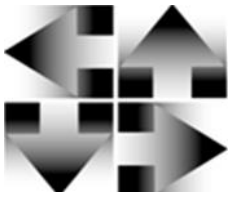

Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) III

MANUAL OF PROCEDURES

March 2012

https://www.crhc.pitt.edu/crispiii

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Chapter 1. Purpose of the CRISP III Manual of Procedures

The purpose of the CRISP III Manual of Procedures (MOP) is to provide study investigators with one all-encompassing source to use as a guide in carrying out CRISP III studies. The CRISP III 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 III 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 III MOP directly from the website, as needed. The Data and Safety Monitoring Board will also have private access to the web-based CRISP III 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.

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 the University of Pittsburgh.

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 III 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.

The goal of CRISP III 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.

2.3.2. 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.

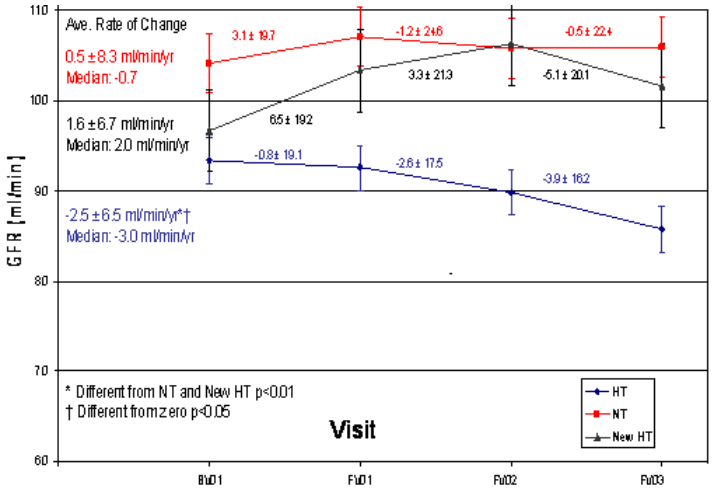


Figure 2.1. GRF by Visit
Annual rate of change in glomerular filtration rate measured by iothalamate renal clearance in normotensive (squares), new hypertensives (triangles) and hypertensives (diamonds) in CRISP I. A significant decline in glomerular filtration rate was found in the hypertensive (-3.0 mL/yr/1.73m^2) subjects that was significantly different from both normotensives and new hypertensives.

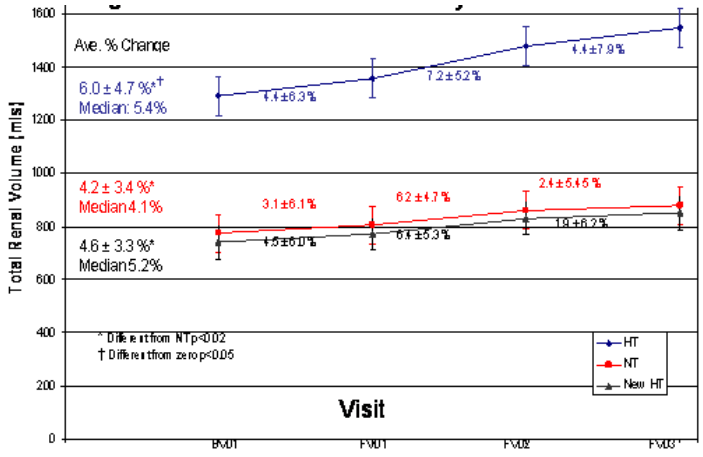


Figure 2.2. Total Renal Volume by Visit
Annual rate of change in renal volume in normotensive (squares), new hypertensives (triangles) and hypertensives (diamonds) in CRISP I. A significant increase in renal volume from baseline was found the hypertensive subjects and a significantly greater rate of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

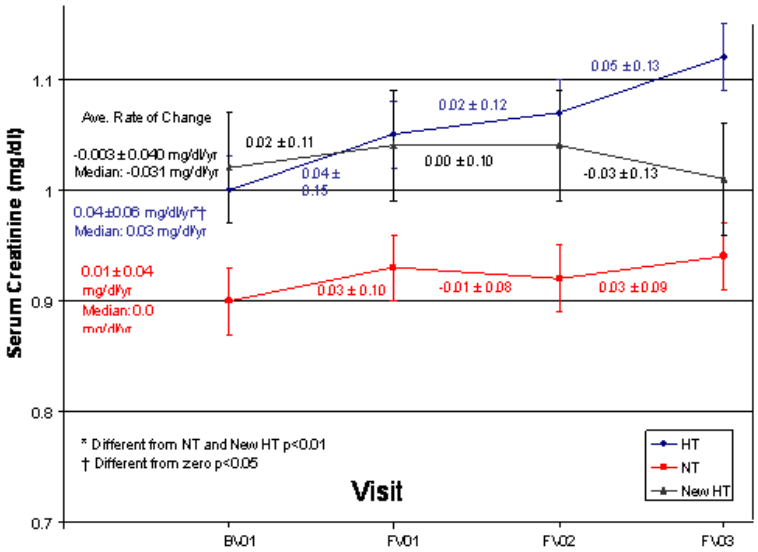


Figure 2.3. Serum Creatinine by Visit
Annual serum creatinine levels in normotensive (squares), new hypertensives (triangles) and hypertensives (diamonds) in CRISP I. The average annual rate of change was significantly increased only in the subjects who were hypertensive at baseline.

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.

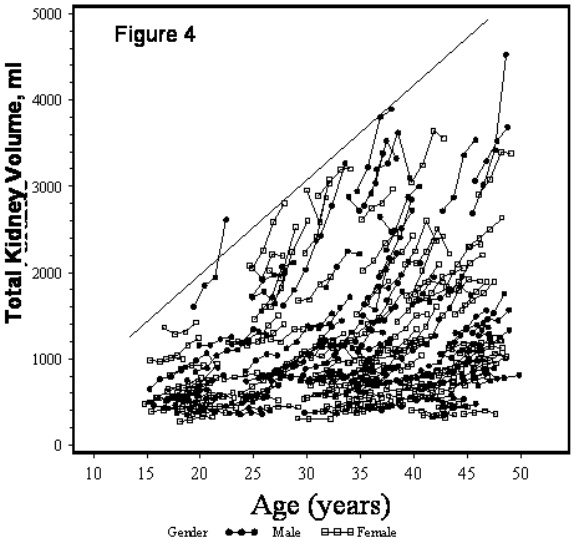


Figure 2.4. Time-course plot of TKV growth curves.

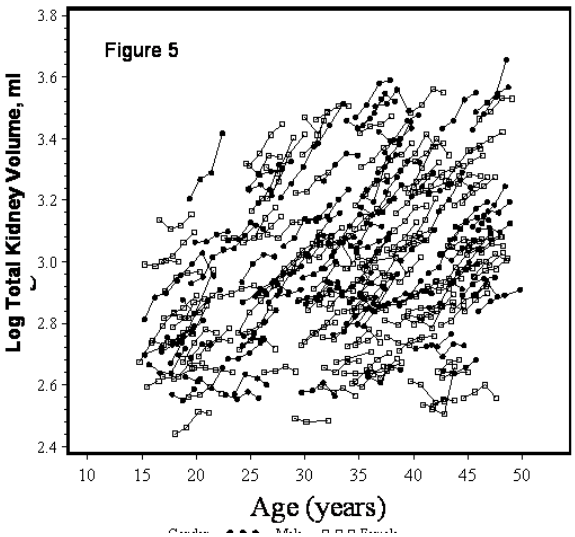
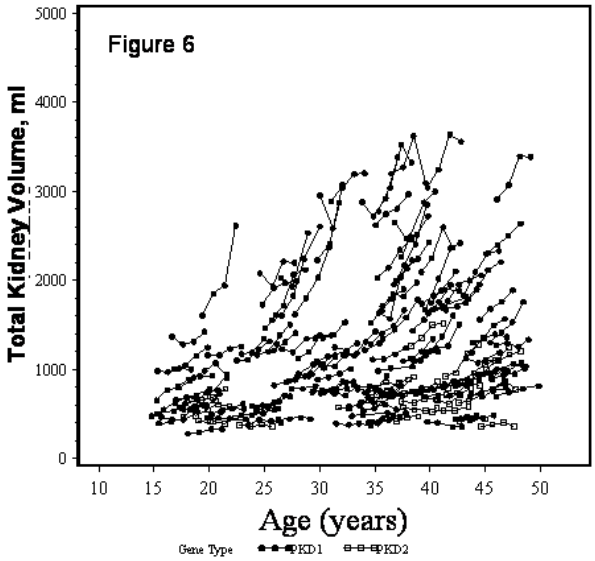


Figure 2.5. Time-course plot of TKV growth curves.

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.

2.5. CRISP III Study: Overview and Specific Aims

2.5.1. Overview of Study Design

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.

CRISP is a uniquely characterized population of 241 ADPKD patients on which comprehensive clinical information, MR determined total kidney volume (TKV), liver cyst volume (LCV) and renal blood flow (RBF), and genotyping data are available. Longitudinal follow-up over an average of 7.3 years during CRISP I and II has established the exponential nature of TKV growth, but also illustrated the considerable variability seen within the population. Increasingly, as patients reach renal insufficiency endpoints, the predictive nature of baseline TKV in terms of severity of renal disease and other qualitative complications has been established. The predictive value of RBF has also been suggested.

CRISP III will build on the findings from this unique population with studies to address five specific aims as outlined below. These will further collect and analyze data and develop models to better utilize the predictive nature of TKV, RBF and LCV. The characteristics of individual cysts and the predictive value of the pattern of cyst development will be explored. Genetic and proteomic studies will be facilitated to aid the identification of genetic risk factors and biomarkers, and a pilot study will explore the role of sodium intake in influencing disease severity. The overall goal of this project is to maximize the use of the national resource that is CRISP to improve the predictive value of early imaging and other data, and hence, facilitate clinical trials of this common cause of ESRD.

2.5.2. Specific AIM 1

Extend the serial quantification of total kidney (TKV) and liver (TLV) and of kidney (KCV) and liver cyst (LCV) volumes in order to develop and test new models for predicting the risk of developing renal insufficiency

Hypothesis 1a. Baseline TKV and change in TKV predict loss of kidney function.

Hypothesis 1b. The progression of polycystic liver volume (LCV) will be similar to but distinct from that of TKV; baseline LCV, adjusted for covariates, will independently predict the rate of increase in LCV and complications arising within the liver.

2.5.3. Specific AIM 2

Determine the extent to which age and sex-adjusted measurements of renal blood flow (RBF), determined by MR imaging, predict the rate of change in TKV and determine if RBF and TKV independently predict the risk of developing renal insufficiency.

Hypothesis 2. Baseline RBF predicts the rate of increase in TKV and, independent of and in addition to baseline TKV, predicts renal insufficiency.

2.5.4. Specific AIM 3

Develop methods to quantify total cyst number, individual cyst volumes, and pattern of distribution of cysts in each kidney and apply these to analyze the influence of renal cyst

number, volume, and topography at baseline on the subsequent course of TKV and GFR and the risk of developing renal insufficiency.

Hypothesis 3a. Renal cyst number and volume will be associated with rates of change in TKV and GFR and risk of developing renal insufficiency. These relationships may vary by genotype.

Hypothesis 3b. Renal cyst topography (medullary vs. non-medullary) will be associated with rates of change in TKV and GFR and risk of developing renal insufficiency. These relationships may vary by genotype.

Hypothesis 3c. Individual renal cyst growth is continuous and exponential (similar to the growth pattern in TKV) and patterns of renal cyst growth or involution will be associated with rates of change in TKV and GFR and risk of developing renal insufficiency. These relationships may vary by genotype.

2.5.5. Specific AIM 4

Expand and analyze CRISP biological samples collected in NIDDK repositories to improve genotype/phenotype and biomarker studies, and facilitate independently funded ancillary studies.

Sub-aim 4.1 Collect and analyze DNA samples and clinical data from CRISP family members for enhanced genotype/phenotype studies and to facilitate other genetic studies.

Sub-aim 4.2 In conjunction with the NIDDK Biomarkers Consortium and ongoing ancillary studies utilizing CRISP samples, determine specificity and sensitivity of urinary and serological markers to: 1) detect severity of renal and extra-renal ADPKD manifestations (e.g., TKV and LCV); and 2) predict rates of their progression.

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 Expert Group (EEG) has been formed and reports directly to NIDDK.

3.2. CRISP III 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 (Michal Mrug) 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 is located at the University of Pittsburgh, Pittsburgh, Pennsylvania, where K. Ty Bae is the Principal Investigator and Douglas Landsittel 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. Michael Flessner (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.crhc.pitt.edu/crispiii

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

Dr. Michael Flessner serves as the NIDDK Project Director for CRISP and is a voting member of the Steering Committee. In her role as Project Director, Dr. Flessner 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. Flessner is also responsible for forming and coordinating the activities of the CRISP External Expert Group and subsequent Data Safety and Monitoring Board.

3.4. External Expert Group

An External Expert Group (EEG) 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 External Expert Group (EEG) will act in an advisory capacity to the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK) to monitor patient safety and evaluate the data collection and analysis. This study is funded by the NIDDK. The CRISP protocol requires EEG approval before the study can begin. Once recruitment is underway, members of the EEG will serve on the Data Safety and Monitoring Board (DSMB).

The members of the CRISP EAC are as follows:

John R. Sedor, MD
MetroHealth Research Endowment Professor
Kidney Disease Research Center
Departments of Medicine and Physiology and Biophysics
Case Western Reserve University
Cleveland, OH

David A. Bluemke, MD, PhD
Clinical Director, MRI
Russel H. Morgan Dept. of Radiology
Johns Hopkins Medical Institutions
Baltimore, MD
NIH: Radiology and Imaging Sciences
Bethesda, MD

Martin Pollak, MD
Beth Israel Deaconess Medical Center
Chief, Division of Nephrology, Department of Medicine
Boston, MA

Shona Pendse, MD
Medical Officer
CDER Division of Cardiovascular and Renal Products
FDA
White Oak, MD

James Hodges, PhD
Associate Professor, Division of Biostatistics
University of Minnesota School of Public Health
Minneapolis, MN

Nancy J. Cox, PhD
Professor, Department of Medicine
Section of Genetic Medicine
The University of Chicago
Chicago, Il

Terry J. Watnick, MD
Professor, Medicine
PI JHU PKD Research and Clinical Core Center
855 N. Wolfe St
Rangos Building, Room 550
Baltimore, MD 21205

3.5. Data Safety and Monitoring Board

Once participant recruitment for CRISP begins, the External Expert Group (EEG) 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.crhc.pitt.edu/crispiii/

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 – Douglas Landsittel, Chair

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

- Requested modifications to the CRISP III 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. Douglas Landsittel and Dr. Ty Bae as well as key data management and imaging staff and the CRISP III 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 III 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 FV-10 and FV-12, 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 III 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. 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 patients and draw an electronic pedigree for each family. Identified affected family members who agree to participate will be consented into the study and a blood sample will be collected for DNA extraction.

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=10925637151082500795

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].

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.

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

MC4091-23

Iothalamate Glomerular Filtration Rate (GFR) Test #81476

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

3.13. Information for Study Personnel

3.13.1. Training

The Data Coordinating and Image Analysis Center (DCIAC) is responsible for training all CRISP III personnel in the correct procedures for carrying out the study. A WebEx training session for Study Coordinators was conducted on November 3rd, 2011. Principal investigators reviewed the CRISP III Protocol, updated forms and discussed the Manual of Procedures during the Steering Committee meeting on October 17, 2011, 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 CRISPIII@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>

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

3.13.5. Setting up New CRISP Personnel

When a new staff member joins the CRISP III team, the site coordinator should download the New Personnel Form, complete the "CRISP Information and Web Access Form" form and fax or email to the Study Coordinator (available for download on the CRISPIII website). 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 III 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 III 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 III 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 available on the CRISP III website and 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 available on the CRISP III website and 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 III 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 III DCIAC, with access limited to CRISP III 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 III 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, M. Flessner, D. Landsittel, W. M. Bennett (chair)

Ancillary Studies Committee – J.J. Grantham (chair), D. Landsittel, A.B. Chapman, V.E. Torres, K.T. Bae, M. Flessner

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 III 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 III website, a password−protected content accessible to only study personnel. The address of the CRISP III website is: https://www.crhc.pitt.edu/crispiii/.

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 III Study Design and Protocol

7.1. Overview of Design

The CRISP III Study is a prospective, observational study that is an extension of CRISP I and CRISP II. CRISP I was 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. 201 CRISP I participants completed follow-up in CRISP II. It is anticipated that all CRISP I subjects not yet on dialysis or having received a transplant (n= 3) are eligible to enroll in CRISP III. CRISP III 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 has 40 CRISP subjects in Study A (which includes MR imaging identical to that proposed in this submission) and 23 subjects in Study B (no MR imaging). In addition 25 CRISP participants are currently enrolled in interventional trials involving V2 receptor antagonists. Importantly, the co-Principal Investigators (Dr. Ty Bae, and Dr. D. Landsittel) and personnel for the Imaging Center for both HALT and CRISP III are the same. The CRISP/HALT liaison committee will review and approve dual participation in both CRISP III and HALT and the CRISP and HALT Steering Committees will approve the CRISP III protocol. To minimize subject burden and to maintain retention throughout CRISP III, those CRISP III 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 III that are not included in HALT.

General Protocol: Measurements of TKV, KCV, TLV, LCV, RBF, GFR and other laboratory evaluations (CRISP website, MOP) will be made twice during CRISP III (year 10 and 12 of the longitudinal study) in participants utilizing a similar approach to CRISP I and II. Plasma creatinine concentration will be measured annually. Medical histories and ADPKD specific patient reported outcomes will be obtained every 3 months. The frequency of these visits are increased from CRISP II as patients are more likely to present with complications specifically related to TKV and TLV on a more frequent basis. Unique additions or changes to the parent CRISP III protocol, e.g. AIM 5 Pilot Study, are noted in association with each Specific Aim.

