chapman, MD	(404) 686-8280	(404) 686-8299
Catherine M. Meyers, MD	(301) 594-7717	(301) 480-3510
Vicente E. Torres, MD, PhD	(507) 284-0944	(507) 266-7891

	Email Addresses
Chairman Jared J. Grantham, MD	jgrantha@kumc.edu
K. Ty Bae, MD, PhD	baek@upmc.edu
James E. Bost, MS, PhD	bostje@upmc.edu
Arlene B. Chapman, MD	arlene.chapman@emoryhealthcare.org
Catherine M. Meyers, MD	meyersc@extra.niddk.nih.gov
Vicente E. Torres, MD, PhD	torres.vicente@mayo.edu

Clinical Committee

	Phone	Fax
Chairman Arlene B. Chapman, MD	(404) 686-8280	(404) 686-8299
James E. Bost, MS, PhD	(412) 246-6932	(412) 246-6954
Jared J. Grantham, MD	(913) 588-7605	(913) 588- 9251
Michal Mrug, MD	(205) 975-6129	(205) 975-5689
Vicente E. Torres, MD, PhD	(507) 284-0944	(507) 266-7891

	Email Addresses
Chairman Arlene B. Chapman, MD	arlene.chapman@emoryhealthcare.org
James E. Bost, MS, PhD	bostje@upmc.edu
Jared J. Grantham, MD	jgrantha@kumc.edu
Michal Mrug, MD	mmrug@uab.edu
Vicente E. Torres, MD, PhD	torres.vicente@mayo.edu

Data Management and Quality Control Committee

	Phone	Fax
Chairman James E. Bost, MS, PhD	(412) 246-6932	(412) 246-6954
K. Ty Bae, MD, PhD	(412) 383-1980	(412) 383-2306
William M. Bennett, MD	(503) 413-7349	(503) 413-6563
Jared J. Grantham, MD	(913) 588-7605	(913) 588-9251
Johana Schafer, MS	(412) 641-2328	(412) 641-2582

	Email Addresses
Chairman James E. Bost, MS, PhD	bostje@upmc.edu
K. Ty Bae, MD, PhD	baek@upmc.edu
William M. Bennett, MD	bennettw@lhs.org
Jared J. Grantham, MD	jgrantha@kumc.edu
Johana Schafer, MS	schaferj@upmc.edu

Forms Committee

	Phone	Fax
Chairman Arlene B. Chapman, MD	(404) 686-8280	(404) 686-8299
Jared J. Grantham, MD	(913) 588-7605	(913) 588-9251
Teresa Chacana, RN, BSN, CPN	(205) 934-7649	(205) 975-0814
Yoosun Han	(404) 727-3845	(404) 727-3425
Vickie Kubly	(507) 266-9207	(507) 255-0770
Johana Schafer, MS	(412) 641-2328	(412) 641-2582
Beth Stafford, RN	(913) 588-7609	(913) 588-7606

	Email Addresses
Chairman Arlene B. Chapman, MD	arlene.chapman@emoryhealthcare.org
Jared J. Grantham, MD	jgrantha@kumc.edu
Teresa Chacana, RN, BSN, CPN	tchacana@uab.edu
Yoosun Han	yhan2@emory.edu
Vickie Kubly	Kubly.vickie@mayo.edu
Johana Schafer, MS	schaferj@upmc.edu
Beth Stafford, RN	bstafford@kumc.edu

Genetics Committee

	Phone	Fax
Chairman Peter C. Harris, PhD	(507) 266-0541	(507) 266-3774
James E. Bost, MS, PhD	(412) 246-6932	(412) 246-6954
Arlene B. Chapman, MD	(404) 686-8280	(404) 686-8299
Jared J. Grantham, MD	(913) 588-7605	(913) 588-9251
Lisa M. Guay-Woodford, MD	(205) 934-7308	(205) 975-5689
Catherine M. Meyers, MD	(301) 594-7717	(301) 480-3510
Vicente E. Torres, MD, PhD	(507) 284-0944	(507) 266-7891

	Email Addresses
Chairman Peter C. Harris, PhD	harris.peter@mayo.edu
Bost, James E. MS, PhD	bostje@upmc.edu
Arlene B. Chapman, MD	arlene.chapman@emoryhealthcare.org
Jared J. Grantham, MD	jgrantha@kumc.edu
Lisa Guay-Woodford, MD	lgw@uab.edu
Catherine M. Meyers, MD	meyersc@extra.niddk.nih.gov
Vicente E. Torres, MD, PhD	torres.vicente@mayo.edu