7.2. Study Timeline

April 2011-September 2011
Protocol refinement, IRB approvals
Forms development, MOP development
External Expert group review and approval
Continued analysis of longitudinal data from CRISP I and II

October 2011-March 2013 (Baseline or YR 1 VISIT)
Initial PCC Visit 1
Quarterly contacts with participants via telephone for detailed review of medications, medical visits, and hospitalizations

April 2013-March 2014
Finish PCC Visit 1
Quarterly contacts continue
Acquisition of plasma creatinine (duplicate determination)

April 2014-March 2015
PCC Visit 2
Quarterly contacts continue

April 2015-March 2016 (YR 4 VISIT)
Finish PCC Visit 2
Quarterly contacts continue
Acquisition of plasma creatinine (duplicate determination)

April 2016-March 2017
Complete analysis and prepare for CRISP IV

7.2. Study Calendar

STUDY CALENDAR

Time Line	Visit Number	Form Name	Date Expected
Initial Clinic Visit Year 10	FV-10	Consent Form Registration [#2] Identification Form [#51] Biannual Med & Events [#28] Biannual Labs [#27] Quality of Life (SF-36v2) [#41] Pain Questionnaire [#42] Symptoms [#12] Physical Findings [#11] Women's OB-GYN [#40] GFR Collection [#9] GFR Reporting [#10] Archived Blood Sample [#53] Archived Urine Sample [#47] MRI Status verification [#55] MR Session RBF [#7] Visit Checklist (PI signature) [#46]	
3 Month Phone Call Post Year 10	FV-10.3	Follow-Up Study & Events [#13]	Initial Visit + 3 months
6 Month Phone Call Post Year 10	FV-10.6	Follow-Up Study & Events [#13]	Initial Visit + 6 months
9 Month Phone Call Post Year 10	FV-10.9	Follow-Up Study & Events [#13]	Initial Visit + 9 months
Lab Visit Year 11	FV-11	Alternate Year Labs Lab Visit [#33] Follow-Up Study & Events [#13]	Initial Visit + 12 months
3 Month Phone Call Post Year 11	FV-11.3	Follow-Up Study & Events [#13]	Initial Visit + 15 months
6 Month Phone Call Post Year 11	FV-11.6	Follow-Up Study & Events [#13]	Initial Visit + 18 months
9 Month Phone Call Post Year 11	FV-11.9	Follow-Up Study & Events [#13]	Initial Visit + 21 months
Biannual Clinic Visit Year 12	FV-12	Biannual Med & Events [#28] Biannual Labs [#27] Quality of Life (SF-36v2) Pain Questionnaire [#42] Symptoms [#12] Physical Findings [#11] Women's OB-GYN [#40]	Initial Visit + 24 months

		GFR Collection [#9] GFR Reporting [#10] Archived Blood Sample [#53] Archived Urine Sample [#47] MRI Status verification [#55] MR Session RBF [#7] Visit Checklist (PI signature) [#46]	
3 Month Phone Call Post Year 12	FV-12.3	Follow-Up Study & Events [#13]	Initial Visit + 27 months
6 Month Phone Call Post Year 12	FV-12.6	Follow-Up Study & Events [#13]	Initial Visit + 30 months
9 Month Phone Call Post Year 12	FV-12.9	Follow-Up Study & Events [#13]	Initial Visit + 33 months
Lab Visit Year 13	FV-13	Alternate Year Labs Lab Visit [#33] Follow-Up Study & Events [#13]	Initial Visit + 36 months
3 Month Phone Call Post Year 13	FV-13.3	Follow-Up Study & Events [#13]	Initial Visit + 39 months
6 Month Phone Call Post Year 13	FV-13.6	Follow-Up Study & Events [#13]	Initial Visit + 42 months
9 Month Phone Call Post Year 13	FV-13.9	Follow-Up Study & Events [#13]	Initial Visit + 45 months
Special Events	When Needed	Shipping Manifest-Plasma [#48] Shipping Manifest-Urine [#47] Shipping Manifest-DNA [#56] Shipping Manifest-Cleveland Clinic [#50] Shipping Manifest Checklist [#62] Missed Visit [#24] Study Withdrawal [#19] Transfer [#18] Death Notification [#15] Transitional Symptoms [#63] Endpoints Form [#64] HALT ID [#59]	

7.2.1. Development Phase (April 2011-September 2011)

- Protocol refinement, consent form development for CRISP III, local IRB approval
- Forms and MOP development
- Review and concept approval of CRISP III protocol by the EEG.
- Continue analyses of longitudinal data initiated in CRISP I and II
- Complete transfer of data and biologic samples to NIDDK repositories

7.2.2. YR10 visit or baseline (October 2011-March 2013)

- First PCC visit for CRISP III participants
- Quarterly (every 3 months) contact with participants via telephone for detailed review of medications, medical visits, hospitalizations
- Annual acquisition of plasma creatinine (duplicate determination)

7.2.3. YR11 (October 2012-September 2013)

- Annual acquisition of plasma creatinine (duplicate determination)
- Quarterly (every 3 months) contact with CRISP extension participants for detailed review of medications, medical visits and hospitalizations
- Initiate analyses of combined CRISP II and CRISP III longitudinal data

7.2.4. YR12 visit (October 2013-March 2015)

- Second full PCC visit of CRISP III participants
- Quarterly (every 3 months) contact with participants via telephone for detailed review of medications, medical visits and hospitalizations
- Continue analyses

7.2.5. YR13 (October 2014-March 2016)

- Annual acquisition of plasma creatinine (duplicate determination)
- Quarterly (every 3 months) contact with CRISP extension participants for detailed review of medications, medical visits and hospitalizations.
- Continue analyses

7.2.6. (April 2016-March 2017)

- Data analysis, close out visits, transfer of CRISP III data and samples to NIDDK repositories, completion of ancillary studies.
- Complete analysis and prepare for CRISP IV

7.3. Eligibility and patient recruitment for CRISP III

All CRISP I participants not yet on dialysis or receiving renal transplantation will be invited to participate in CRISP III. At entry into CRISP I participants met a number of inclusion and exclusion criteria. Exclusion criteria for participation in CRISP III are:

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
4. Currently receiving renal replacement therapy or having received a renal transplant.

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 III, but will not undergo MR studies.

To enroll in CRISP III, 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 III 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 III protocol does not exclude participants that enroll in other interventional trials. If CRISP III participants are recruited into an interventional trial (e.g HALT clinical trial) that also requires imaging studies, the visits for CRISP III 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 III analysis. Analysis of the data obtained on subsequent visits will be held until the interventional trial is completed. The CRISP III 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 III 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 III will in part be collected in other trials, but there will be some CRISP III specific information that may need to be acquired by the CRISP III 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 III 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; quarterly 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 year 1 (2012/2013) and year 3 (2014/2015) 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

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.
(i.e., correction of magnetic field inhomogeneity).

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 ≤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. <u>(For renal blood flow measurement)</u> Breath-hold, <u>oblique-coronal</u> 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. <u>(For renal blood flow measurement)</u> 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. Guidelines for Participants at End Stage Renal Disease

Participants who have reached End Stage Renal Disease do not need to return to the PCC for regular study visits. ESRD participants will be contacted by telephone follow-up every three months until Death.

Laboratory blood or urine samples will not be collected. No additional clinical and/or imaging data, in addition to eGFR and creatinine values, will be retrieved from patients' clinical records.

Form #64: Endpoints Form should be updated every three months until Death has occurred. Form 64 is to be completed by study coordinator once the participant has reached End Stage Renal Disease or Death.

7.4.5. Family History Collection of CRISP III Participants

A major component of CRISP III is to collect more exhaustive family histories of all CRISP I patients. 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 transformed 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.* 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.

The CRISP participants will be asked to complete a family history questionnaire to extend the traceable family. When possible, the most recent CT or MR examination of the abdomen will be retrieved for the analysis of kidney and liver morphology at the Data Coordinating Image Analysis Center (DCIAC). If these examinations are 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 participants, it will be a relatively reliable means to assess renal disease severity in all patients. 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).

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 serial quantification of total kidney (TKV) and liver (TLV) and of kidney (KCV) and liver cyst (LCV) volumes in order to develop and test new models for predicting the risk of developing renal insufficiency.

7.5.1.1. Hypothesis 1a

Baseline TKV and change in TKV predict loss of kidney function.

To characterize the development of renal insufficiency, we will employ a battery of GFR measurements based on iothalamate clearance and serum creatinine concentration (MDRD equation). For example, we will evaluate the pattern of GFR decline over time to determine if individual participants slopes are appropriate or not. In conjunction with our evaluation of slopes, we will employ a repeated measures mixed model (hierarchical model) using all time points to assess the effects of our predictors, time, and the interactions between predictors, such as TKV and time, to predict decline in GFR We will also assess hard endpoints such as GFR thresholds defined by K/DOQI stages 3, 4 and 5, 4) 50% decrease in GFR from the CRISP I baseline, 5) dialysis, transplantation, and death from ESRD.

Multivariable analysis will be extended to include more individuals with renal insufficiency outcomes predicted to occur in CRISP III in order to obtain more rigorous testing of the hypothesis that TKV predicts renal insufficiency. ROC analysis will be used to determine the sensitivity and specificity of TKV to predict renal insufficiency. By including continuous changes in GFR we will demonstrate trends of change relatively early in the course of individual patients, and thereby determine more precisely the earliest clear indication of renal insufficiency in relation to TKV and change in TKV. To measure annual change over time for TKV, iothalamate clearance and plasma creatinine concentration we will calculate within participant intercepts and slopes, transforming the measurement if appropriate. For continuous outcomes (slope of GFR) we will use linear regression, for dichotomous outcomes (50% decrease in iothalamate clearance) logistic regression and for ordinal outcomes (K/DOQI stage) ordinal logistic regression. During our model building process we will also test the benefit of 1) inclusion of other variables, known to associate with TKV that occur in advance of the development of renal insufficiency (hypertension, pain, gross hematuria) to determine if they enhance the identification of patients destined to develop renal insufficiency beyond what htTKV provides, and 2) the addition of other variables explored in Specific Aim 2, 3, and 5) in empirical models utilizing new candidate biomarkers.

Preliminary hierarchical linear modeling [10] of iothalamate clearance trajectories indicates that: 1) the decline of renal function over time varies among individuals, and 2) the rate of decline can be predicted from patient gender and baseline TKV values (e.g., based on the CRISP baseline visit data, this model predicts iothalamate clearance at the third year follow up with

r=0.76 for training and r=0.71 for validation datasets, both p<0.0001). We will further develop these trajectory models using extended iothalamate clearance data and inclusion of time-varying predictors (e.g., TKV). These analyses will be complemented by Generalized Estimation Equations (GEE) modeling.

7.5.1.2. Hypothesis 1b

The progression of polycystic liver volume (LCV) will be similar to but distinct from that of TKV; baseline LCV, adjusted for covariates, will independently predict the rate of increase in LCV and complications arising within the liver.

We have determined previously in this cohort that LCV and TKV increase with age. In CRISP III we will determine the correlation of change in LCV and TKV in individual patients adjusting for appropriate covariates such as gene and mutation type. Our analytic approach will be similar to that used for the kidneys when the outcome is continuous.

7.5.2. Specific AIM 2

Determine the extent to which age and sex-adjusted measurements of renal blood flow (RBF), determined by MR imaging, predict the rate of change in TKV and determine if RBF and TKV independently predict the risk of developing renal insufficiency.

7.5.2.1. Hypothesis 2a

Baseline RBF predicts the rate of increase in TKV and, independent of and in addition to baseline TKV, predicts renal insufficiency.

Our analytic approach to RBF will be to first determine the patterns of decline in RBF over time using repeated measures ANOVA testing for linear or quadratic trend and to see whether these patterns change over time. Next, we will add baseline RBF to the existing baseline analyses and models developed in Aim 1 and assess whether adding baseline RBF improves the ability to predict loss of renal function. Potential RBF and TKV or TCV interaction (potentially using ROC cutpoints) will also be considered. Lastly, we will add all RBF values to the longitudinal / hierarchical models developed in Aim 1.

7.5.3. Specific AIM 3

Develop methods to quantify total cyst number, individual cyst volumes, and pattern of distribution of cysts in each kidney and apply these to analyze the influence of renal cyst number, volume, and topography at baseline on the subsequent course of TKV and GFR and the risk of developing renal insufficiency.

7.5.3.1. Hypothesis 3a

Renal cyst number and volume will be associated with rates of change in TKV and GFR and risk of developing renal insufficiency. These relationships may vary by genotype.

First, we will perform Pearson or Spearman correlations comparing cyst number and volume with TKV and GFR at each time point. Second, we will perform correlations of cyst number and volume at each time point with the slopes of appropriately transformed TKV or GFR values, which represent average change. Third, we will regress the slopes on baseline cyst number and volume including appropriate covariates, genotype, or clinical markers. Finally we will use

mixed models or GEE including cyst number and volume at each time point, a time effect and appropriate interactions.

7.5.3.2. Hypothesis 3b

Renal cyst topography (medullary vs. non-medullary) will be associated with rates of change in TKV and GFR and risk of developing renal insufficiency. These relationships may vary by genotype.

For this hypothesis we will assess the following predictors: 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; and 3) The ratio of number of cysts in the medullary region to the number of cysts in the cortical area (MNCN) at baseline. 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. 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 vs. 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. Similar models will be built using CCD but this predictor will have 5 or 2 (if we dichotomize as primarily medullary vs non-medullary) levels so a baseline adjustor would not be necessary.

7.5.3.3. Hypothesis 3c

Individual renal cyst growth is continuous and exponential (similar to the growth pattern in TKV) and patterns of renal cyst growth or involution will be associated with rates of change in TKV and GFR and risk of developing renal insufficiency. These relationships may vary by genotype.

First, we will plot the cyst growth patterns over time for each cyst and assess whether the pattern is linear or exponential or some other trend. Second, we will create slopes for each cyst based on the appropriate transformation. Third, we will use GEE modeling to see if genotype, age, gender or other factors predict cyst growth using the slopes as our outcome measure. GEE is necessary because we have multiple cysts per person. We will also need to adjust for whether or not the cyst merged with another at a particular time point and account for whether or not the participant is potentially receiving treatment due to their participation in HALT-PKD or TEMPO.

Chapter 8. CRISP Imaging

8.1. Participants

8.1.1. Frequency of Imaging Exams

Imaging studies will be obtained at FV-10 and FV-12, 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 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.

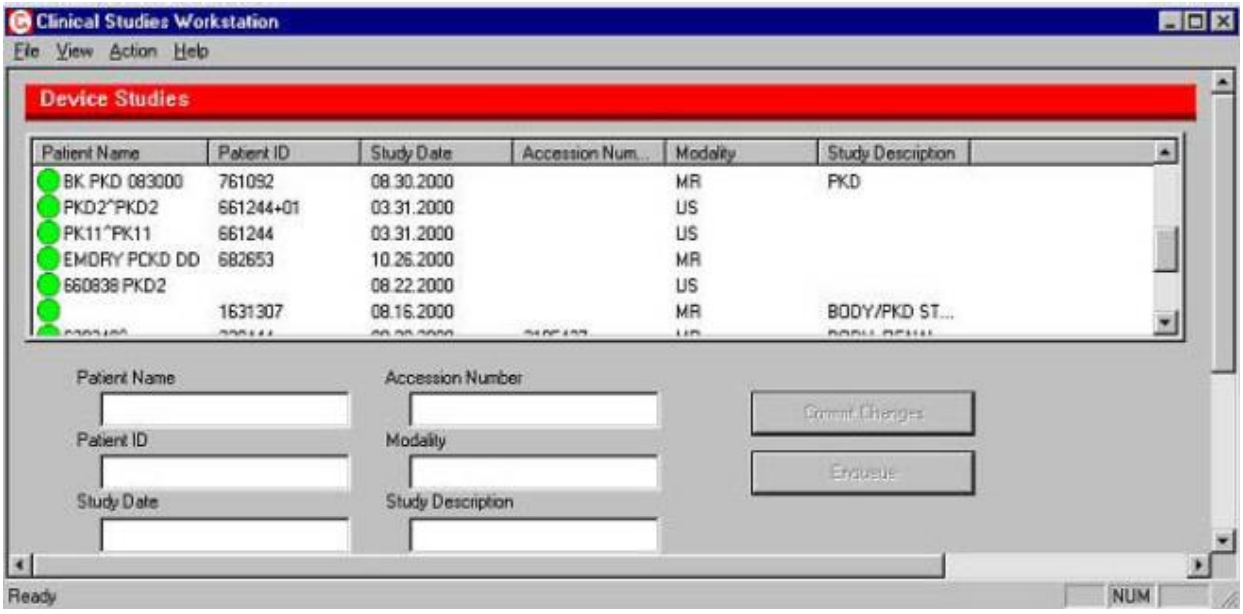


Figure 8.1. Screenshot – Study View from CSW Application

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.

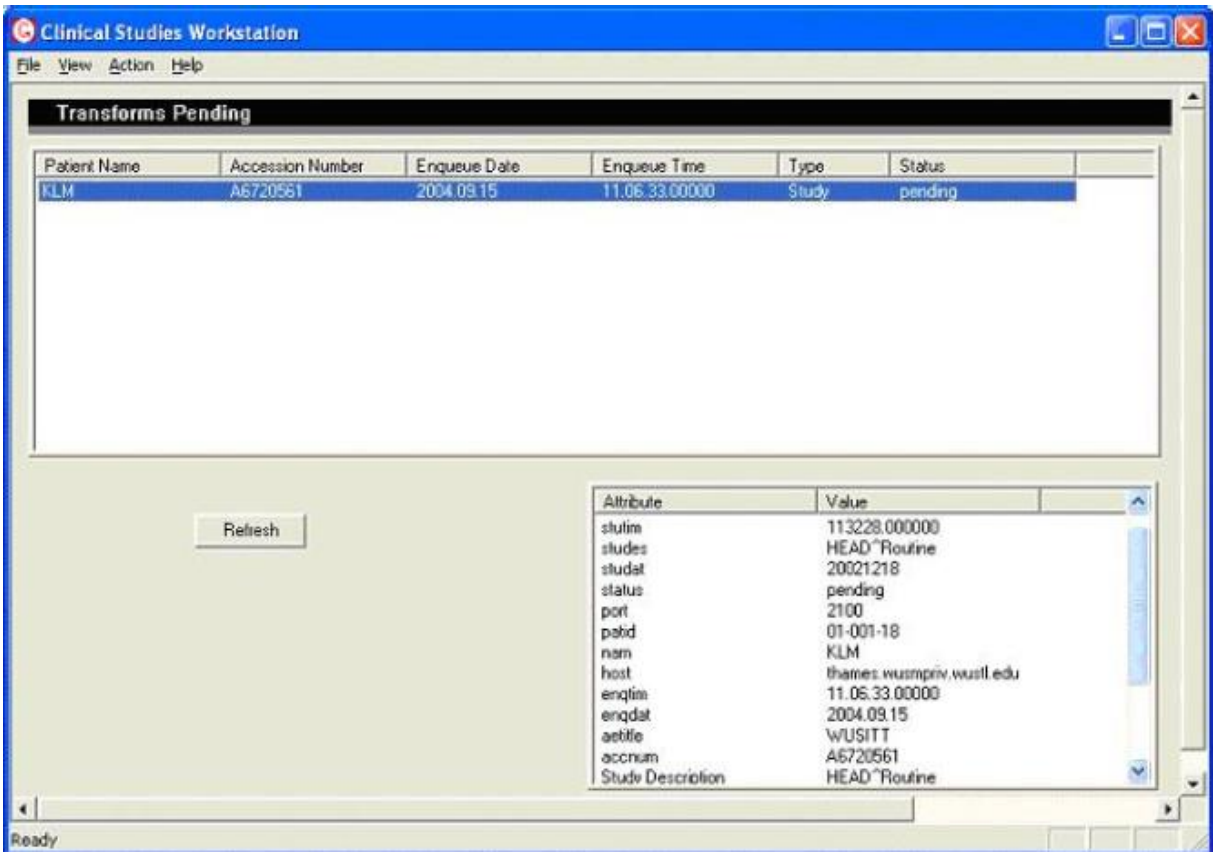


Figure 8.2. Screenshot – Current Status of Studies being Transmitted

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 III.

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.