Imaging Committee

	Phone	Fax
Chairman K. Ty Bae, MD, PhD	(412) 383-1982	(412) 383-2306
Bernard F. King, MD	(507) 538-1200	(507) 284-9245
Mark E. Lockhart, MD	(205) 934-7130	(205) 975-7213
Diego R. Martin, MD, PhD	(404) 778-3800	(404) 778-3080
Louis H. Wetzel, MD	(913) 588-7894	(913) 588-7899

	E-mail Addresses
Chairman K. Ty Bae, MD, PhD	baek@upmc.edu
Bernard F. King, MD	bfking@mayo.edu
Mark E. Lockhart, MD	mlockhar@uab.edu
Diego R. Martin, MD, PhD	diego_martin@emory.org
Louis H. Wetzel, MD	lwetzel@kumc.edu

Publications Committee

	Phone	Fax
Chairman Vicente E. Torres, MD, PhD	(507) 284-0944	(507) 266-7891
James E. Bost, MS, PhD	(412) 246-6932	(412) 246-6954
Arlene B. Chapman, MD	(404) 686-8280	(404) 686-8299
Jared J. Grantham, MD	(913) 588-7605	(913) 588-9251
Catherine M. Meyers, MD	(301) 594-7717	(301) 480-3510

	Email Addresses
Chairman Vicente E. Torres, MD, PhD	torres.vicente@mayo.edu
James E. Bost, MS, PhD	bostje@upmc.edu
Arlene Chapman, MD	arlene.chapman@emoryhealthcare.org
Jared J. Grantham, MD	jgrantha@kumc.edu
Catherine M. Meyers, MD	meyersc@extra.niddk.nih.gov

Data Coordinating Image Analysis Center
University of Pittsburgh
Pittsburgh, Pennsylvania

BAE, K. Ty, MD, PhD
Principal Investigator
University of Pittsburgh
3362 Fifth Avenue
Pittsburgh, PA 15213
Telephone: (412) 641-2657
Fax: (412) 641-2582
email: baek@upmc.edu

BOST, James E., MS, PhD
Co-Investigator
University of Pittsburgh
Data Center, Center for Research on Health Care
200 Meyran Avenue, Suite 200
Pittsburgh, PA 15213
Telephone: (412) 246-6932
Fax: (412) 246-6954
email: bostje@upmc.edu

BRAGG, Tim
Systems Analyst
University of Pittsburgh
Data Center, Center for Research on Health Care
200 Meyran Avenue, Suite 200
Pittsburgh, PA 15213
Telephone: (412) 692-4898
Fax: (412) 586-9672
email: braggtj@upmc.edu

CHANG, Samuel
Research Associate
University of Pittsburgh
3362 Fifth Avenue
Pittsburgh, PA 15213
Telephone: (412) 641-2591
Fax: (412) 641-2582
email: changs@upmc.edu

SCHAFER, Johana, MS
Project Coordinator
University of Pittsburgh
3362 Fifth Avenue
Pittsburgh, PA 15213
Telephone: (412) 641-2328
Fax: (412) 641-2582
email: schaferj@upmc.edu

SEFCIK, Terry, MSIS
Systems Analyst
University of Pittsburgh
Data Center, Center for Research on Health Care
200 Meyran Avenue, Suite 200
Pittsburgh, PA 15213
Telephone: (412) 692-4851
Fax: (412) 246-6954
email: sefcikth@upmc.edu

SIAN, Layla S.
Systems Analyst
University of Pittsburgh
Data Center, Center for Research on Health Care
200 Meyran Avenue, Suite 200
Pittsburgh, PA 15213
Telephone: (412) 692-2693
Fax: (412) 586-9672
email: sianls@upmc.edu

TAO, Cheng, MD
Telephone: (412) 641-2671

Research Associate
University of Pittsburgh
3362 Fifth Avenue
Pittsburgh, PA 15213

Fax: (412) 641-2582
email: taoc@upmc.edu

Data Coordinating Image Analysis Center
University of Pittsburgh
Pittsburgh, Pennsylvania
(continue)