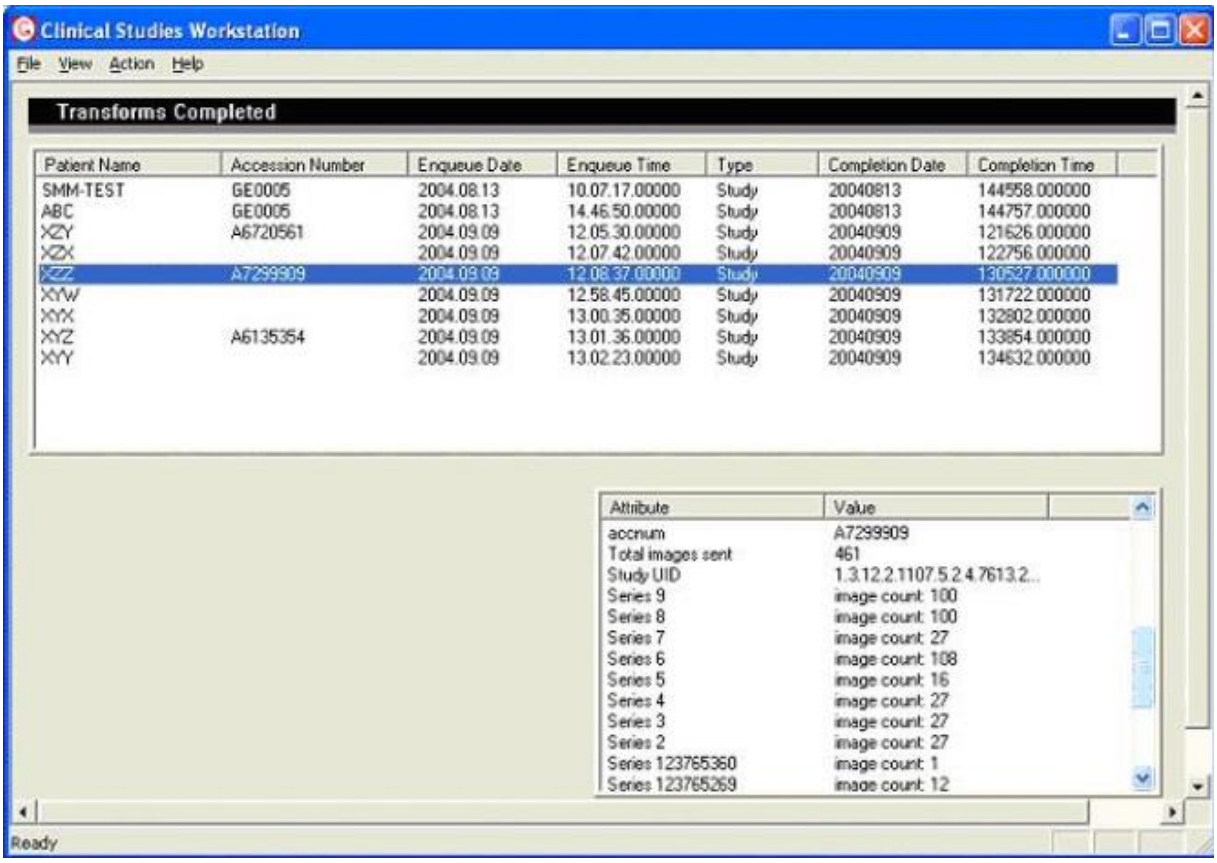


Figure 8.3. Screenshot – List of all Transmitted Studies

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 https://www.crhc.pitt.edu/crispiii/
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/CRISP3/MAYO_CRISP3

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

2. Window 2

cd /crisp3a/pcc-images / MAYO_CRISP3
ls (make sure there is no duplicated case)
mkdir xxxxxxx

3. Window 1

cp –rp *42512 /crisp3a/pcc-images/CRISP3-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 /crisp3a/pcc-images/CRISP3-MAYO/xxxxxxx
cd xxxxxxx/*42512

5. Go to website http://pkd2:8080/CRISP3/, click “DICOM conversion to AVW”.

6. Open up the study from the site. Click the UID.

7. Choose “YES” for kidney, liver series; “NO” for RBF and other useless series.

8. Window 3

Cd /crisp3a/pkd/conversions/scripts/production/7xx/7xxxxx 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.

9. Window 4

cd /crisp3b/pkd/pat/fv10/7xx
chmod –R 775 7xxxxxx

cd 7xxxxxx
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/CRISP3/
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 crisp3 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 11.0 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 CRISP3 website (https://www.crhc.pitt.edu/crispiii/).

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

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 III Study Forms

Forms development and updating will be done during the initial phase of the CRISP III 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 October of 2012 to review the CRISP II forms for CRISP III modification and to discuss potential new forms.
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 III Web Data Entry System

Website access is given to site personnel affiliated with the study. A registration form must be completed and sent to the DCIAC. When information has been received, login information will be provided. All new study personnel are required to perform training before access is given.

In addition to the web form portal for data entry, the website provides minutes of all committee meetings, with additional resources such as the MOP and Protocol, printable forms and tracking reports.

9.2.1. Accessing the Website

The website is https://www.crhc.pitt.edu/crispiii/. 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.

APPENDICES

CRISP III Clinical and Administrative Forms

Table 4. List of CRISP II Data Collection Forms

Form ID	Data Collection Forms [https://www.crhc.pitt.edu/crispiii]
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
13	Follow Up Study and Events Clinical Form
15	Death Notification Administrative Form
18	Transfer Form Administrative Form
19	Study Withdrawal Administrative Form
24	Missed Visit Administrative 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
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
51	Identification Form Administrative Form
53	Archived Blood Sample Clinical Form
55	MRI Status Verification Clinical Form
56	Genetics Phlebotomy Form (Shipping Manifest - Rutgers) Clinical Form

	Administrative Forms
	MR Tech registration Administrative Form
	Web Access Administrative Form
	Application for a CRISP Ancillary Study

Form ID	Family Member Data Collection Forms [https://www.crhc.pitt.edu/Modifier/Login.aspx]
1	Family History Questionnaire form (PCC only)
2	ADPKD Genetic Modifier Study Questionnaire (non CRISP participant / family member)
4	Rutgers shipping manifest
6	MRI/CT Session form
8	Assessment of Quality of Radiologic Studies
9	ADPKD Genetic Modifier Study Questionnaire for CRISP participants (Miniform for CRISP proband)

CRISP III

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:

Registration Form

This form is to be completed at visit 10, 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 ***(Please complete Halt ID Form)***
2 ☐ Tempo
3 ☐ Other, Specify: _____ *enrolsp*

Date of Enrollment *enroldt* __/__/__ or **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* 0 ☐ No 1 ☐ Yes

CRISP III

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:

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

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:

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*
- ☐ Embolization coils *emcoil*

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:

Registration Form

- ☐ 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*

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:

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. It is to be entered promptly and data transferred to the Imaging Analysis Center (AC) right after the scan.

Was an MR Scan done by the Halt Study for this participant visit? *scand* ☐ Yes ☐ No

*If Yes, enter Halt Accession Number for this visit and STOP*_____ *haccn*

If No, complete this form.

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*
_____ *ns4*	_____ *ed4*
_____ *ns5*	_____ *ed5*

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*

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*

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*

CRISP II

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

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

visit: Accession ID: _____ *accn*

MR Session Information/Renal Blood Flow Form

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*

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**

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: _____ *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:

GFR Reporting Form

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

☐ Refused ☐ Original ☐ Repeat 1 ☐ Repeat 2 *redo*

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: _____ *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:

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*

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

Note: The CRISP III 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 III

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 III

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 III

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* Date: __ __ / __ __ / __ __ __ __ *vsbldt*
Impotence/Decreased Libido *impot*			*impotspy*
Urinary Tract Infection *uti*			*utispy* Date: __ __ / __ __ / __ __ __ __ *utidt*
Kidney Stone *kidst*			*kidstspy* Date: __ __ / __ __ / __ __ __ __ *kidstdt*
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 III

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 III

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	555555 ☐ Unknown	
3b.	**Have you ever had epididymal cysts?** *epidcysts*	☐ N/A	0 ☐ No	1 ☐ Yes	555555 ☐ Unknown	

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 III

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 4 Month Post and 8 Month Post 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*_____

_____

_____

2a. **Have you been newly diagnosed with hypertension since last contact?** *hypert* 0 ☐ No 1 ☐ Yes

If yes, **Date of diagnosis:** __ __/__ __/__ __ __ __ *hypyr*
hypmt *hypda* Month Day Year

How were you diagnosed with hypertension? *hyphdia* 1 ☐ Home BP monitor 2 ☐ Doctor visit
3 ☐ Hospital stay 4 ☐ Other Specify: _____ *hypspc*

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: _____

Address: _____

City, State, Zip: _____

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

_____

CRISP III

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: _____

Address: _____

City, State, Zip:_____

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: _____

Address: _____

City, State, Zip:_____

d. Specify reason for visit: *pv2reason2*_____

_____

_____

CRISP III

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: _____

Address: _____

City, State, Zip:_____

d. Specify reason for visit: *pv2reason3*_____

_____

_____

Please continue on the next page

CRISP III

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:_____

Address:_____

City, State, Zip:_____

f. Name and address of physician treating participant:

Name:_____

Address:_____

City, State, Zip:_____

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

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

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*

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:_____

Address:_____

City, State, Zip:_____

f. Name and address of physician treating participant:

Name:_____

Address:_____

City, State, Zip:_____

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 III

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:_____

Address:_____

City, State, Zip:_____

f. Name and address of physician treating participant:

Name:_____

Address:_____

City, State, Zip:_____

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 III

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:_____

Address:_____

City, State, Zip:_____

f. Name and address of physician treating participant:

Name:_____

Address:_____

City, State, Zip:_____

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*

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 *(Go to #6b)* 1 ☐ Yes

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*
pma6	*dpmamt6* ___/___ *dpmadate6*
pma7	*dpmamt7* ___/___ *dpmadate7*
pma8	*dpmamt8* ___/___ *dpmadate8*
pma9	*dpmamt9* / *dpmadate9*
pma10	*dpmamt10* ___/___ *dpmadate10*
pma11	*dpmamt11* ___/___ *dpmadate11*
pma12	*dpmamt12* ___/___ *dpmadate12*
pma13	*dpmamt13* ___/___ *dpmadate13*
pma14	*dpmamt14* ___/___ *dpmadate14*
pma15	*dpmamt15* ___/___ *dpmadate15*
pma16	*dpmamt16* / *dpmadate16*
pma17	*dpmamt17* ___/___ *dpmadate17*
pma18	*dpmamt18* ___/___ *dpmadate18*
pma19	*dpmamt19* ___/___ *dpmadate19*
pma20	*dpmamt20* ___/___ *dpmadate20*
pma21	*dpmamt21* ___/___ *dpmadate21*

CRISP III

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

pma22	*dpmamt22* ___/___ *dpmadate22*
pma23	*dpmamt23* / *dpmadate23*
pma24	*dpmamt24* ___/___ *dpmadate24*
pma25	*dpmamt25* ___/___ *dpmadate25*

6b. Since the last visit, have prescribed drugs been stopped/discontinued? 0 ☐ No 1 ☐ Yes
pdyn *(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*
pmd6	*dpmdmt6* / *dpmddate6*
pmd7	*dpmdmt7* ___/___ *dpmddate7*
pmd8	*dpmdmt8* ___/___ *dpmddate8*
pmd9	*dpmdmt9* ___/___ *dpmddate9*
pmd10	*dpmdmt10* ___/___ *dpmddate10*
pmd11	*dpmdmt11* ___/___ *dpmddate11*
pmd12	*dpmdmt12* ___/___ *dpmddate12*
pmd13	*dpmdmt13* ___/___ *dpmddate13*
pmd14	*dpmdmt14* ___/___ *dpmddate14*
pmd15	*dpmdmt15* ___/___ *dpmddate15*
pmd16	*dpmdmt16* ___/___ *dpmddate16*
pmd17	*dpmdmt17* ___/___ *dpmddate17*

CRISP III

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

pmd18	*dpmdmt18* __ __/__ __ __ __ *dpmddate18*
pmd19	*dpmdmt19* __ __/__ __ __ __ *dpmddate19*
pmd20	*dpmdmt20* __ __/__ __ __ __ *dpmddate20*
pmd21	*dpmdmt21* __ __/__ __ __ __ *dpmddate21*
pmd22	*dpmdmt22* __ __/__ __ __ __ *dpmddate22*
pmd23	*dpmdmt23* __ __/__ __ __ __ *dpmddate23*
pmd24	*dpmdmt24* __ __/__ __ __ __ *dpmddate24*
pmd25	*dpmdmt25* __ __/__ __ __ __ *dpmddate25*

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*

CRISP III

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

omd4	*domdmt4* __ __/__ __ __ __ *domddate4*
omd5	*domdmt5* __ __/__ __ __ __ *domddate5*

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.

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: _____ *deidnum* Date: __ __/__ __/__ __ __ __ *dedate*

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

CRISP III

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 10 and 12.

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 III

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: _____ *deidnum* Date: __ __/__ __/__ __ __ __ *dedate*

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

CRISP III

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 Visits 10 and 12.

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*_____

_____

_____

2a. Have you been newly diagnosed with hypertension since last contact?*hypert* 0 ☐ No 1 ☐ Yes

If yes, Date of diagnosis: __ __/__ __/__ __ __ __ *hypyr*
hypmt *hypda* Month Day Year

How were you diagnosed with hypertension? *hyphdia* 1 ☐ Home BP monitor 2 ☐ Doctor visit
3 ☐ Hospital stay 4 ☐ Other Specify: _____ *hypspc*

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: _____

Address: _____

City, State, Zip: _____

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

_____

_____

_____

CRISP III

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: _____

Address: _____

City, State, Zip:_____

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: _____

Address: _____

City, State, Zip:_____

d. Specify reason for visit: *pv2reason2*_____

_____

_____

CRISP III

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: _____

Address: _____

City, State, Zip:_____

d. Specify reason for visit: *pv2reason3*_____

_____

_____

Physician #4

a. Date of additional physician visit: __ __/__ __ /__ __ __ __ *pv2yr4*
pv2mt4 *pv2da4* Month Day Year

b. Were there multiple visits to this physician? *m2vc4* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____

Address: _____

City, State, Zip:_____

d. Specify reason for visit: *pv2reason4*_____

_____

_____

CRISP III

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 #5

a. Date of additional physician visit: __ __/__ __/__ __ __ __ *pv2yr5*
pv2mt3 *pv2da3* Month Day Year

b. Were there multiple visits to this physician? *m2vc5* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____

Address: _____

City, State, Zip:_____

d. Specify reason for visit: *pv2reason5*_____

_____

_____

Physician #6

a. Date of additional physician visit: __ __/__ __/__ __ __ __ *pv2yr6*
pv2mt6 *pv2da6* Month Day Year

b. Were there multiple visits to this physician? *m2vc6* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____

Address: _____

City, State, Zip:_____

d. Specify reason for visit: *pv2reason6*_____

_____

_____

CRISP III

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 #7

a. Date of additional physician visit: __ __/__ __ /__ __ __ __ *pv2yr7*
pv2mt7 *pv2da7* Month Day Year

b. Were there multiple visits to this physician? *m2vc7* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____

Address: _____

City, State, Zip:_____

d. Specify reason for visit: *pv2reason7*_____

_____

_____

Physician #8

a. Date of additional physician visit: __ __/__ __ /__ __ __ __ *pv2yr8*
pv2mt8 *pv2da8* Month Day Year

b. Were there multiple visits to this physician? *m2vc8* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____

Address: _____

City, State, Zip:_____

d. Specify reason for visit: *pv2reason8*_____

_____

_____

CRISP III

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 #9

a. Date of additional physician visit: __ __/__ __/__ __ __ __ *pv2yr9*
pv2mt9 *pv2da9* Month Day Year

b. Were there multiple visits to this physician? *m2vc9* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____

Address: _____

City, State, Zip:_____

d. Specify reason for visit: *pv2reason9*_____

_____

_____

Physician #10

a. Date of additional physician visit: __ __/__ __/__ __ __ __ *pv2yr10*
pv2mt10 *pv2da10* Month Day Year

b. Were there multiple visits to this physician? *m2vc10* 0 ☐ No 1 ☐ Yes

c. Name and address of physician treating participant:

Name: _____

Address: _____

City, State, Zip:_____

d. Specify reason for visit: *pv2reason10*_____

_____

_____

Please continue on the next page

CRISP III

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:_____

Address:_____

City, State, Zip:_____

f. **Name and address of physician treating participant:**

Name:_____

Address:_____

City, State, Zip:_____

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

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

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 III

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 #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 (in days) : _____*lenst2*

e. Name and address of hospital:

Name:_____

Address:_____

City, State, Zip:_____

f. Name and address of physician treating participant:

Name:_____

Address:_____

City, State, Zip:_____

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 III

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:_____

Address:_____

City, State, Zip:_____

f. Name and address of physician treating participant:

Name:_____

Address:_____

City, State, Zip:_____

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 III

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:_____

Address:_____

City, State, Zip:_____

f. Name and address of physician treating participant:

Name:_____

Address:_____

City, State, Zip:_____

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 III

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 1 ☐ Yes *cigar*

6h. *If yes,* **how many cigars since the last visit?** __ __ *cignm*

6i. Pipe 0 ☐ No 1 ☐ Yes *pipeyn*

6j. Chewing Tobacco/Snuff 0 ☐ No 1 ☐ Yes *chewyn*

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*

0 ☐ Per day
1 ☐ Per week **Number of 8 ounce cups per interval**__ __ *ccafunit*
2 ☐ Per month

CRISP III

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*

0 ☐ Per day
1 ☐ Per week **Number of 12 ounce portions per interval** __ __ *scafunit*
2 ☐ 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)
0 ☐ Per day
1 ☐ Per week **Number of drinks per interval** __ __ *alconit*
2 ☐ 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*

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 10 and the participant is in Crisp II, or if this is Visit 12, Go to # 11.

If this is Visit 10 and the participant is in Crisp I only,

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 III

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

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*
pma6	*dpmamt6* __ __/__ __ __ __ *dpmadate6*
pma7	*dpmamt7* __ __/__ __ __ __ *dpmadate7*
pma8	*dpmamt8* __ __/__ __ __ __ *dpmadate8*
pma9	*dpmamt9* __ __/__ __ __ __ *dpmadate9*
pma10	*dpmant10* __ __/__ __ __ __ *dpmandate10*
pma11	*dpmant11* __ __/__ __ __ __ *dpmandate11*
pma12	*dpmant12* __ __/__ __ __ __ *dpmandate12*
pma13	*dpmant13* __ __/__ __ __ __ *dpmandate13*
pma14	*dpmant14* __ __/__ __ __ __ *dpmandate14*
pma15	*dpmant15* __ __/__ __ __ __ *dpmandate15*
pma16	*dpmant16* __ __/__ __ __ __ *dpmandate16*

CRISP III

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

11b. Since the last visit, have prescribed drugs been stopped/discontinued? 0 ☐ No 1 ☐ Yes
pdyn *(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*
pmd6	*dpmdmt6* __/____ *dpmddate6*
pmd7	*dpmdmt7* __/____ *dpmddate7*
pmd8	*dpmdmt8* __/____ *dpmddate8*
pmd9	*dpmdmt9* __/____ *dpmddate9*
pmd10	*dpmdmt10* __/____ *dpmddate10*
pmd11	*dpmdmt11* __/____ *dpmddate11*
pmd12	*dpmdmt12* __/____ *dpmddate12*
pmd13	*dpmdmt13* __/____ *dpmddate13*
pmd14	*dpmdmt14* __/____ *dpmddate14*
pmd15	*dpmdmt15* __/____ *dpmddate15*

CRISP III

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

12. Over-the-counter medications changes:

12a. Since the last visit, have OTC drugs been added? *oayn* 0 ☐ No *(Go to #12b)* 1 ☐ Yes

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*
oma6	*domamt6* __ __/__ __ __ __ *domadate6*
oma7	*domamt7* __ __/__ __ __ __ *domadate7*

12b. Since the last visit, have OTC drugs been stopped/discontinued ? *odyn* 0 ☐ No *(Go to #13a)* 1 ☐ Yes

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 III **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

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 III

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 11 and 13

This form is to be completed at the participant's lab visit during years 11 and 13.