WANG, JinHong, MD
Research Associate
University of Pittsburgh
3362 Fifth Avenue
Pittsburgh, PA 15213

Telephone: (412) 641-2590
Fax: (412) 641-2582
email: wangj4@upmc.edu

Data Coordinating Image Analysis Center
Washington University
St. Louis, Missouri

COMMEAN, Paul K., BEE
Imaging Project Manager
Mallinckrodt Institute of Radiology
4525 Scott Avenue, Suite 3361
St. Louis, MO 63110

Telephone: (314) 362-8497
Fax: (314) 362-6971
email: commeanp@mir.wustl.edu

GAINES, Mary Virginia, BS
Imaging Project Coordinator
Mallinckrodt Institute of Radiology
4525 Scott Avenue, Suite 3337
St. Louis, MO 63110

Telephone: (314) 362-2962
Fax: (314)362-7259
email: gainesm@mir.wustl.edu

VENDT, Bruce
Systems Manager
Mallinckrodt Institute of Radiology
4525 Scott Avenue, Suite 3338
St. Louis, MO 63110

Telephone: (314) 362-1882
Fax: (314) 362-6971
email: vendtb@mir.wustl.edu

Participating Clinical Center
Emory University
Atlanta, Georgia

CHAPMAN, Arlene B., MD
Principal Investigator
Department of Medicine-Nephrology
Emory University School of Medicine
WMB 338
1639 Pierce Drive
Atlanta, GA 30322

Telephone: (404) 686-8280
Fax: (404) 686-8299
email: arlene.chapman@emoryhealthcare.org

MARTIN, Diego R., MD, PhD
Department of Radiology
Emory University Hospital
Building A, AT622
1365 Clifton Road, NE
Atlanta, GA 30322

Telephone: (404) 778-3800
Fax: (404) 778-3080
email: diego_martin@emory.org

RAHBARI-Oscoui, Frederic, MD
Renal Division, Department of Medicine
Emory University School of Medicine
101 Woodruff Circle, Suite 338
Atlanta, GA 30322

Telephone: (404) 727-2590
Fax: (404) 727-3425
email: frahbar@emory.edu

HAN, Yoosun
Study Coordinator
Emory University School of Medicine
Woodruff Memorial Research Building
Suite 338
101 Woodruff Circle
Atlanta, GA 30322

Telephone: (404) 727-3845
Fax: (404) 727-3425
email: yhan2@emory.edu

WATKINS, Diane
Study Coordinator
Emory University School of Medicine
Center for Hypertension and Renal Disease
Crawford W. Long Hospital
550 Peachtree Street NE
Atlanta, GA 30308-2225

Telephone: (404) 712-1354
Fax: (404) 686-8299
email: dpwatki@emory.edu

Participating Clinical Center
University of Kansas
Kansas City, Kansas

GRANTHAM, Jared J., MD
Principal Investigator
Kidney Institute-6018 WHE
University of Kansas Medical Center
3901 Rainbow Blvd.
Kansas City, KS 66160

Telephone: (913) 588-7605
Fax: (913) 588-9251
email: jgrantha@kumc.edu

WINKLHOFER, Franz, MD
Co-Investigator
Kidney Institute
University of Kansas Medical Center
4015 Sudler Building
3901 Rainbow Blvd.
Kansas City, KS 66160

Telephone: (913) 588-7609
Fax: (913) 588-7606
email: fwinklho@kumc.edu

WETZEL, Louis H., MD
Co-Investigator
University of Kansas Medical Center
Department of Radiology
3901 Rainbow Blvd.
Kansas City, KS 66160-7234

Telephone: (913) 588-7894
Fax: (913) 588-7899
email: lwetzel@kumc.edu

STAFFORD, Beth, RN
Study Coordinator
University of Kansas Medical Center
4015 Sudler Building
3901 Rainbow Blvd.
Kansas City, KS 66160-7382

Telephone: (913) 588-7609
Fax: (913) 588-7606
email: bstafford@kumc.edu
Pager: (913) 917-2810

LANZA, Pam, RN
Study Coordinator
University of Kansas Medical Center
4015 Sudler Building
3901 Rainbow Blvd.
Kansas City, KS 66160