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

2. Location where samples were obtained: *labloc* 1 ☐ PCC 2 ☐ Other

3. Laboratory where samples were processed: *samproc* 1 ☐ PCC 2 ☐ Other

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 III

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: 1☐ 2☐ 3☐ 4☐ 5☐ *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 III

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: 1☐ 2☐ 3☐ 4☐ 5☐ *livacep*

Comment: _____ *livcom*

_____

10. Was the protocol followed? Score: 1☐ 2☐ 3☐ 4☐ 5☐ *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: 1☐ No 2☐ No 3☐ No 4☐ No 5☐ No *rbacep*

Comment: _____ *rbcom*

_____

13. Was the protocol followed? Score: 1☐ 2☐ 3☐ 4☐ 5☐ *rbprot*

Comment: _____ *rbprcom*

_____

14. Is a rescan necessary? *rbres* 0☐ No 1☐ Yes

CRISP III

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? *dttrans*	0 ☐ No	0 ☐ Yes
Indicate any problem below: _____ *dtprob*		

CRISP III

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*

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 III

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*

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*

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 III

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*

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*

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 III

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 *lcgroc*	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 III

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 III

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 III

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 III

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 III

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

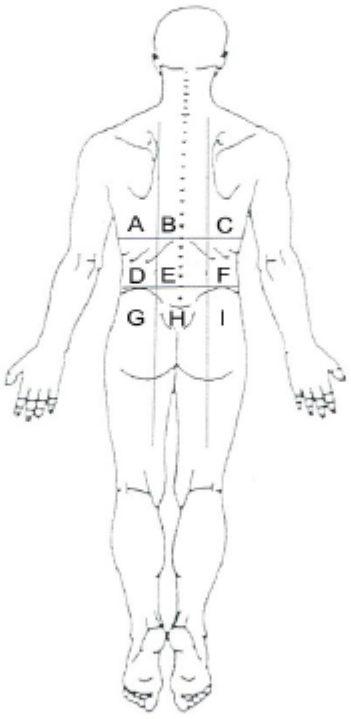
BACK PAIN

3. **Over the past 3 months,** how often 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
bklocа	*bklocb*	*bklocc*	*bklocd*	*bkloce*	*bklocf*	*bklocg*	*bkloch*	*bkloci*	*bklocu*

*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 one number that best describes how you would rate your back pain at its worst **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 one number that best describes how you would rate your back pain on average **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 <u>often</u> did you experience back pain radiating to your buttocks, hips or legs? *rdpnfrq*

(Choose one response only)

1 ☐ Never *(Go to #12)* | 2 ☐ Rarely | 3 ☐ Sometimes | 4 ☐ Often | 5 ☐ Usually | 6 ☐ Always

If you answered "Never", please go to #12

10. Check the <u>one</u> number that best describes how you would rate your back pain radiating into your buttocks, hips or legs <u>at its worst</u> **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 <u>one</u> number that best describes how you would rate your back pain radiating into your buttocks, hips or legs <u>on average</u> **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

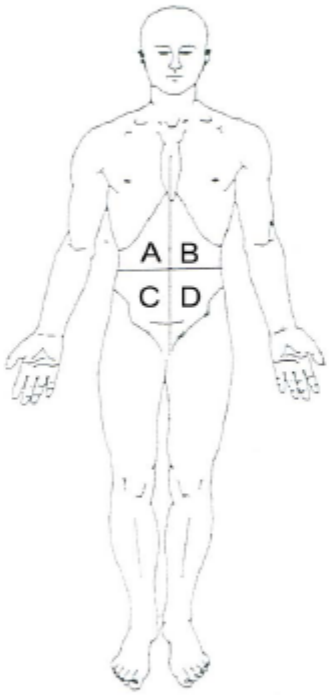
ABDOMINAL PAIN

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
abloca	*ablocb*	*ablocc*	*ablocd*	*ablocu*

*If you chose one letter only in **#13, please go to #15***

CRISP III

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.** *abpnmloc*

☐ 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*

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

No Pain — 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*

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

No Pain — 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 III

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 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
Never	Rarely	Sometimes	Often	Usually	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 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
Never	Rarely	Sometimes	Often	Usually	Always

20. How often was your appetite poor because of nausea in the past 3 months? *nausea*

(Choose one response only)

1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐
Never	Rarely	Sometimes	Often	Usually	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 III

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 III

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 __ __/__ __/__ __ __ __

CRISP III

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 10 and Year 12, the PI should review check off each form that has been completed and entered and sign below.

#	Form Description	Completed	Entered	Comments
2	Registration (visit 10 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 12 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*
59	Halt ID	☐ *haltcp*	☐ *haltent*	*haltcom*

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 III

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 10 and 12.

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.

Date of Collection: ____/____/_____ *dtcoll*

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 III

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:

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	Sample Not Shipped	Reason Sample Will Never Be Sent
1	**SST** Tiger-top for serum			*ttsh* ☐	*ttnotsh* ☐	
2	**SST** Green/gray for plasma			*gssh* ☐	*gsnotsh* ☐	

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 III

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:

Shipping Manifest: Repository – Urine Samples

This form is to be completed for the urine samples to be collected from the study participant and shipped to the NIDDK Repository at Fisher Bioservices. Samples are to be stored at the collection site (-80 degrees Celsius) and shipped to Fisher 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.

To complete this form:

1. Verify the number of tubes per sample and enter it in the appropriate field below.
2. Enter Specimen Box ID(s) in which tubes are stored. Cell IDs are optional. Note: Boxes are to be filled sequentially. Ideally, cells are filled from left to right and top to bottom for quicker cross checks when samples are received at Fisher.
3. Number the pages in sequence (lower right hand corner) and store then in the PCC freezer until time of shipment.
4. 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.
5. 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	Box ID	Cell ID	Check When Shipped	Provide Reason if Sample Will Never be Shipped
1	Fresh Void				*fvsh* ☐	
2	Pellet				*pelish* ☐	

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.

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: _____ *ufedexnum* **Date of Shipment:** ____/____/____ *urshipdt*

Name of Shipper/Form Completer: _____ **E-mail Address:** _____ */*

Phone: (_____)_____ **Fax:** (____)_____

Temperature: _____ ☐ Celsius ☐ Fahrenheit **Number of Boxes:** _____ *urnumbox* **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 III Shipping Manifest: Repository-Urine Samples, Form 49
Version 1,10/01/2011

CRISP III **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*

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	Accession ID	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 III

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 Visit 10 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 III

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 III

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 Blood Sample Collection Form

This form is to be completed at visit 10 and 12. Samples must be shipped on the day of collection to the NIDDK Biosample Repository at Fisher BioServices.

Date of Collection: ____/____/_____ *dtcoll*

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 __ __/__ __/__ __ __ __

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 III Missing Date Report, Form 54
Version 1, 10/01/2011

CRISP III

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 III Missing Date Report, Form 54
Version 1, 10/01/2011

CRISP III

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 12, 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 III

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*

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 III

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 LAB USE ONLY:

TO:

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 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: _____ ____/____/____ (DATE *emfxdt*) _____ AM/PM (TIME)

PACKAGE TRACKING #: _____ *packtrk* (CHECK SATURDAY DELIVERY ON DELIVERY FORM IF APPLICABLE)

TO BE COMPLETED BY 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 III

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:

Shipping Manifest Checklist

Once the forms below have been completed and entered for the participant's visit during Year 10 and Year 12, the PI should review check off each form that has been completed and entered and sign below.

#	Form Description	Completed	Entered	Comments
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	☐ *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 III Manifest Visit Checklist, Form 62
Version 1, 10/01/2011

CRISP III

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:

Transfer Form

This form is to be completed by the Study Coordinator whenever a participant transfers between clinics. The clinic of origin should complete this form. Please contact the destination clinic to coordinate date of transfer and other participant information.

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 III

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 reason for withdrawal. *otenr* *If yes, please specify briefly: otensp* _____ _____	0 ☐ No 1 ☐ Yes

CRISP III

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 III

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:

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: _____ Date: __ __/__ __/__ __ __ __ *dedate*
deidnum

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

CONSORTIUM FOR RADIOLOGIC IMAGING STUDIES OF POLYCYSTIC KIDNEY DISEASE

CRISP III

MRI Technologist Registration Form

Institution _____

Name _____

Telephone _____

E-mail Address _____

Equipment you will use for study (scanner manufacturer and name) _____

_____

Indicate Education and Experience:

Education _____

_____

Experience _____

_____

Are you a registered radiologic technologist? ( ) yes ( ) no

Have you passed the advanced registry in Magnetic Resonance Imaging? ( ) yes ( ) no

Have you read and reviewed the attached CRISP scanning protocol? ( ) yes ( ) no

Have you scanned a patient or phantom using the CRISP protocol? ( ) yes ( ) no

Can you provide us with any other pertinent information?

_____

_____

Signature _____ Date _____

Please complete and EMAIL or fax to Johana Schafer at schaferj@upmc.edu or fax: (412) 641-2582.

CRISP

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 III

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:

TRANSITIONAL SYMPTOMS FORM

This form is to be completed for any participant not in Crisp II for the time period between their last CRISP I contact and their Initial CRISP III visit.

Date of visit: *dvdate* ☐☐/☐☐/☐☐☐☐

1. **Enter symptoms experienced.**

CONSTITUTIONAL

Malaise/Feeling sickly or ill *tmal*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tmalspy* _____

HEAD/NECK

Headache *thead*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *theadspy* _____

Blurred Vision/Visual Changes *tblur*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tblurspy* _____

Dry Eyes/Nasal Passages *tdry*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tdryspy* _____

Nasal Congestion *tnas*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tnasspy* _____

Sore Throat *tsore*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tsorespy* _____

Dry Mouth/Excessive Thrist *tdrym*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tdrymspy* _____

CRISP III

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:

TRANSITIONAL SYMPTOMS FORM

CARDIOVASCULAR

Chest Pain *tchest*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tchestspy* _____

Heart Palpitations *theart*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *theartspy* _____

Dizziness/Lightheadedness *tdiz*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tdizspy* _____

Fatigue/Weakness *tfatig*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tfatigspy* _____

Leg Swelling/Edema *tleg*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tlegspy* _____

RESPIRATORY

Shortness of Breath with Exertion *tshbex*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tshbexspy* _____

Shortness of Breath at Rest *tshre*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tshrespy* _____

Cough *tcough*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tcoughspy* _____

MUSCULOSKELETAL

Joint Pain/Aches *tjoint*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tjointspy* _____

Muscle Pain/Cramping/Spasm *tmusc*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tmuscspy* _____

CRISP III

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:

TRANSITIONAL SYMPTOMS FORM

GENITOURINARY

Urinary Changes *turin*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *turinspy*_____

Visible Blood in Urine *tvsbl* Date __ __/__ __ /__ __ __ __ *tvsbldt*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tvsblspy*_____

Impotence/Decreased Libido *timpot*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *timpotspy*_____

Urinary Tract Infection *tuti* Date __ __/__ __ /__ __ __ __ *tutidt*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tutispy*_____

Kidney Stone *tkidst* Date __ __/__ __ /__ __ __ __ *tkidstdt*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tkidstspy*_____

DEMATOLOGIC

Changes of the Skin or Hair *tskin*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tskinspy*_____

GASTROINTESTINAL

Nausea/Vomiting *tnaus*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tnausspy*_____

Diarrhea *tdiar*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tdiarspy*_____

CRISP III

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:

TRANSITIONAL SYMPTOMS FORM

GASTROINTESTINAL (Continued)

Constipation *tconst*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tconstspy*_____

Stomach Discomfort/Abdominal Pain *tstom*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tstomspy*_____

Changes in Appetite *tappe*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tappespy*_____

NEUROLOGICAL

Mood Changes like Anxiety, Restlessness, Depression *tmood*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tmoodspy*_____

Tingling/Numbness *tnumb*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tnumbspy*_____

Problems with Memory *tmem*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tmemspy*_____

Drowsiness *tdrow*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tdrowspy*_____

Insomnia/Problems Sleeping *tinsom*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *tinsomspy*_____

Other Symptoms

totsm1 _____ *totsm1yn*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *totsm1spy*_____

CRISP III

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:

TRANSITIONAL SYMPTOMS FORM

Other Symptoms (Continued)

totsm2 _____ *totsm2yn*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *totsm2spy*_____

totsm3 _____ *totsm3yn*

0 ☐ Never 1 ☐ Once 2 ☐ Once a year 3 ☐ Around 6 time a year 4 ☐ Monthly 5 ☐ Weekly 6 ☐ Daily

Specify/Describe if applicable *totsm3spy*_____

Please complete History of Renal Pain on next page

CRISP III

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:

TRANSITIONAL SYMPTOMS FORM

2. History of Renal Pain in the last year.

2a. Was there pain in the right kidney since last Crisp I visit? *tlocrp* 0 ☐ No 1 ☐ Yes
If no, go to 2d *Go to 2b*

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

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 *tsevere*

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

2d. Was there pain in the left kidney since last Crisp I visit? *toclp* 0 ☐ No 1 ☐ Yes
If no, **Stop** *Go to 2e*

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

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 *tseverel*

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

CRISP III

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:

TRANSITIONAL SYMPTOMS FORM

3.	**For Males Only.**					
				If female, select N/A for Not Applicable		
3a.	**Have you ever had seminal vesicle cysts?** *tsemcysts*	☐ N/A	0 ☐ No	1 ☐ Yes	555555 ☐ Unknown	
3b.	**Have you ever had epididymal cysts?** *tepidcysts*	☐ N/A	0 ☐ No	1 ☐ Yes	555555 ☐ Unknown	

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 III

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:

Endpoints Form

This form is to be completed by designated personnel once the participant has reached KDOQI Stage IV, End Stage Renal Disease, or Death. The form should be updated every three months until Death has occurred.

NOTE: KDOQI Stage IV occurs when eGFR (using MDRD formula) falls below 30.

NOTE: ESRD is defined as the start of hemodialysis, peritoneal dialysis or kidney transplantation, at the discretion of the subject's primary nephrologist. This form, in addition to other lab and chart information, will be adjudicated by the medical advisor to ensure the start of dialysis or kidney transplantation is reasonable.

Date of Visit: *dvdate* ☐☐ / ☐☐ / ☐☐☐☐

Please document endpoint currently reached. *endpt*

1 ☐ KDOQI Stage IV *(Complete Section A & STOP)*
2 ☐ ESRD *(Complete Section B & STOP)*
3 ☐ Death *(Complete Section C & STOP)*

A. KDOQI Stage IV

Date KDOQI *kdoqidt* ☐☐ / ☐☐ / ☐☐☐☐

Serum creatinine value that triggered the Stage IV designation *(Not to be completed by site)* *scriv1* _____

eGFR that triggered the Stage IV designation *(Note to be completed by site)* *egfriv1* _____

If different, the most recent serum creatinine value *scriv2* _____ mgdL

eGFR calculated from most recent serum creatinine value *(Not to be completed by site)* *egfriv2* _____

B. ESRD

Date ESRD *esrddt* ☐☐ / ☐☐ / ☐☐☐☐

Type of Renal Replacement Therapy: *renrepther*

1 ☐ Decreased Donor Kidney Transplantation
2 ☐ Living Donor Kidney Transplantation
3 ☐ Hemodialysis
4 ☐ Peritoneal Dialysis
5 ☐ Other **Specify:** *renrepsp* _____

CRISP III

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:

Endpoints Form

Date of Transplantation or Start of Dialysis *dialdt* ☐☐/☐☐/☐☐☐☐

NOTE: If dialysis is started in the hospital and continues in an outpatient setting, use the date of the first in-house dialysis session. Do not include transient dialysis for acute renal failure that does not continue in the outpatient setting.

Was a nephrectomy performed prior to beginning dialysis and/or transplant? *neph*

0 ☐ No
1 ☐ Partial
2 ☐ Full
3 ☐ Unknown

Most recent serum creatinine value prior to start of dialysis and/or transplant _____mgdL *recsercr*

C. **Death**

Date of Death *deathdt* ☐☐/☐☐/☐☐☐☐

Was death kidney related? *deatkidrel*	0 ☐ No	1 ☐ Yes
Was an autopsy performed? *deatautper*	0 ☐ No	1 ☐ Yes
Was the death certificate obtained? *deatcert*	0 ☐ No	1 ☐ Yes

Cause of Death *deathcaus*_____

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 __ __/__ __/__ __ __ __

ADPKD Genetic Modifier Study

Family History Questionnaire

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

The following document is to collect information on your family history of kidney and liver disease. Please complete as much as possible if you have consented to take part in the study. The information from the form will be used to construct a family tree. The names and contact information of your family members is requested but we will not contact your relatives without permission from you to approach them.

Your name: _____
lname, fname

Mayo Clinic Number: _____
clinicnum

Telephone Number: _____
phone

1. Are you adopted? *adopted*

No ☐ Please complete the following information

Yes ☐ Please complete the following information only on your **biological** relatives (relatives *not adopted*, and *not by marriage*. Stop here if you do not have this information)

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

2. Please complete information about your father and mother

Name of Father _____ (*mblast, mbfirst, fammi*)

Address _____ (*street1, streeet2*)

_____ (*city, state, zip*)

Date of Birth _____ (*dob*)

Name of Mother _____

Address _____

_____

Date of Birth _____

Alive (*live*) yes ☐ no ☐ don't know ☐

If dead, cause and age

Cause_____ (*cause*)

Age _____ (*aged*)

Alive yes ☐ no ☐ don't know ☐

If dead, cause and age

Cause_____

Age _____

IF DECEASED, Did he have kidney or liver disease? (*dis*) yes ☐ no ☐ Don't know ☐

IF DECEASED, Did she have kidney or liver disease? yes ☐ no ☐ Don't know ☐

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

3. Please complete for your grandparents

Father's Parents

Name of grandfather_____
Address _____
_____
Date of Birth _____

Alive — yes ☐ no ☐ don't know ☐

If dead, cause and age — Cause_____ Age _____

IF DECEASED, Did he have kidney or liver disease? — Yes ☐ no ☐ Don't know ☐

Name of grandmother_____
Address _____
_____
Date of Birth _____

Alive — yes ☐ no ☐ don't know ☐

If dead, cause and age — Cause_____ Age _____

IF DECEASED, Did she have kidney or liver disease? — yes ☐ no ☐ Don't know ☐

Mother's Parents

Name of grandfather_____
Address _____
_____
Date of Birth _____

Alive — yes ☐ no ☐ don't know ☐

If dead, cause and age — Cause_____ Age _____

IF DECEASED, Did he have kidney or liver disease? — yes ☐ no ☐ Don't know ☐

Name of grandmother_____
Address _____
_____
Date of Birth _____

Alive — yes ☐ no ☐ don't know ☐

If dead, cause and age — Cause_____ Age _____

IF DECEASED, Did she have kidney or liver disease? — yes ☐ no ☐ Don't know ☐

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

4. Please complete for your brothers and sisters including half-brothers and half-sisters

Brother or Sister *rel relmblast, relmbfirst,relfammi, reladdress1 reladdress2 relcity, relstate relzip reldob*	**Relationship** _____ **Name** _____ **Address**_____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name** _____ **Address** _____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name** _____ **Address** _____ _____ _____ _____ **Date of Birth**_____
Alive	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐
If dead	cause _____ age _____	cause _____ age _____	cause _____ age _____
IF DECEASED, Did they have kidney or liver disease?	Don't yes no know ☐ ☐ ☐	Don't yes no know ☐ ☐ ☐	Don't yes no know ☐ ☐ ☐

Brother or Sister	**Relationship**_____ **Name**_____ **Address**_____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name**_____ **Address** _____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name**_____ **Address** _____ _____ _____ _____ **Date of Birth**_____
Alive	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐
If dead	cause _____ age _____	cause _____ age _____	cause _____ age _____
IF DECEASED, Did they have kidney or liver disease?	Don't yes no know ☐ ☐ ☐	Don't yes no know ☐ ☐ ☐	Don't yes no know ☐ ☐ ☐

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___ ___

5. Please complete for your father's brothers and sisters including half-brothers and half-sisters

Paternal Aunt or Uncle	**Relationship**_____ **Name**_____ **Address** _____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name** _____ **Address**_____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name**_____ **Address** _____ _____ _____ _____ **Date of Birth**_____
Alive	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐
If dead	cause _____ age _____	cause _____ age _____	cause _____ age _____
IF DECEASED, Did they have kidney or liver disease?	Don't yes no know ☐ ☐ ☐	Don't yes no know ☐ ☐ ☐	Don't yes no know ☐ ☐ ☐

Paternal Aunt or Uncle	**Relationship**_____ **Name**_____ **Address**_____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name** _____ **Address**_____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name**_____ **Address**_____ _____ _____ _____ **Date of Birth**_____
Alive	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐
If dead	cause _____ age _____	cause _____ age _____	cause _____ age _____
IF DECEASED, Did they have kidney or liver disease?	Don't yes no know ☐ ☐ ☐	Don't yes no know ☐ ☐ ☐	Don't yes no know ☐ ☐ ☐

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

6. Please complete for your mother's brothers and sisters, including half-brothers and half-sisters

Maternal Aunt or Uncle	**Relationship**_____ **Name**_____ **Address** _____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name**_____ **Address** _____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name**_____ **Address** _____ _____ _____ _____ **Date of Birth**_____
Alive	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐
If dead	cause _____ age _____	cause _____ age _____	cause _____ age _____
IF DECEASED, Did they have kidney or liver disease?	yes no Don't know ☐ ☐ ☐	yes no Don't know ☐ ☐ ☐	yes no Don't know ☐ ☐ ☐