Telephone: (913) 588-8983
Fax: (913) 588-7606
email: planza@kumc.edu

Participating Clinical Center
Mayo Clinic
Rochester, Minnesota

TORRES, Vicente E., MD, PhD
Principal Investigator
Mayo Clinic
Department of Internal Medicine-Nephrology
Eisenberg Building – S 24
200 First Street SW
Rochester, MN 55905

Telephone: (507) 266-7093
Fax: (507) 266-7891
email: torres.vicente@mayo.edu

KING, Bernard F., MD
Co-Investigator
Department of Radiology
Mayo Clinic
200 First Street SW
Rochester, MN 55905

Telephone: (507) 538-1200
Fax: (507) 284-9245
email: bfking@mayo.edu

GLOCKNER, James F., MD, PhD
Radiologist
Mayo Clinic
Department of Radiology
Old Marion Hall 1, Radiology
200 First Street SW
Rochester, MN 55905

Telephone: (507) 266-3350
Fax: (507) 255-4068
email: glockner.james@mayo.edu

HARRIS, Peter C., PhD
Division of Nephrology, Stabile 7
Mayo Clinic
200 First Street
Rochester, MN 55905

Telephone: (507) 266-0541 or
(507) 255-3774
Fax: (507) 266-9315
email: harris.peter@mayo.edu

KUBLY, Vickie
Study Coordinator
Department of Nephrology
Mayo Clinic
200 First Street, SW
Eisenberg S-33J
Rochester, MN 55905

Telephone: (507) 266-9207
Fax: (507) 255-0770
email: kubly.vickie@mayo.edu

SPENCER, Dorothy
Study Coordinator
Department of Nephrology
Mayo Clinic
200 First Street, SW
Eisenberg S-33G
Rochester, MN 55905

Telephone: (507) 266-3868
Fax: (507) 255-0770
email: spencer.dorothy@mayo.edu

Participating Clinical Center
University of Alabama-Birmingham
Birmingham, Alabama

GUAY-WOODFORD, Lisa M., MD
Principal Investigator
University of Alabama at Birmingham
Kaul Building, Room 740
1530 3rd Avenue South
Birmingham, AL 35294-0024
Telephone: (205) 934-7308
Fax: (205) 975-5689
email: lgw@uab.edu

MRUG, Michal, MD
University of Alabama at Birmingham
Kaul Building, Room 752A
1530 3rd Avenue South
Birmingham, AL 35294-0005
Telephone: (205) 975-6129
Fax: (205) 975-5689
email: mmrug@uab.edu

LOCKHART, Mark E., MD, MPH
Department of Radiology, JTN358
University of Alabama at Birmingham
619 South 19th Street
Birmingham, AL 35294
Telephone: (205) 934-7130
Fax: (205) 975-7213
email: mlockhar@uabmc.edu

CHACANA, Teresa, RN, BSN, CPN
Study Coordinator
University of Alabama at Birmingham
Kaul Building, Room 705
1530 Third Avenue South
Birmingham, AL 35294-0024
Telephone: (205) 934-7649
Fax: (205) 975-0814
email: tchacana@uab.edu

CRISP II Study Electronic Mailing Lists

Last updated October 31, 2007.

CRISP Steering Committee
crispsteer@list.pitt.edu

William M. Bennett
K. Ty Bae
James E. Bost
Arlene B. Chapman
Lisa M. Guay-Woodford
Jared J. Grantham
Peter C. Harris
Catherine M. Meyers
Laura K. Moen
Michal Mrug
Vicente E. Torres
Mary V. Gaines
Johana Schafer

CRISP Coordinators
crispcoord@list.pitt.edu
Teresa Chacana
Yoosun Han
Vickie Kubly
Dorothy Spencer
Beth Stafford
Mary V. Gaines
Johana Schafer

CRISP Imaging Committee
crispimage@list.pitt.edu
K. Ty Bae
James F. Glockner
Bernard King
Mark Lockhart
Diego Martin
Louis Wetzel
Samuel Chang
Cheng Tao
Jinhong Wang
Mary V. Gaines
Johana Schafer

CRISP Genetics Committee
crispgenetics@list.pitt.edu
Peter C. Harris
James E. Bost
Arlene B. Chapman
Lisa M. Guay-Woodford
Jared J. Grantham
Catherine M. Meyers
Vicente E. Torres

All on CRISP Mailing Lists
crispall@list.pitt.edu