Maternal Aunt or Uncle	**Relationship**_____ **Name**_____ **Address**_____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name** _____ **Address** _____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name**_____ **Address** _____ _____ _____ _____ **Date of Birth**_____
Alive	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐
If dead	cause _____ age _____	cause _____ age _____	cause _____ age _____
IF DECEASED, Did they have kidney or liver disease?	yes no Don't know ☐ ☐ ☐	yes no Don't know ☐ ☐ ☐	yes no Don't know ☐ ☐ ☐

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

7. Please complete for your children

Sons and Daughters

	Relationship_____	**Relationship**_____	**Relationship**_____
	Name_____ **Address**_____ _____ _____ _____ **Date of Birth**_____	**Name**_____ **Address**_____ _____ _____ _____ **Date of Birth**_____	**Name**_____ **Address**_____ _____ _____ _____ **Date of Birth**_____
Alive	yes ☐ no ☐ don't know ☐	yes ☐ no ☐ don't know ☐	yes ☐ no ☐ don't know ☐
If dead	cause _____ age _____	cause _____ age _____	cause _____ age _____
IF DECEASED, Did they have kidney or liver disease?	yes ☐ no ☐ Don't know ☐	yes ☐ no ☐ Don't know ☐	yes ☐ no ☐ Don't know ☐

Sons and Daughters

	Relationship_____	**Relationship**_____	**Relationship**_____
	Name_____ **Address**_____ _____ _____ _____ **Date of Birth**_____	**Name**_____ **Address** _____ _____ _____ _____ **Date of Birth**_____	**Name**_____ **Address**_____ _____ _____ _____ **Date of Birth**_____
Alive	yes ☐ no ☐ don't know ☐	yes ☐ no ☐ don't know ☐	yes ☐ no ☐ don't know ☐
If dead	cause _____ age _____	cause _____ age _____	cause _____ age _____
IF DECEASED, Did they have kidney or liver Disease?	yes ☐ no ☐ Don't know ☐	yes ☐ no ☐ Don't know ☐	yes ☐ no ☐ Don't know ☐

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

8. Please complete for any biological relatives, not included above, such as grand-uncles, grand-aunts, cousins, nephews, or nieces, with kidney or liver disease

	Relationship_____ **Name**_____ **Address** _____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name**_____ **Address**_____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name**_____ **Address**_____ _____ _____ _____ **Date of Birth**_____
Alive	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐
If dead	cause _____ age _____	cause _____ age _____	cause _____ age _____
IF Deceased, Did they have kidney or liver disease?	yes no Don't know ☐ ☐ ☐	yes no Don't know ☐ ☐ ☐	yes no Don't know ☐ ☐ ☐

	Relationship_____ **Name**_____ **Address**_____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Name**_____ **Address** _____ _____ _____ _____ **Date of Birth**_____	**Relationship**_____ **Nam** _____ **Address**_____ _____ _____ _____ **Date of Birth**_____
Alive	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐	yes no don't know ☐ ☐ ☐
If dead	cause _____ age _____	cause _____ age _____	cause _____ age _____
IF DECEASED, Did they have kidney or liver disease?	yes no Don't know ☐ ☐ ☐	yes no Don't know ☐ ☐ ☐	yes no Don't know ☐ ☐ ☐

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

Modifier Study 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 __ __/__ __/__ __ __

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

ADPKD Genetic Modifier Study NIDDK– Genetics 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

INITIAL: _____

YELLOW ML: _____

ID#: _____

FROM (SITE):

SHIPMENT TO INCLUDE BLOOD SAMPLES FOR CELL LINES

YELLOW TOP TUBES: ____

PLACE TUBE LABEL HERE OR COMPLETE BY HAND
(VERIFY INFO AGAINST INFO ON BLOOD TUBES!!!)

Sex: M ___ F ___ Age: _____

Alternate ID#: _____

FAMILY MEMBER 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 ____/____/____

Modifier Study 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 __ __/__ __/__ __ __

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

Accession Number: _____ **Date of Session** __ __/__ __/ __ __ __ __ **Repeat Scan** ____

MRI/CT Session FORM

☐ This accession number WILL NOT BE USED *numnotused*

☐ No scan – participant refused *norescan*

This form is to be completed by a radiology technologist or other designated personnel and reviewed by the radiologist at the time of the MRA. Readings are entered and averaged for each artery. The form is to be entered promptly and data transferred to the Imaging Analysis Center (IAC) right after the scan.

Date of Session: ☐☐ / ☐☐ / ☐☐☐☐ *mdsdate*
Month Day Year

Scan Type: *scantype*

☐ **PROSPECTIVE/RESEARCH - MR**
☐ **RETROSPECTIVE/CLINICAL - MR**
☐ **RETROSPECTIVE/CLINICAL - CT**

1. **Start Time:** _____:_____ (24 hr—participant on the table) *mrstarttime*

2. **Machine Model:**_____ *midnum /midname*
Technologist:_____ *tidnum*
Radiologist:_____ *ridnum/ridname*

3. **Scan Series Information**

4. **Adverse Events:** ☐ **None** *mraenone*

Series # *aeseries*	Event Description *aeevent*
_____	_____
_____	_____
_____	_____

5. **Stop Time:** _____:_____ (24 hr—participant off the table) *mrstophr : mrstopmin*

****

Modifier staff member completing this form: _____ **Date:** ____/____/____
cmidnum Month *cdm* Day *cdd* Year *cdy*

Reviewed by Radiologist (signature required): _____ **Date:** ____/____/____
Month Day Year

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

Primary Entered by: _____ Date: __ __/__ __/__ __ __
deidnum *dem* Month *ded* Day *dey* Year

3A. Renal Scan Series Information: Accession Number: ______________________ *mraid* MRI Form #6, page 2 (renal) 02.07.2012

* For 3mm T2, 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)x3=66mm. The **2nd shift mean** = -60 + 66 =6mm.

Series # *mrsid*	Name of MR/CT Sequence (circle one) *mrdesc*					Comments *mrcom*	# of Slices	Duration (seconds)	FOV
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer		*mrsn*	*mrsd*	*mrfov1* x *mrfov2*
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x
	T2 FatSat 9mm 3mm*	T2 Non-FatSat Adj-kidney Adj-liver	Pre T1	Post T1 120s 180s	Localizer				x

Omitted Series	Reason series was omitted
omseries	*omreas*

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

Accession Number: _____ **Date of Session** __ __/__ __/ __ __ __ __ **Repeat Scan** ____

3B. Cardiac Scan Series Information: Accession Number: _____ *mraid*

A set of cine-cardiac images should be obtained at each slice level using 2D-Cine Short Axis True FISP (FIESTA) sequence. The scan should cover starting from the apex to the atrioventricular ring. We prefer each set to be sent separately as individual series instead of combining all sets as a single series.

Series #	Comments *ccom*	# of Slices	FOV
csid		*csn*	*cfov1* X *cfov2*
			X
			X
			X
			X
			X
			X
			X
			X
			X
			X
			X
			X
			X
			X
			X
			X
			X
			X
			X
			X

Attention - DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

Accession Number: _____

ASSESSMENT OF QUALITY OF RADIOLOGIC STUDIES FORM

Studies Included: ☐ Kidney *kid* ☐ Liver *liv* ☐ Heart *hrt* ☐ RBF *rbf*

Date Received at IAC _____ *recdate* Quality Control Date _____ *qcdate*

Kidney

1. Is the quality of the images acceptable? (Excellent = 5, Poor = 1) *kdeval*

☐ 5 ☐ 4 ☐ 3 ☐ 2 ☐ 1

1a. Kidney scan decision. *kdevalq*

1 ☐ Scan is O.K. 0 ☐ Scan needs to be re-done 2 ☐ Not Applicable

1b. Indicate any problem: _____ *kdprob*

2. Was the protocol followed? (Excellent = 5, Poor = 1) *kdprot*

☐ 5 ☐ 4 ☐ 3 ☐ 2 ☐ 1

2a. Indicate any deviation below: *kddev*

_____

_____

Liver

3. Is the quality of the images acceptable? (Excellent = 5, Poor = 1) *lveval*

☐ 5 ☐ 4 ☐ 3 ☐ 2 ☐ 1

3a. Liver scan decision. *lvevalq*

1 ☐ Scan is O.K. 0 ☐ Scan needs to be re-done 2 ☐ Not Applicable

3b. Indicate any problem: _____ *lvprob*

4. Was the protocol followed? (Excellent = 5, Poor = 1) *lvprot*

☐ 5 ☐ 4 ☐ 3 ☐ 2 ☐ 1

4a. Indicate any deviation below: *lvdev*

_____

_____

Heart

5. Is the quality of the images acceptable? (Excellent = 5, Poor = 1) *cdeval*

☐ 5 ☐ 4 ☐ 3 ☐ 2 ☐ 1

Attention - DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

Accession Number: _____

ASSESSMENT OF QUALITY OF RADIOLOGIC STUDIES FORM

5a. Heart scan decision. *cdevalq*

1 ☐ Scan is O.K. 0 ☐ Scan needs to be re-done 2 ☐ Not Applicable

5b. Indicate any problem: _____ *cdprob*

6. Was the protocol followed? (Excellent = 5, Poor = 1) *cdprot*

☐ 5 ☐ 4 ☐ 3 ☐ 2 ☐ 1

6a. Indicate any deviation below: *cddev*

_____

_____

Renal Blood Flow (RBF)

7. Is the quality of the images acceptable? (Excellent = 5, Poor = 1) *rbfeval*

☐ 5 ☐ 4 ☐ 3 ☐ 2 ☐ 1

7a. Renal Blood Flow decision. *rbfevalq*

1 ☐ Scan is O.K. 0 ☐ Scan needs to be re-done 2 ☐ Not Applicable

7b. Indicate any problem: _____ *rbfprob*

8. Was the protocol followed? (Excellent = 5, Poor = 1) *rbfprot*

☐ 5 ☐ 4 ☐ 3 ☐ 2 ☐ 1

8a. Indicate any deviation below: *rbfdev*

_____

_____

Data Transmission

9. Were there any problems with the transmission of the data? *done* 0 ☐ No 1 ☐ Yes

9a. Indicate any problem below: *dttm*

_____

_____

****

Modifier staff member completing this form: _____ *cmidnum* **Date:** ___/___/___ ___ ___
Month *cdm* Day *cdd* Year *cdy*

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

Primary Entered by: _____ Date: ___ ___/___ ___/___ ___ ___
deidnum *dem* Month *ded* Day *dey* Year

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

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

ADPKD Genetic Modifier Study Questionnaire for CRISP participants

Please provide the following information to the best of your knowledge. For dates, if you do not know the specific date, please fill in the month and year. If month and day are both unknown, please fill in the year.

1. Today's date: ☐☐ / ☐☐ / ☐☐☐☐ *dtdate*
Month *dtmon* Day *dtday* Year *dtyear*

2. Have you signed and dated the written consent for this Research Study? *consent* 0 ☐ No 1 ☐ Yes

If no, PLEASE STOP – DO NOT COMPLETE ANY MORE QUESTIONS.

2a. If yes, date of Consent: ☐☐ / ☐☐ / ☐☐☐☐ *dcdate*
Month *dcmon* Day *dcday* Year *dcyear*

3. Are you currently enrolled in any observational or clinical trials for ADPKD *enroll* 0 ☐ No 1 ☐ Yes

3a. If *yes*, which study?

haltpkd 0 ☐ No 1 ☐ Yes HALT If HALT, HALT ID to be completed by staff _____ *haltid*
crisp 0 ☐ No 1 ☐ Yes CRISP If CRISP, CRISP ID to be completed by staff _____ *crispid*
tempo 0 ☐ No 1 ☐ Yes TEMPO If TEMPO, TEMPO ID to be completed by staff _____ *tempoid*
ostudy 0 ☐ No 1 ☐ Yes Other, Specify: _____ *spostdy* Duration: *drmons* months *dryrs* years

4. Grandparents Country of Origin
_____ *origin1*
_____ *origin2*

Complications

5. Have you had renal (flank) pain? 0 ☐ No 1 ☐ Yes *renalpain*

5a. If yes, frequency of renal (flank) pain: *renalpainnof*

1 ☐ Once
2 ☐ Less than once a year
3 ☐ 1 – 5 times a year
4 ☐ Monthly
5 ☐ Weekly
6 ☐ Daily/Constant
9998 ☐ Unknown

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

ADPKD Genetic Modifier Study Questionnaire for CRISP participants

5b. At what age did you first notice PKD related flank pain? _____ ☐ Check if age is unknown.
renalpainage *renalpainageunk*

5c. How severe has your worst pain been in the last month? *renalpainmth*

0 ☐ No pain in last month
1 ☐ Not requiring medication
2 ☐ Requiring analgesics
3 ☐ Requiring narcotic pain relief

6. Have you ever seen blood in your urine? 0 ☐ No 1 ☐ Yes *urineblood*

6a. If yes, frequency of blood in your urine: *ubldnof*

1 ☐ Once
2 ☐ Less than once a year
3 ☐ 1 – 5 times a year
4 ☐ Monthly
5 ☐ Weekly
6 ☐ Daily/Constant
9998 ☐ Unknown

7. Have you ever had a urinary tract infection? 0 ☐ No 1 ☐ Yes *uti*

7a. If yes, frequency of urinary tract infection: *utinof*

1 ☐ Once
2 ☐ Less than once a year
3 ☐ 1 – 5 times a year
4 ☐ Monthly
5 ☐ Weekly
6 ☐ Daily/Constant
9998 ☐ Unknown

Attention – DO NOT enter family member data on this form if the header does not contain *preprinted* Family Member ID, Family ID and Site specific ID.

Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

ADPKD Genetic Modifier Study Questionnaire for CRISP participants

8. Have you ever had a kidney stone? *kdnystn* 0 ☐ No 1 ☐ Yes

8a. If yes, frequency of kidney stones: *kdnystnnof*

1 ☐ Once
2 ☐ Less than once a year
3 ☐ 1 – 5 times a year
4 ☐ Monthly
5 ☐ Weekly
6 ☐ Daily/Constant
9998 ☐ Unknown

Other Diseases

9a. Have you ever been diagnosed with cancer of any kind (except for squamous or basal cell carcinoma non-melanoma skin cancer)
cancer

0 ☐ No 1 ☐ Yes

If yes, type: _____ *cancertype*

9b. Do you have an existing condition that would affect kidney function? (e.g. other primary kidney disease, systemic disease such as diabetes or amyloidosis, or nephrectomy due to polycystic kidney. *othercond*

0 ☐ No 1☐ Yes

If yes, specify: _____ *othercondsp*

Environmental

10a. Cigarette Smoking
Have you ever smoked cigarettes regularly? *cigar*

0 ☐ No 1 ☐ Yes

If yes, how many cigarettes/day, on average? _____ *cignm* For how many years? _____ *cigyr*

Are you currently a smoker? *smoker*

0 ☐ No 1 ☐ Yes

10b. Alcohol Intake
Do you drink alcohol regularly? *alcdr*

0 ☐ No 1 ☐ Yes

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Family Member ID:_____ **Family ID:**_____ **Site specific ID:** ___ ___ ___ ___ ___ ___ ___

ADPKD Genetic Modifier Study Questionnaire for CRISP participants

If yes, how many?
(12 oz) Bottles of beer/week: _____ *beernm* (4 oz) Glasses of wine/week: _____ *winenm* Shots of Liquor/week: _____ *liquornm*

For how many years? _____ *drinkyr*

10c. Tea/Coffee Drinking
Have you been a regular drinker of tea or coffee? *teacoffee*

1 ☐ Yes, tea 2 ☐ Yes, coffee 3 ☐ Yes, both 4 ☐ No, both

If yes, how many cups/day, on average? _____ *cupshm* For how many years? _____ *tcyr*

10d. Exercise and Activity

(a) Which of the following best describes your level of activity on the job? *activity*
1 ☐ Sedentary (e.g. office work);
2 ☐ Moderate Activity (requires considerable, but not constant lifting, walking, bending, pulling - e.g. homemaker without domestic assistance; policeman; student taking physical education course)
3 ☐ Strenuous Activity (requires almost constant lifting, walking, bending, pulling - e.g. furniture mover; heavy domestic work).
4 ☐ Not Applicable

(b) Do you exercise regularly (i.e. enough to work up a sweat ~ 30 minutes)? *exercise*
0 ☐ No 2 ☐ Yes

If yes, how long per session: _____ minutes *exlast*

How many times per week: _____ *exnm*

Modifier Study 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

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.

CRISPIII 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 CRISPIII investigators are:

Aim 1:. Extend the serial quantification of total kidney (TKV) and liver (TLV) and of kidney (KCV) and liver cyst (LCV) volumes in order to develop and test new models for predicting the risk of developing renal insufficiency.

Aim 2: Determine the extent to which age and sex-adjusted measurements of renal blood flow (RBF), determined by MR imaging, predict the rate of change in TKV and determine if RBF and TKV independently predict the risk of developing renal insufficiency.

Aim 3: Develop methods to quantify total cyst number, individual cyst volumes, and pattern of distribution of cysts in each kidney and apply these to analyze the influence of renal cyst number, volume, and topography at baseline on the subsequent course of TKV and GFR and the risk of developing renal insufficiency.

Aim 4: Expand and analyze CRISP biological samples collected in NIDDK repositories to improve genotype/phenotype and biomarker studies, and facilitate independently funded ancillary studies.

CRISPIII 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: Develop and evaluate models of renal insufficiency dependent on the local effects of cysts and the effects of chemokine and cytokine products synthesized by cysts.

Members of the ***CRISP Steering Committee*** include (Patient Care Site PIs noted in bold): W. M. Bennett (chair), **A. B.Chapman,** D. Landsittel **J.J.Grantham, M. Mrug**, M. Flessner, **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 CRISPIII 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 CRISPIII; 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 2001-200?? 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
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 III Study Biosample Repository

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.

07 Mar 2007

Biosample Repository

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.

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 III Study IRB Approval Letters

Data Coordinating Center Image Analysis Center IRB Approval Letter

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

To: Kyongtae Bae MD PHD
From: Sue Beers PHD, Vice Chair
Date: 9/6/2011
IRB#: PRO11070208
Subject: Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP)

The University of Pittsburgh Institutional Review Board reviewed and approved the above referenced study by the expedited review procedure authorized under 45 CFR 46.110 and 21 CFR 56.110. Your research study was approved under:
45 CFR 46.110.(5)
45 CFR 46.110.(6)
45 CFR 46.110.(7)

This study is supported by the following federal grant application:
2U01DK056961-12 Consortium for Radiologic Imaging Studies in Polycystic Kidney Disease (CRISP)

Approval Date: 9/6/2011
Expiration Date: 9/5/2012

For studies being conducted in UPMC facilities, no clinical activities can be undertaken by investigators until they have received approval from the UPMC Fiscal Review Office.

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 Events Coordinator at 412-383-1480.

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).

Emory University IRB Approval Letter

EMORY UNIVERSITY | Institutional Review Board

TO: Arlene Chapman, MD
Principal Investigator
Renal

DATE: September 30, 2011 (replaces version from September 22, 2011)

RE: **Full Board Approval**
IRB00052434
RENAL IMAGING TO ASSESS PROGRESSION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): EXTENSION (CONSORTIUM FOR RADIOLOGIC IMAGING STUDIES OF POLYCYSTIC KIDNEY DISEASE III)

Thank you for submitting a new application for this protocol. The Emory IRB reviewed it at its convened meeting on 8/24/2011 and granted approval pending minor changes. Upon receipt of the requested changes from study team, the IRB granted full approval effective from **8/24/2011** through **8/23/2012.** Thereafter, continuation of human subjects research activities requires the submission of another renewal application, which must be reviewed and approved by the IRB prior to the expiration date noted above. Please note carefully the following items with respect to this approval:

- Approved under 45 CFR 46.404 as research that poses no more than minimal risk to subjects
- One parent's signature required for the purposes of obtaining the consent of a minor
- Sensitive Study status confirmed; Key Points Summary for study #52434, submitted 7/22/2011, approved
- Study protocol, submitted 7/22/2011 , approved
- Main consent form, version date 9/15/2011, approved
- Family Sub-Aim consent form, version date 9/15/2011, approved
- Assent form, version date 9/15/2011, approved
- HIPAA Authorization form, version date 9/15/2011, approved
- Revocation letter, version date 7/22/2011, approved

Any reportable events (e.g., unanticipated problems involving risk to subjects or others, noncompliance, breaches of confidentiality, HIPAA violations, protocol deviations) must be reported to the IRB according to our Policies & Procedures at www.irb.emory.edu, immediately, promptly, or periodically. Be sure to check the reporting guidance and

contact us if you have questions. Terms and conditions of sponsors, if any, also apply to reporting.

Before implementing any change to this protocol (including but not limited to sample size, informed consent, study design, you must submit an amendment request and secure IRB approval.

In future correspondence about this matter, please refer to the IRB file ID, name of the Principal Investigator, and study title. Thank you.

Sincerely,

Sam Roberts, CIP
Research Protocol Analyst
This letter has been digitally signed

CC:			
	Ali	Nagzah	MedRenal
	Han	Yoosun	MedRenal
	Hitchcock	Stacie	MedRenal
	Jolley	Andee	MedRenal
	Watkins	Diane	MedRenal
	Williams	Olubunmi	MedRenal
	Masoumi	Amirali	GEN PED EGLESTON
	Mittal	Pardeep	Radiology - Main
	Rahbari Oskoui	Frederic	MedRenal

Emory University
1599 Clifton Road, 5th Floor - Atlanta, Georgia 30322
Tel: 404.712.0720 - Fax: 404.727.1358 - Email: irb@emory.edu - Web: http://www.irb.emory.edu/
An equal opportunity, affirmative action university

Mayo Clinic IRB Approval Letter

Protocol ID : 11-005494

Protocol Title: RENAL IMAGING TO ASSESS PROGRESSION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): EXTENSION (CRISP III)

Administrative Inquiry

Committee Name - (Project ID)	IRB-C - (11-005494)
Meeting Date	10/7/2011
Decision	Approve
Agenda Type	New Protocol
Link to:	View/Print Study
Letter to PI	**DECISION:** The Committee reviewed and approved the above referenced application and noted that all requirements for approval of research (45CFR46.111) were met. This approval is valid for one year unless during that time the IRB determines that it is appropriate to halt or suspend the study earlier. IRB approval will expire on October 06, 2012. The Committee approved the accrual of 358 male and female adult subjects. The Committee approved the following site to conduct this study: Mayo Clinic in Rochester, MN. **REVIEW:** The Committee noted receipt of the undated protocol. The Committee noted that the Data Safety Monitoring Plan was appropriate for the study. Funding for the study is provided by The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The Committee noted that travel expense reimbursement up to $500.00 per visit (for probands) will be provided. **CONTACT MATERIALS:** The Committee approved the subject contact letter, questionnaires, and telephone scripts as written. **CONSENT:** The Committee approved the consent forms (00 & 01) as written with updates to Mayo template. The final approved consent forms will be provided under the Documents tab of the main study workspace in IRBe. **REMINDERS:** The Committee: • Reminds the investigator that, per HIPAA regulations, protected health information collected during the screening of prospective subjects who do not subsequently sign the consent form and/or HIPAA authorization form must be discarded or de-identified. • Reminds the investigator to submit a continuing review report prior to the expiration date (reminder will be sent prior to expiration).
	DISCUSSION: The Committee noted no controverted issues.
Additional minutes	**REVIEW/CRITERIA:** The Committee approved the application in accordance with the following criteria: Approval of Research (45CFR46.111), Elements of Informed Consent (45CFR46.116), and Documentation of Informed Consent (45CFR46.117). **ADDITIONAL COMMITTEE APPROVAL:** The Committee noted the following committee approvals: Biospecimen Subcommittee dated September 6, 2011; Nephrology/Hypertension Research Committee dated August 18, 2011. **VOTE:** The Committee approved the above referenced application. A quorum was present during the vote. Vote Total = 9; For = 9; Opposed = 0; Abstained = 0.

University of Alabama-Birmingham IRB Approval Letter Approval Letter

OMB No. 0990-0263
Approved for use through 1/31/2012

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 Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP III) (PID, Innovative Imaging to Assess Progression (PCC))		5. Name of Principal Investigator, Program Director, Fellow, or Other MRUG, MICHAL

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 08/29/2016 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) 10/26/2011 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 F110901006
Protocol subject to Annual continuing review.	Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP III) (PID, Innovative Imaging to Assess Progression (PCC))

IRB Approval Issued: 10-26-11

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 University of Alabama at Birmingham 701 20th Street South Birmingham, AL 35294
11. Phone No. *(with area code)* (205) 934-3789 12. Fax No. *(with area code)* (205) 934-1301 13. Email: dhball@uab.edu	
14. Name of Official Ferdinand Urthaler, M.D.	15. Title Chairman, IRB
16. Signature Ferdinand Urthaler, MD/JC	17. Date 10-26-11

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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, S.W., 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

November 7, 2011

Project Number:	12891
Project Title:	CRISP III Protocol: Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP III)
Sponsor:	National Institutes of Health
Protocol Number:	2U01DK056943-11
Protocol Version/Date:	20 July 2011
Primary Investigator:	Jared J. Grantham, M.D.
Department	Internal Medicine
Meeting Date:	09/20/2011
HSC Approval Date:	11/04/2011
HSC Expiration Date:	11/03/2012
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 appropriate Problem Report, found on the HSC website.
(4) Report deviations from previously approved research by using the Report of Non-Compliance, found on the HSC website.
(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
NOV 08 2011
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 III Study Consent Forms

Emory University Consent Form

Study No.: IRB00052434 | **Emory University IRB** IRB use only | Document Approved On: 8/24/2011 Project Approval Expires On: **8/23/2012**

Emory University
Consent to be a Research Subject

Title: **CONSORTIUM FOR RADIOLOGIC IMAGING STUDIES OF POLYCYSTIC KIDNEY DISEASE (CRISP III)**

Principal Investigator: **Arlene B. Chapman, MD**
Co-Investigator: **Pardeep Mittal, MD,**
Sub-Investigators: **Frederic Rahbari Oskoui, MD; Amirali Masoumi, MD**

Sponsor: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH)

If you are the legal guardian of a child who is being asked to participate, the term "you" used in this consent refers to your child

Introduction

You are being asked to be in a medical research study funded by the National Institutes of Health (NIH). This form is designed to tell you everything you need to think about before you decide to consent (agree) to be in the study or not to be in the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most the website will include a summary of the results. You may search this website at any time.

Study Overview

You are being asked to participate because you have autosomal dominant polycystic kidney disease (ADPKD), 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 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 United States 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 Clinical

Interaction Network (CIN) inpatient or outpatient unit at Emory University Hospital and the Satellite CIN at Emory Midtown Hospital.

Procedures

The CRISP III protocol includes participants that enroll in other interventional trials. If CRISP III participants are recruited into an interventional trial (e.g. HALT clinical trial that also requires imaging studies) the visits for CRISP III 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 III 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 de-identified 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 de-identified 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 III study. As part of 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 Clinical Interaction Network (CIN) at Emory University Hospital for testing.

B: CLINICAL INTERACTION NETWORK (CIN) STAY at Year 1 and Year 3:

You will spend as few as one and as many as two days at the inpatient or outpatient CIN at Emory University Hospital. These visits will occur at Year 1 and Year 3 of your participation in 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 and/or CRISP II. 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 CIN 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 60ml (4 tablespoons) of blood will be taken for these tests. De-identified (identified by CRISP ID number only) blood and urine samples will be shared with other CRISP site investigators. Some of these blood and urine samples will be sent to the NIDDK Central Repositories (described below).

NIDDK CENTRAL REPOSITORIES:

We are asking you to provide a sample of blood, urine, which will be sent to the NIDDK Central Repositories, 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 ADPKD, 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 ADPKD.

The Repository will take measures to protect your privacy, although no guarantee of confidentiality can be absolute. Before the researchers in this study send samples to the Repository, each sample will be given a code number. Your name, and all personal identifying information, such as address, social security number, and date of birth, will be removed. Therefore, the Repository will not be able to give out your name, or other information that identifies you to the scientists who receive the samples. However, the Repository and scientists will have some data about you, such as age, sex, diagnosis, race, and outcomes of the initial study.

You will not receive any direct benefit or payment for participating, but your sample may benefit the future health of the community at large or some particular group. Because other researchers will not have access to your identity, neither you nor your physician will get the eventual results of studies that might be performed using your sample. It is possible that data resulting from use of your sample may eventually be used in a research publication. In that event, your name or other identifying information will not be included, as this information will not be available to the researchers.

It is important for you to understand that there is a small chance that some research may yield results that may indirectly have a negative impact on insurability, employability, and/or family relationships of some individuals or groups of people.

Sometimes, research results in findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery. Some of the profits from this may be paid back to the researchers and the organizations doing this study, but you will not receive any financial benefits.

Your donation is voluntary, and if you choose not to participate there will be no penalty or loss of benefits to which you are entitled. Please *initial* your choice below.

_____ Yes, I agree to have my blood and urine samples stored in the NIDDK Biosample Repository.

_____ No, I do not agree to have my blood and urine samples stored in the NIDDK Biosample Repository.

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.

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 while pictures of your kidneys are taken. 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 genetic testing or DNA analysis, if needed, will be obtained once.

C: OPTIONAL CLINICAL INTERACTION NETWORK (CIN) VISIT at Year 2 and Year 4:

At years 2 and 4, you will have 20 ml of blood samples (2 tablespoons) collected either at the CIN 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 CIN to be processed.

OUTPATIENT FOLLOW-UP:

After the CIN tests are done, you will be discharged from the CIN and continue under the care of your own primary care 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 three months between CIN 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.

Risks and Discomforts

There may be side effects from the study procedures that are not known at this time.

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 drawing blood 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.

New Information

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Benefits

This study is not designed to benefit you directly. Your ADPKD may improve while you are in this study but it may not, and it may even get worse. This study is designed to learn more about ADPKD. The study results may be used to help others in the future. 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.

Compensation

You will receive $200 for each CIN Stay (Year 1 and Year 3 visits). You will not be compensated for the two outpatient visits (Year 2 and Year 4 visits). If you do not finish the study, you will be paid for the visits you have completed. Compensation will be paid by check 3-4 weeks after the completion of each visit. You will receive $400 total, if you complete all study visits.

Other Treatment Outside this Study

If you decide not to enter this study, there is care available to you outside of this research. The study doctor will discuss these options with you. You do not have to be in this study to be treated for ADPKD.

If you decide to participate in this study, 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

Given the hereditary nature of ADPKD, extra care will be taken to maintain your anonymity. Certain offices and people other than the researchers may look at your medical charts and study records. Government agencies and Emory employees overseeing proper study conduct may look at your study records. These offices include the Office for Human Research Protections, the Emory Institutional Review Board, the Emory Office of Research Compliance, the Office for Clinical Research, the Clinical Trials Audit & Compliance Office. The National Institutes of Health, the study sponsor, may also look at your study records. Emory will keep any research records we create private to the extent we are required to do so by law. A study number rather than your name will be used on study records wherever possible. Your name and other facts that might point to you will not appear when we present this study or publish its results.

Study records can be opened by court order. They may also be produced in response to a subpoena or a request for production of documents.

Research Information That Will and Will Not Go Into the Medical Record:

If you are or have been an Emory Healthcare patient, you have an Emory Healthcare medical record. If you are not and have never been an Emory Healthcare patient, you do not have one. Please note that an Emory Healthcare medical record **will** be created if you have any services or procedures done by an Emory provider or facility for this study.

If you agree to be in this study, a copy of the consent form and HIPAA patient form that you sign **will not** be placed in your Emory Healthcare medical record. Emory Healthcare may create study information about you that can help Emory Healthcare take care of you. For example, the results of study tests or procedures. These useful study results will be placed in your Emory Healthcare medical record. Anyone who has access to your medical record will be able to have

access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA Privacy Rule. On the other hand, some state and federal laws and rules may not protect the research information from disclosure.

Emory does not control results from tests and procedures done at other places, so these results would not be placed in your Emory Healthcare medical record. They will not likely be available to Emory Healthcare to help take care of you. Emory also does not have control over any other medical records that you may have with other healthcare providers. Emory will not send any test or procedure results from the study to these providers. If you decide to be in this study, it is up to you to let them know.

The researchers will review the results of certain study tests and procedures only for the research. The researchers **will not** be looking at the results of these tests and procedures to make decisions about your personal health or treatment. For this study, those things include: the GFR test, MRI, and analysis of genetic samples.

In Case of Injury

If you get ill or injured from being in the study, Emory would help you to get medical treatment. Emory and the sponsor have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proved that your injury or illness is directly caused by the negligence of an Emory or sponsor employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this trial, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Arlene Chapman at telephone number 404-727-1993. You should also let any health care provider who treats you know that you are in a research study.

Costs

There will be no costs to you for participating in this study, other than basic expenses like transportation. You will not be charged for any of the research activities.

Withdrawal from the Study

You have the right to leave a study at any time without penalty. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers and sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interest;
- You were to object to any future changes that may be made in the study plan;
- or for any other reason.

Contact Information

Contact Dr. Arlene Chapman at 404-712-1993:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent

Please, print your name and sign below if you agree to be in this study. By signing this consent form, you will not give up any of your legal rights. We will give you a copy of the signed consent, to keep.

_____
Name of Subject

_____ _____
Signature of Subject Date Time

_____ _____
Signature of Person Conducting Informed Consent Discussion Date Time

_____
Name of Person Conducting Informed Consent Discussion

_____ _____
Signature of Legally Authorized Representative Date Time

_____
Authority of Legally Authorized Representative or Relationship to Subject

_____ _____
Signature of Assent for 17 year old Subject Date Time

Study No.: IRB00052434 **Emory University IRB** IRB use only Document Approved On: 8/24/2011 Project Approval Expires On: **8/23/2012**

Emory University Research Subject HIPAA Authorization to Use or Disclose Health Information that Identifies You for a Research Study

Title: CONSORTIUM FOR RADIOLOGIC IMAGING STUDIES OF POLYCYSTIC KIDNEY DISEASE (CRISP III)

Principal Investigator: Arlene B. Chapman, MD
Co-Investigator: Pardeep Mittal, MD, -
Sub-Investigators: Frederic Rahbari Oskoui, MD; Amirali Masoumi, MD

Sponsor: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH)

Introduction
The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act (HIPAA). We refer to all of these laws in this form as the Privacy Rules. This form explains how we will use your PHI for this study.

Please read this form carefully and if you agree with it, sign it at the end.

Description of Research Study
You are being asked to participate 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. A GFR test will be done, and blood and urine samples will be taken. You will also complete questionnaires.

PHI That Will Be Used/Disclosed
The PHI that we may use or disclose (share) for this research study includes: results of blood tests and imaging studies, entire medical record, and answers to survey questions.

Purposes for Which Your PHI Will Be Used
If you sign this form, you give us your permission to use your PHI for the conduct and oversight of this research study.

People That Will Use or Disclose Your PHI and Purpose of Use/Disclosure
Different people and groups will use and disclose your PHI. They will do this only in connection with the research study. The following persons or groups may use and/or disclose your PHI:

- The Principal Investigator and the research staff.
- The Principal Investigator may use other people and groups to help conduct the study. These people and groups will use your PHI to do this work.
- The NIH is the Sponsor of this Research. The Sponsor may use and disclose your PHI to make sure the research is done correctly. They may also use your PHI to collect and analyze the results of the research. The Sponsor may have other people and groups help conduct, oversee, and analyze the study. These people or groups will use your PHI.

- The following groups may also use and disclose your PHI. They will do this to make sure the research is done correctly and safely. The groups are:
  - the Emory University Institutional Review Board
  - the Emory University Office for Clinical Research
  - the Emory University Office of Research Compliance
  - research monitors and reviewers
  - data and safety monitoring boards
  - any government agencies who regulate the research including the Office of Human Subjects Research Protections
  - public health agencies
  - researchers working on this study at the other CRISP III sites:
    University of Pittsburg, Pittsburg, PA
    Mayo Foundation, Rochester, MN
    Kansas Medical Center, Kansas City, KS
    University of Alabama, Birmingham, AL

We will use or disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or elder abuse. We also will comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Revoking Your Authorization

You do not have to sign this form. Even if you do, at any time later on you may revoke (take back) your permission. If you want to do this, you must write to:

Dr. Arlene Chapman
Emory University School of Medicine/Renal Division
1010 Woodruff Circle Room 338
Atlanta GA 30322

After that point, the researchers would not collect any more of your PHI. But they may use or pass along the information you already gave them so they can follow the law, protect your safety, or make sure the research was done properly. If you have any questions about this, please ask.

Other Items You Should Know

If we disclose information to people who do not have to follow the Privacy Rules, your information will no longer be protected by the Privacy Rules. People who do not have to follow the Privacy Rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them. Let us know if you have questions about this.

You do not have to sign this form. If you do not sign, you may not participate in the research study.

We will **not** put a copy of your signed informed consent form for the research study and your signed HIPAA Authorization form into any medical record that you may have with Emory Healthcare facilities.

During the study you will generally not have access to records related to the research study. This is to preserve the integrity of the research. You may have access to these records when the study is

complete. These records may include research related PHI your health care providers use to make decisions about your care. If necessary for your care, this information may be available to your doctor before the end of the study.

If identifiers are removed from your PHI, then the remaining information will not be subject to the Privacy Rules. It may be used or disclosed with other people or organizations, and/or for other purposes.

Expiration Date
Your permission to use and disclose your PHI will **not** expire. The researchers will add your PHI to a database that they are compiling for research purposes.

Contacts
If you have any questions regarding the study, you may call Dr. Arlene Chapman at 404-712-1993.

If you have any questions about the study, or your rights as a study subject, you may contact the Emory University Institutional Review Board at 404-712-0720 or 1-877-503-9797, by email at irb@emory.edu.

Authorization
A copy of this form will be given to you.

_____
Signature of Study Subject OR Subject's Legal Authorized Representative

_____ _____
Date Time

_____
Printed Name of Study Subject OR Subject's Legally Authorized Representative

If Representative, Relationship to Study Subject: _____

_____
Signature of Person Obtaining Authorization

_____ _____
Date Time

_____
Printed Name of Person Obtaining Authorization

_____ _____
Date Time

Emory University Relative Consent Form

Study No.: IRB00052434 | **Emory University IRB** IRB use only | Document Approved On: 8/24/2011 Project Approval Expires On: **8/23/2012**

Emory University
Consent to be a Research Subject

Title: CRISP FAMILY STUDY: CONSORTIUM FOR RADIOLOGIC IMAGING STUDIES OF POLYCYSTIC KIDNEY DISEASE (CRISP III) – **SubAim 4.1**

Principal Investigator: Arlene B. Chapman, MD
Co-Investigator: Pardeep Mittal, MD,
Sub-Investigators: Frederic Rahbari Oskoui, MD; Amirali Masoumi, MD

Sponsor: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH)

If you are the legal guardian of a child who is being asked to participate, the term "you" used in this consent refers to your child

Introduction

You are being asked to be in a medical research study funded by the National Institutes of Health (NIH). This form is designed to tell you everything you need to think about before you decide to consent (agree) to be in the study or not to be in the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

Study Overview

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 in Birmingham, AL and Kansas University Medical Center in Kansas City, KS.

Procedures

A spot check urine sample will be obtained during your CIN visit. The urine will be processed and stored locally for future biomarker studies. A blood sample (50 mL or less than four tablespoonfuls) will be obtained by venipuncture for a measurement of serum creatinine, extraction of DNA and for future biomarker studies. 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 for review. The entire procedure should take 30 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. 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.

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* your choice below:

_____ Yes, I agree that the Principal Investigator may retain information that links my sample with my name.

_____ No, I do not agree that the Principal Investigator may retain information that links my sample with my name.

Risks and Discomforts
There may be side effects from the study procedures that are not known at this time. There are risks related to drawing blood that include pain, bruising and infection.

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 the Principal Investigator for this study.

New Information
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. Your name will not be given to scientists for research purposes.

Benefits
This study is not designed to benefit you directly. This study is designed to learn more about ADPKD. The study results may be used to help others in the future.

Compensation
You will not be offered payment for being 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.

Confidentiality

Given the hereditary nature of ADPKD, extra care will be taken to maintain your anonymity. Certain offices and people other than the researchers may look at your medical charts and study records. Government agencies and Emory employees overseeing proper study conduct may look at your study records. These offices include the Office for Human Research Protections, the Emory Institutional Review Board, the Emory Office of Research Compliance, the Office for Clinical Research, the Clinical Trials Audit & Compliance Office. The National Institutes of Health, the study sponsor, may also look at your study records. Emory will keep any research records we create private to the extent we are required to do so by law. A study number rather than your name will be used on study records wherever possible. Your name and other facts that might point to you will not appear when we present this study or publish its results.

Study records can be opened by court order. They may also be produced in response to a subpoena or a request for production of documents.

Research Information That Will and Will Not Go Into the Medical Record:

If you are or have been an Emory Healthcare patient, you have an Emory Healthcare medical record. If you are not and have never been an Emory Healthcare patient, you do not have one. Please note that an Emory Healthcare medical record **will** be created if you have any services or procedures done by an Emory provider or facility for this study.

If you agree to be in this study, a copy of the consent form and HIPAA patient form that you sign **will not** be placed in your Emory Healthcare medical record. Emory Healthcare may create study information about you that can help Emory Healthcare take care of you. For example, the results of study tests or procedures. These useful study results will be placed in your Emory Healthcare medical record. Anyone who has access to your medical record will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA Privacy Rule. On the other hand, some state and federal laws and rules may not protect the research information from disclosure.

Emory does not control results from tests and procedures done at other places, so these results would not be placed in your Emory Healthcare medical record. They will not likely be available to Emory Healthcare to help take care of you. Emory also does not have control over any other medical records that you may have with other healthcare providers. Emory will not send any test or procedure results from the study to these providers. If you decide to be in this study, it is up to you to let them know.

The researchers will review the results of certain study tests and procedures only for the research. The researchers **will not** be looking at the results of these tests and procedures to make decisions about your personal health or treatment. For this study, those things include: analysis of genetic samples.

In Case of Injury

If you get ill or injured from being in the study, Emory would help you to get medical treatment. Emory and the sponsor have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proved that your injury or illness is directly caused by the negligence of an Emory or sponsor employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this trial, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Arlene Chapman at telephone number 404-727-1993. You should also let any health care provider who treats you know that you are in a research study.

Costs

There will be no costs to you for participating in this study, other than basic expenses like transportation. You will not be charged for any of the research activities.

Withdrawal from the Study

You have the right to leave a study at any time without penalty. If you leave the study before the final planned study visit, the researchers may ask you to have some of the final steps done.

The researchers and sponsor also have the right to stop your participation in this study without your consent if:

- They believe it is in your best interest;
- You were to object to any future changes that may be made in the study plan;
- or for any other reason.

Contact Information

Contact Dr. Arlene Chapman at 404-712-1993:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study drug, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent

Please, print your name and sign below if you agree to be in this study. By signing this consent form, you will not give up any of your legal rights. We will give you a copy of the signed consent, to keep.

_____

Name of Subject

_____ _____

Signature of Subject Date Time

_____ _____

Signature of Person Conducting Informed Consent Discussion Date Time

_____

Name of Person Conducting Informed Consent Discussion

Study No.: IRB00052434 **Emory University IRB** IRB use only Document Approved On: 8/24/2011 Project Approval Expires On: **8/23/2012**

Signature of Legally Authorized Representative Date Time

Authority of Legally Authorized Representative or Relationship to Subject

Signature of Assent for 17 year old Subject Date Time

Mayo Clinic Consent Form

MAYO CLINIC

Name and Clinic Number

To be completed by IRB office:
IRB # 11-005494 01
Consent form approved October 7, 2011;
This consent valid through October 6, 2012;

1. General Information About This Research Study

Study Title: Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP III) (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 or the CRISP II extension 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.

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. 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 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.

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C. Additional Information You Should Know

The NIH (National Institutes of Health) 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.

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 two visits. These visits will occur at years one and three of this study. At years two and four you will be asked to provide a blood sample and you have a choice of whether or not you are seen.

A. Year 1 and Year 3 Visits

For these visits you will be admitted to the In-Patient Clinical Research Unit (CRU) at St. Marys Hospital. After you are finished at the CRU, you will see one of the research doctors on this study. The following tests and examinations will be performed at the CRU for these visits:

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/CRISP II.

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. 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. De-identified 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.

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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.

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.

A major part of CRISP III is to collect more complete and updated family histories of all CRISP I and CRISP II 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

At Years 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. If you would like to be seen at these time points we will schedule an appointment for you.

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C. Quarterly Telephone Interviews

Every three 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 have 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 III protocol does not exclude participants that enroll in other interventional trials. If, as a CRISP III participant, you are recruited into an interventional trial (e.g. HALT clinical trial that also requires imaging studies) the visits for CRISP III 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 III 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 de-identified 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 de-identified 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: _____

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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 two phases of the CRISP study (CRISP I and CRISP II) in which you participated have helped us to understand how polycystic kidney disease progresses. CRISP III 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 and 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 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.

The risks of performing an MRI are minimal. 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 III 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.

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As with all research studies, there may be risks we are not aware of which could include life threatening reactions.

Pregnancy and Birth Control:

1) Will women of child-bearing-potential (able to become pregnant) be allowed to participate in this study?

   Yes: Women of child-bearing-potential will be able to participate in this study if they have a negative pregnancy test and agree to use acceptable birth control (see #5) since the risks to an unborn child are either unknown or potentially serious.

2) Will 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.

3) 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 urine pregnancy test will be given by submitting a urine sample to be tested.

   You will be told the results of the pregnancy test. If the pregnancy test is positive, you will be delayed in any participation for this study until after delivery and lactation ends.

4) Will men who are able to father a child be allowed to participate in this study?

   Yes: Men who are able to father a child are allowed to take part in this study.

5) What types of birth control are acceptable?

   Surgical sterilization
   Approved hormonal contraceptives (such as birth control pills, Depo-Provera)
   Barrier methods (such as a condom or diaphragm) used with a spermicide
   An intrauterine device (IUD)
   Abstinence

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 less uncomfortable. Talk to the researcher and/or your healthcare provider about side effects and ask any other questions.

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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, 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:

- Physical examination
- Medical history
- MRI
- GFR test
- Blood tests (creatinine, chemistry, cholesterol profile)
- Urine pregnancy test

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.

If you have study related questions regarding billing, insurance or reimbursement, stop by: Admission and Business Services office, or call Patient Account Services at (507) 266-5670.

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9. Will You Be Paid for Participating in this Research Study?

You will be reimbursed for mileage, parking, hotels, meals, airfare, etc. up to $500.00 per visit. In order to receive reimbursement, you must provide a copy of the original receipts for those expenses.

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.

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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.

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 de-identified and Mayo will take steps to help other parties understand the need to keep this information confidential.

This authorization lasts forever.

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.

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13. What Will Happen to Your Samples?

Your sample of blood will be kept at The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) repository located at Rutgers University in New Brunswick, New Jersey for use in this study. The NIDDK receives blood samples collected in many different studies and processes them to create immortalized cell lines (An immortalized cell-line means a portion of your sample will be treated in such a way that the cells continue to grow in a test tube. This allows researchers to have an unlimited supply of your cells in the future without asking for more samples from you.) and DNA samples. In addition, the Genetics Repository also cryopreserves blood cells, extracts DNA from blood samples, stores samples of DNA under optimal conditions, and distributes DNA samples to qualified investigators. The Contractor for the Genetics Repository is Rutgers, The State University of New Jersey, New Brunswick, NJ. Rutgers University is the site that will be running the analysis on your blood samples for this research. This is being done at Rutgers because there are multiple sites participating (including Mayo).

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 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:

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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.

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I permit Mayo to give my sample to researchers at other institutions:
Please mark one box:

☐ Yes ☐ No Please initial here: _____Date: _____

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. 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 Operator)	**Questions about the study tests and procedures** **Research-related injuries or emergencies**
Study Coordinator: Vickie Kubly	(507) 266-9207	**Any research-related concerns or complaints**
Mayo Clinic IRB **Research Subject Advocate**	**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) 266-5670	**Billing / Insurance Questions**

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15. Summary and Enrollment Signatures

You have been asked to take part in a research study at Mayo Clinic. The information about this study has been provided to you to inform you about this study.

- I have read the whole consent form, and all of my questions have been answered to my satisfaction.
- I am satisfied that I have been given enough information about the purpose, methods, risks, and possible benefits of the study to decide if I want to join.
- I know that joining the study is voluntary and I agree to join the study.
- I know that I can call the investigator and research staff at any time with any questions or to tell them about side effects.
- I know that I may withdraw from the study at any time.
- A copy of this form will be put in my medical records and I will be given a copy of this completed form.

Please sign and date to show that you have read all of the above guidelines. Please do not sign unless you have read this entire consent form. 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 Relative Consent Form

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Name and Clinic Number

To be completed by IRB office:
IRB # 11-005494 00
Consent form approved October 7, 2011;
This consent valid through October 6, 2012;

1. General Information About this Research Study

Study Title: Renal Imaging to Assess Progression in Autosomal Dominant Polycystic Kidney Disease (ADPKD): Extension (CRISP III) (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 or the CRISP II extension study. The purpose of this study is to collect more complete family histories of all CRISP patients and draw a family tree (pedigree) of each family and to identify genetic factors that may influence the severity of the cystic disease.

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. 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 to take part in this study.

If you are unclear about anything along the way, please ask questions until you feel you understand.

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B. Number of Participants

Up to 300 affected relatives of CRISP participants will be enrolled into this study at the Mayo Clinic, 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 National Institutes of Health (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.

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 to assess kidney disease and to isolate DNA to identify genetic risk factors that influence the course of your disease. 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 may be asked to have a new MRI of your abdomen. If this MRI is done at Mayo, signing this form will allow us to use the MRI for this study as well as studies directly related to this one, which includes the possibility of a site beyond Mayo (our collaborators). If your MRI is done somewhere other than Mayo, we will ask that you complete the *"Authorization to Release Medical Information to Mayo Clinic"* form. When using MRI images or data outside of Mayo your information will be de-identified as it is for all information shared outside of Mayo. If you have an MRI that is recent enough for use in this study, the same processes will apply if you have it at Mayo or a different institution.

3. How Long Will You Be in This Research Study?

You will be in this study for one day.

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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, and rarely, infection at the site of the needle stick.

The risks of performing an MRI of your abdomen are minimal. An MRI is a non-invasive, diagnostic test which uses magnetic imaging to take pictures of your abdomen. 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.

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.

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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 include:

- Blood draw
- Measurement of serum creatinine
- Extraction of blood DNA for genetic testing
- MRI, if an MRI is ordered for this study

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.

If you have study related questions regarding billing, insurance or reimbursement, stop by: Admission and Business Services office, or call Patient Account Services at (507) 266-5670.

9. Will You Be Paid for Participating in this Research Study?

You will not be paid for taking part in this study.

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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.

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.

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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.

This authorization lasts forever.

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.

13. What Will Happen to Your Samples?

Your sample of blood will be kept at The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) repository located at Rutgers University in New Brunswick, New Jersey for use in this study. The NIDDK Receives blood samples collected in many different studies and processes them to create immortalized cell lines (An immortalized cell-line means a portion of your sample will be treated in such a way that the cells continue to grow in a test tube. This allows researchers to have an unlimited supply of your cells in the future without asking for more samples from you.) and DNA samples. In addition, the Genetics Repository also cryopreserves blood cells, extracts DNA from blood samples, stores samples of DNA under optimal conditions, and distributes DNA samples to qualified investigators. The Contractor for the Genetics Repository is Rutgers, The State University of New Jersey, New Brunswick, NJ. Rutgers University is the site that will be running the analysis on your blood samples for this research. This is being done at Rutgers because there are multiple sites participating (including Mayo).

MAYO CLINIC

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 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.

MAYO CLINIC

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.

I permit Mayo to give my sample to researchers at other institutions:
Please mark one box:

☐ Yes ☐ No Please initial here: _____Date: _____

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. 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 Operator)	**Questions about the study tests and procedures** **Research-related injuries or emergencies**
Study Coordinator: Vickie Kubly	(507) 266-9207	**Any research-related concerns or complaints**
Mayo Clinic IRB **Research Subject Advocate**	**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) 266-5670	**Billing / Insurance Questions**

MAYO CLINIC

15. Summary and Enrollment Signatures

You have been asked to take part in a research study at Mayo Clinic. The information about this study has been provided to you to inform you about this study.

- I have read the whole consent form, and all of my questions have been answered to my satisfaction.
- I am satisfied that I have been given enough information about the purpose, methods, risks, and possible benefits of the study to decide if I want to join.
- I know that joining the study is voluntary and I agree to join the study.
- I know that I can call the investigator and research staff at any time with any questions or to tell them about side effects.
- I know that I may withdraw from the study at any time.
- A copy of this form will be put in my medical records and I will be given a copy of this completed form.

Please sign and date to show that you have read all of the above guidelines. Please do not sign unless you have read this entire consent form. 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

UAB

Consent Form to Participate in Research at UAB

TITLE OF RESEARCH: **"Polycystic Kidney Disease: Innovative Imaging to Assess Progression (PCC)"- CRISP III**
IRB PROTOCOL: **F110901006**

PRINCIPAL INVESTIGATOR: Michal Mrug, MD

SPONSOR: National Institutes of Health

PURPOSE OF THE STUDY

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 five 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 Polycystic Kidney Disease (PKD). This study is funded by the National Institutes 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 the original CRISP (including participants from UAB) will be enrolled in CRISP III and at least 194 subjects from the centers will be enrolled altogether. At UAB, we expect 15 participants (not including family members); the study's activities will be performed at the Clinical Research Unit (CRU), 15th floor Jefferson Tower, at the UAB Hospital.

EXPLANATION OF PROCEDURES

1. ELIGIBILITY DETERMINATION

You are eligible if you participated in the past CRISP studies. 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 III 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 scheduled to come to the CRU for testing.

2. WHAT WILL HAPPEN TO YOU WHILE YOU ARE IN THIS RESEARCH STUDY?

If you agree to participate in the study, you will be scheduled for two visits: initial (Year 1) and Year 3.

a. Initial (Year 1) and Year 3 visits:

For these visits you will be come to the CRU. These visits will last at most 8 hours. Prior to the initial (Year 1) visit, we will mail you the study consent to give you time to review it and a family history questionnaire to gather data about your relatives affected by the disease.

On the evening before to coming to the CRU, you must hold the evening dose of any medicine taken to treat high blood pressure, between 9 and 10 PM drink at least three (8 oz) glasses of water (with no ice), start fasting (do not eat) after 10 PM , and go to bed at 10:00 PM.
On the day coming to the CRU, you should remain fasting (except for water), do not eat, do not drink beverages with caffeine in it and do not smoke until the end of this visit. You must be at the CRU by 7 AM. Bring all medications, including herbal medicines and vitamins that you are taking or have used. Bring your parking ticket with you.

On arrival, you will discuss the study, and consent document with the research coordinator or investigator, and sign the consent form. After it, a medical history interview, medication history (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 and II. A family history questionnaire will also be obtained. You will undergo a complete physical examination including height, weight, and blood pressure measurements. You will have the blood pressure measured at least three times in the same arm that was used in CRISP II.

Blood and urine samples will be obtained during the initial (year 1) and year 3 visits. If you are a woman with childbearing potential, a urine pregnancy test to determine if you are pregnant will be performed prior to undergoing any test. You will be told if you are pregnant.

The blood samples will be to determine your serum chemistries and cholesterol profile, and other markers that may identify risk for renal failure in PKD. If you want, an intravenous line can be

placed in your arm to draw blood samples (avoiding sticking you three times to get blood samples). About 50 ml or 4 tablespoons of blood will be taken for these tests.

Blood and urine samples, identified by CRISP ID code number only, and without your name or other identifier (this is called de-identified), will be stored in a central repository (Fisher BioServices) and shared with other CRISP investigators. When these studies are completed, the researchers may wish to perform additional tests related to this disease on these samples.

You do not have to save urine for 24 hr. Urine samples from random urine will be collected when you arrive to the CRU.

A special test called GFR Test (Glomerular Filtration Rate test) involving blood and urine collections to measure your kidney function will be performed at baseline (Year 1) and Year 3. 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 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 skin and a probe that measures bladder volume will be moved over the skin. The nurse will obtain a small blood samples from your vein (1 teaspoon [5ml]) at two different times during the test. The GFR test will take approximately three 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. 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 or contrast dye use associated with this procedure. The total duration of the MRI will be, at most, one hour. The MRI will be done at baseline and Year 3 visits.

Recruitment of Family Members

A major part of CRISP II is to collect more complete family histories of all CRISP patients and create a family tree (pedigree) for each family. We are asking you to share the study information letter (given to you at the CRU visit) with your relatives who might have Polycystic Kidney Disease and to ask them to contact the Research Nurse Coordinator, Ms. Teresa Chacana, at 205-934-7649, 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 below:

_____I will give the information to my family members

_____I will not give the information to my family members

b. Year 2 and Year 4 Visits

In Years 2 and 4 you will be asked to provide a blood sample for measurement of serum creatinine. The blood sample can be obtained either at the UAB CRU 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 on how to mail the sample back to us.

c. Quaterly Telephone Interviews

Every three months, the CRISP study coordinator will contact you to obtain information regarding any medication changes, hospitalizations, doctor visits and outpatient procedures. We will ask for your permission to contact your doctor and obtain information regarding your health from any physician who has examined or treated you since your last visit or telephone interview. These phone calls will last at most 30 minutes.

3. HOW LONG WILL YOU BE IN THIS RESEARCH STUDY?

This is a five year study. Initial (Year 1) and Year 3 visits will be at the CRU -15 Jefferson Tower at the UAB Hospital. Visits at Year 2 and Year 4 can be completed at the CRU or with your local physician. There will be telephone follow-up visits every 3 months after each yearly visit. You will continue to be under the care of your primary physician at home.

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. Mrug 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.

The risk of allergic reaction to iothalamate meglumine is less than 1 in 50,000. As with any infusion, there is a 5% risk of infiltration (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 no radiation exposure or contrast dye use associated with this procedure.

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.

Incidental findings discovered during the review of blood, urine and MRI results will be informed to you. We will give you a copy of the blood and urine test's reports. The MRI report will not be given to you; this test is limited to review research goals and not a complete clinical study.

BENEFITS

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. There is a possibility that results from this investigation may provide important insight for the future management of patients with these diseases. There is no clear indication that these studies will be of any direct benefit to you or your family.

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

Information obtained about you for this study will be kept private to the extent allowed by law. However, research information that identifies you may be shared with the UAB Institutional Review Board (IRB) and others who are responsible for ensuring compliance with laws and regulations related to research, including people on behalf of National Institutes of Health; the U.S. Food and Drug Administration (FDA); and the Office for Human Research Protections (OHRP).The results of the treatment may be published for scientific and educational purposes. These results could include your lab tests and MRIs. However your identity will be not revealed in any publications. If any part of this study takes part at University of Alabama Hospital, this consent will be placed in your file at that facility. The document will become part of your medical record chart.

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 no radiation exposure or contrast dye use associated with this procedure.

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.

Incidental findings discovered during the review of blood, urine and MRI results will be informed to you. We will give you a copy of the blood and urine test's reports. The MRI report will not be given to you; this test is limited to review research goals and not a complete clinical study.

BENEFITS

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. There is a possibility that results from this investigation may provide important insight for the future management of patients with these diseases. There is no clear indication that these studies will be of any direct benefit to you or your family.

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

Information obtained about you for this study will be kept private to the extent allowed by law. However, research information that identifies you may be shared with the UAB Institutional Review Board (IRB) and others who are responsible for ensuring compliance with laws and regulations related to research, including people on behalf of National Institutes of Health; the U.S. Food and Drug Administration (FDA); and the Office for Human Research Protections (OHRP).The results of the treatment may be published for scientific and educational purposes. These results could include your lab tests and MRIs. However your identity will be not revealed in any publications. If any part of this study takes part at University of Alabama Hospital, this consent will be placed in your file at that facility. The document will become part of your medical record chart.

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the Office of the Institutional Review Board for Human Use (OIRB) at (205) 934-3789 or 1-800-822-8816. If calling the toll-free number, press the option for "all other calls" or for an operator/attendant and ask for extension 4-3789. Regular hours for the Office of the IRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

LEGAL RIGHTS

You are not waiving any of your legal rights by signing this consent form.

WHAT WILL HAPPEN TO YOUR SAMPLES?

De-identified small samples of your blood and urine will be stored for future research studies of Polycystic Kidney Disease. 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 National Institutes of Health (Fisher BioServices and NIDDK Center for Genetics Studies, Rutgers University Cell and DNA Repository).

GENOME-WIDE ASSOCIATION STUDIES (GWAS)

The DNA that composes your genes will be analyzed and that data, which is referred to as your genotype or complete genetic makeup, will be compared to your phenotype, which consists of your observable traits, characteristics, and diseases. Your genotype and phenotype data will be shared for research purposes through the National Institutes of Health (NIH) Genome-Wide Association Studies (GWAS) data repository. The aim of this research is to discover genetic factors that contribute to the development, progression, or therapy for a particular disease or trail.

STORAGE OF BLOOD AND URINE SAMPLES

De-identified (identified by CRISP ID number only) blood and urine samples will be shared with other CRISP site investigators. When these studies are completed, the researchers may wish to perform additional tests, related to this disease, on these samples.

Please initial the option with which you agree below:

_____ I agree to allow my de-identified (identified by CRISP ID number only) 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 de-identified (identified by CRISP ID number only) blood and urine samples, stored in the NIDDK Biosample Repository, to be preserved for future research on Polycystic Kidney Disease.

CLINICAL AND GENETIC INFORMATION COLLECTED DURING THE CRISP STUDIES

Dr. Guay-Woodford, the CRISP I and CRISP II principal investigator and current CRISP III investigator for the UAB site, is assembling a database containing de-identified clinical and genetic information from CRISP participants enrolled in any of the four study centers (the Mayo Foundation, University of Kansas Medical Center, Emory University, and UAB). The investigators at UAB would like to include your CRISP information in the database. Saving the information in a database may help for future management of patients with these diseases.

Please initial the option with which you agree below:

_____I give my permission to have my **de-identified** (identified by CRISP ID number only) data from the CRISP studies used in future research by the CRISP investigators.

_____I do not give my permission to have my **de-identified** (identified by CRISP ID number only) data from the CRISP studies used in future research by the CRISP investigators.

SIGNATURES

Your signature indicates that you have read (or been read) the information provided above. You will receive a signed copy of this informed consent and a copy will be placed in your medical records.

Your signature below indicates that you have had a chance to ask questions, and have received satisfactory answers to all of your questions. Your signature here indicates agreement with choices initialed above.

_____

Signature of Participant Date

_____

Signature of Witness Date

_____

Signature of investigator or other person obtaining consent Date

University of Alabama at Birmingham
AUTHORIZATION FOR USE/DISCLOSURE OF HEALTHINFORMATION 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: _____
Research Protocol: "Polycystic Kidney Disease: Innovative Imaging to Assess Progression (PCC)"- CRISP III
Principal Investigator: Dr. Michal Mrug **UAB IRB Protocol Number:** F110901006
Sponsor: National Institutes 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_____ Date: _____

Printed Name of participant's representative: _____

Relationship to the participant: _____

Consent Form for Family Member to Participate In Research at UAB

TITLE OF RESEARCH: **"Polycystic Kidney Disease: Innovative Imaging to Assess Progression (PCC)"- CRISP III**

IRB PROTOCOL: **F110901006**

PRINCIPAL INVESTIGATOR: Michal Mrug, MD

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. 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.

Blood and DNA samples, identified by CRISP ID code number only, and without your name or other identifier (this is called de-identified), will be stored in a central repository (Fisher BioServices) and shared with other CRISP investigators. When these studies are completed, the researchers may wish to perform additional tests related to this disease on these samples.
If you agree to have your sample(s) stored in the Repository, you can change your mind up until the end of the CRISP III study. When study researchers receive written instructions from you, they will destroy your sample and all information that identifies you. After the CRISP III 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.

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 below:

_____ 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.

_____ I do not give my permission for my DNA to be isolated.

_____ 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. Incidental findings discovered during the review of the creatinine;s result, will be informed to you and you will receive a copy of this blood test's report. 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 III 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

Findings from this study could potentially help others in the future. Information regarding your level of kidney involvement may help to determine how fast your PKD is progressing. You will continue to receive your usual treatment by your primary physician. No changes to your usual care will be instituted by this study. There is a possibility that results from this investigation may provide important insight for the future management of patients with these diseases. There is no clear indication that these studies will be of any direct benefit to you or your family.

ALTERNATIVES

The alternative to participating in this study is not to participate at all.

CONFIDENTIALITY

Information obtained about you for this study will be kept private to the extent allowed by law. However, research information that identifies you may be shared with the UAB Institutional Review Board (IRB) and others who are responsible for ensuring compliance with laws and regulations related to research, including people on behalf of National Institutes of Health; the U.S. Food and Drug Administration (FDA); and the Office for Human Research Protections (OHRP).The results of the treatment may be published for scientific and educational purposes. These results could include your lab tests and MRIs. However your identity will be not revealed in any publications. If any part of this study takes part at University of Alabama Hospital, this

consent will be placed in your file at that facility. The document will become part of your medical record chart.

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. Mrug or his 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 but, when you come to UAB hospital to provide a blood sample for measurement of serum creatinine and extraction of DNA for genetic testing, we will reimburse your travel expenses and parking. Travel is reimbursed at the standard mileage rate set by the Internal Revenue Service, and parking at the rate per day.

PAYMENT FOR RESEARCH RELATED INJURIES

UAB and the NIH have not provided for any payment if you are harmed as a result of taking part in this study. If such harm occurs, treatment will be provided. However, this treatment will not be provided free of charge.

QUESTIONS

If you have any questions, concerns, or complaints about the research or a research- related injury including available treatments, please contact Dr. Mrug or Teresa Chacana, the Research Nurse Coordinator. They will be glad to answer any of your questions. Dr. Mrug's number is

205-934-9509 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. and after hours by Paging her at 205-934-3411 (beeper 6193)
If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the Office of the Institutional Review Board for Human Use (OIRB) at (205) 934-3789 or 1-800-822-8816. If calling the toll-free number, press the option for "all other calls" or for an operator/attendant and ask for extension 4-3789. Regular hours for the Office of the IRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

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.

GENOME-WIDE ASSOCIATION STUDIES (GWAS)

The DNA that composes your genes will be analyzed and that data, which is referred to as your genotype or complete genetic makeup, will be compared to your phenotype, which consists of your observable traits, characteristics, and diseases. Your genotype and phenotype data will be shared for research purposes through the National Institutes of Health (NIH) Genome-Wide Association Studies (GWAS) data repository. The aim of this research is to discover genetic factors that contribute to the development, progression, or therapy for a particular disease or trail.

STORAGE OF SPECIMENS

Blood Sample

Please initial the option with which you agree 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 the option with which you agree below:

_____ I agree to allow my DNA sample, 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, stored in the NIDDK Biosample Repository to be preserved for future research on Polycystic Kidney Disease.

CLINICAL AND GENETIC INFORMATION COLLECTED DURING THE CRISP STUDIES

Dr. Guay-Woodord, the CRISP I and CRISP II principal investigator for the UAB site, is assembling a database containing de-identified clinical and genetic information from CRISP participants enrolled in any of the four study centers (the Mayo Foundation, University of Kansas Medical Center, and Emory University, and UAB). The investigator at UAB would like to include your CRISP information in the database. Saving the information in a database may help for future management of patients with these diseases.

Please initial the option with which you agree below:

_____I give my permission to have my **de-identified** (identified by CRISP ID number only) data from the CRISP studies used in future research by the CRISP investigators.

_____I do not give my permission to have my **de-identified** (identified by CRISP ID number only) data from the CRISP studies used in future research by the CRISP investigators.

SIGNATURES

You will receive a 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 investigator or other person obtaining consent Date

Created: 08-26-11
Reviewed 09-21-11

University of Alabama at Birmingham
AUTHORIZATION FOR USE/DISCLOSURE OF HEALTHINFORMATION 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: _____

Research Protocol: "Polycystic Kidney Disease: Innovative Imaging to Assess Progression (PCC)"- CRISP III

Principal Investigator: Dr. Michal Mrug **UAB IRB Protocol Number: F110901006**

Sponsor: National Institutes 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_____Date: _____

Printed Name of participant's representative: _____

Relationship to the participant: _____

University of Kansas Consent Form

CONSENT FORM

RENAL IMAGING TO ASSESS PROGRESSION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): CRISP III

Sponsor: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)

You are being asked to join a research study. You are being asked to take part in this study because you have Autosomal Dominant Polycystic Kidney Disease (ADPKD). You participated in CRISP and CRISP II studies of polycystic kidney disease.

You do not have to participate in this research study. Participating in research is different from getting standard medical care. The main purpose of research is to create new knowledge for the benefit of future patients and society in general. Research studies may or may not benefit the people who participate.

Research is voluntary, and you may change your mind at any time. There will be no penalty to you if you decide not to participate, or if you start the study and decide to stop early. Either way, you can still get medical care and services at the University of Kansas Medical Center (KUMC).

This consent form explains what you have to do if you are in the study. It also describes the possible risks and benefits. Please read the form carefully and ask as many questions as you need to, before deciding about this research.

You can ask questions now or anytime during the study. The researchers will tell you if they receive any new information that might cause you to change your mind about participating.

This research study will take place at the University of Kansas Medical Center (KUMC) with Dr. Jared J. Grantham as the researcher. About 66 people will be in the study at KUMC. A total of about 194 people will be in the study at 4 centers across the United States.

BACKGROUND

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a genetic disease that affects a great number of people worldwide and can lead to kidney failure. ADPKD is a disease that causes kidney cysts (fluid-filled balloons), worsening kidney function, blood in the urine, kidney pain, high blood pressure, kidney stones, kidney infections, and cysts in the brain or other parts of the body. For those with ADPKD, the kidneys respond abnormally to the hormone vasopressin, which may be involved in cyst development or growth in humans. There is currently no treatment known to delay cyst growth or a cure for the disease.

PURPOSE

By doing this study, researchers hope to learn about the disease and any genetic factors that may influence the severity of the cystic disease.

HSC Submission Date: 9/09/11

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Approval Date: 11/04/11 to 11/03/12
Assurance #: FWA00003411

PROCEDURES

If you decide to participate in this study, your participation will last approximately 4 years and you will be asked to visit the clinic 4 times during this study. You will be asked to come to the Clinical and Translational Science Unit (CTSU) in order to have an MRI or blood draws.
If you are eligible and decide to participate in this study, you will be asked to read and sign this consent form before any tests or procedures can be completed and you will be given a copy.

Year 1 and 3 Visit
The following procedures will occur at this visit:

- You will be asked questions about your health, current medications, and medical history.
- You will be asked demographic questions such as your name, date of birth, sex, ethnicity, etc.
- Your vital signs (blood pressure, heart rate, breathing rate, and temperature) will be taken.
- Study staff will review your family history questionnaire with you.
- You will have a physical exam including height and weight.
- A urine sample will be collected. If you are female and are capable of becoming pregnant, this sample will be tested to determine if you are pregnant. There will be blood draws during the visit totaling approximately 4 tablespoons. The blood will be drawn through a flexible catheter that will be placed into a vein in your arm. The IV catheter will remain in place throughout the visit. Some of these 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.
- You will be asked to have an Magnetic Resonance Imaging (MRI). This measurement is used to measure your kidney volume. During the MRI, you will be asked to lie on a table in a small space inside a tube-shaped machine. This machine is very noisy and uses magnetic fields and radio waves to take pictures of your abdomen. It is important that you do not move during this procedure.
- 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 procedure called Glomerular Filtration Rate (GFR) testing, which is done specifically for research purposes and is not part of standard medical care for patients with ADPKD. 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 will absorbed into the blood and is carried to the kidneys. Prior to the injection, you will be asked about previous allergic reactions to iodine containing products to see if there is any possibility that you would be allergic to the Iothalamate. You will be asked to urinate (or empty your bladder) three times during the course of this test. After each urination, a blood sample will also be drawn from the IV needle. A small machine, called a bladder scanner, will be used to check whether or not your bladder is completely empty after each urination.

- This visit will last 4 hours.

Year 2 and 4 Visit

The following procedures will occur at these visits:

- You will be asked questions about your health, current medications, and medical history.
- Your vital signs (blood pressure, heart rate, breathing rate, and temperature) will be taken.
- You will have a blood draw of 2 tablespoons for lab tests that measure your kidney function.
- This visit will last 1 hour.

Telephone Calls

During this study, you will be regularly contacted by telephone every 3 months. During these calls, you will be asked general questions regarding your well-being, medication changes, hospitalizations, doctor visits, and outpatient procedures. You will be asked to participate with the study team to perform a standardized symptom check list to identify complications and symptoms.

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

☐ Yes ☐ No Please initial here: _____Date: _____

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RISKS

MRI Risks

MRI uses a large magnet, radio waves and computer equipment to produce pictures, or images, of the human body. There are risks with an MRI if you are pregnant, or have one of the following: an artificial heart valve, metal plate, pin or other metallic objects in your body (including gun shot or shrapnel). The MRI scan does not cause any pain and does not expose you to x-ray radiation. However there may be some discomfort. Claustrophobia (fear of being trapped in a narrow place) may occur when undergoing this procedure and the noise of the MRI machine itself could be uncomfortable and awkward. The machine may be stopped at any time during the scan upon your request.

There may be other risks that have not yet been identified and unexpected side effects that have not been previously observed may occur.

GFR Risks.

There may be mild discomfort at the injection site in your upper arm, and although unlikely, there is the possibility of allergic reaction to the injected Iothalamate.

Blood Draw Risks

During the study you will have blood drawn for laboratory tests. The risks of drawing blood from a vein may include bleeding, infection and a slight bruising at the site that is used for the blood draw. This will be minimized by careful and clean techniques.

Confidentiality Risk

There is a small risk that if people other than the researchers were given your genetic facts, they could misuse them. If genetic information was given to employers or insurers it could affect your ability to get a job or be insured. Misuse could cause problems for family members. In order to minimize these risks, your genetic information will be kept confidential as noted in this form.

Possibility of Unknown Risks

There may be other side effects or risks that are not yet known. If any new symptoms occur or if old symptoms increase, alert study staff.

NEW INFORMATION

You will be told about anything new that might change your decision to be in this study. You may be asked to sign a new consent form if this occurs.

BENEFITS

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 researchers understand why the progression of polycystic kidney disease varies from patient to patient even within the same family. This information may eventually improve tests for the disease and may provide clues for new treatments.

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ALTERNATIVES
You can choose not to be in the study.

COSTS
The study will pay for all study-related medical services provided during this study. These services include the study visits, and study related tests and procedures such as the physical exams, laboratory tests, study questionnaire, GFR, and MRIs as listed in this consent form.

Any other medical visits and procedures you have outside of the study due to other standard of care treatments or other health issues are billable to you or your insurance through normal hospital billing practices. Standard of care means necessary for the care of a medical issue as determined by your doctor and not necessary for this study.

Your insurance may not cover some or all of the services if you are part of a research study. You may want to talk to your insurance company and review your specific benefits and coverage before deciding to participate. You will be responsible for normal co-pays, deductibles and non-covered services that are not the responsibility of the study. Pre-certification is not a guarantee of payment.

You can still be in the study even if your insurance denies coverage or if you are uninsured. The hospital has a financial assistance program which it makes available to all subjects who qualify. The study staff will be able to provide more information to you.

FINANCIAL DISCLOSURE
The investigator and the KUMC Research Institute, Inc. will receive payments from the sponsor, National Institute of Health, for conducting this study. Payments will be used for research purposes only.

PAYMENT TO SUBJECTS
There is no payment for this study. However, you may receive reimbursement for traveling and lodging expenses, airfare, and meals. Up to $300 will be offered to all subjects who live more than 50 miles from KUMC. Reimbursement would equal the same as the current IRS Standard Mileage Reimbursement Rate for patients that qualify. You may look this information up on the internet or ask the study coordinator for the current rate. If any travel reimbursement is necessary all original receipts will be required. Payment for traveling reimbursement will be made in the form of a check approximately 30 days after each completed visit.

IN THE EVENT OF INJURY
If you have a serious side effect or other problem during this study, you should immediately contact Dr. Jared J. Grantham at (913) 588-9252. If it is after 5:00 p.m., a holiday or a weekend, you should call (913) 588-5000 and ask the operator to page the Nephrologist on call. A member of the research team will decide what type of treatment,

if any, is best for you at that time.

If you have a bodily injury as a result of participating in this study, treatment will be provided for you at the usual charge. Treatment may include first aid, emergency care and follow-up care, as needed. Claims will be submitted to your health insurance policy, your government program, or other third party, but you will be billed for the costs that are not covered by the insurance. You do not give up any legal rights by signing this form.

INSTITUTIONAL DISCLAIMER

If you think you have been harmed as a result of participating in research at the University of Kansas 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. Under certain conditions, Kansas state law or the Kansas Tort Claims Act may allow for payment to persons who are injured in research at KUMC.

CONFIDENTIALITY AND PRIVACY AUTHORIZATION

The researchers will protect your information, as required by law. Absolute confidentiality cannot be guaranteed because persons outside the study team may need to look at your study records. Your health information is protected by a federal privacy law called HIPAA. By signing this consent form, you are giving permission for KUMC to use and share your health information. If you decide not to sign the form, you cannot be in the study.

The researchers will only use and share information that is needed for the study. To do the study, they will collect health information from the study activities and from your medical record. You may be identified by information such as name, address, phone, date of birth, social security number, or other identifiers. Your health information will be used at KUMC by Dr. Jared J. Grantham, 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. Jared J. 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 National Institute of Diabetes and Digestive and Kidney Diseases (the sponsor of the study), other business partners of the sponsor who help with the study, the U.S. Food and Drug Administration (FDA), and U.S. agencies that oversee human research (if a study audit is performed). These groups or agencies may make copies of study records for audit purposes. The purpose for using and sharing your information is to make sure the study is done properly.

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The HIPAA privacy law may not apply to everyone who receives your health information. Your information might not be protected by HIPAA if persons outside KUMC disclose it. In some cases, there may be other laws that protect your information from improper use.

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 may see and copy any study information that is placed in your KUMC medical record. However, some study information is kept only by the researcher. The records kept only by the researcher may not be available to you until the end of the study.

The researchers may publish the results of the study. If they do, they will only discuss group results. Your name will not be used in any publication or presentation about the study.

QUESTIONS

Before you sign this form, Dr. Jared J. Grantham or other members of the study team should answer all your questions. You can talk to the researchers if you have any more questions, suggestions, concerns or complaints after signing this form. If you have any questions about your rights as a research subject, or if you want to talk with someone who is not involved in the study, you may call the Human Subjects Committee at (913) 588-1240. You may also 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 may stop being in the study at any time. Your decision to stop will not prevent you from getting treatment or services at KUMC. You might be asked to come back for a final study visit.

You have the right to cancel your permission for researchers to use your health information. If you want to cancel your permission, please write to Dr. Jared J. Grantham. The mailing address is Dr. Jared J. Grantham, University of Kansas 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. They may use and share information that was gathered before they received your cancellation.

This study might be stopped, without your consent, by the investigator, the sponsor or by the FDA. Your participation also might be stopped by the investigator or by the sponsor if it is in your best interest or if you do not follow the study requirements.

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CONSENT

Dr. Jared J. Grantham or the research team has 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.

By signing this form, you say that you freely and voluntarily consent to participate in this research study. You have read the information and had your questions answered.
You will be given a signed copy of the consent form to keep for your records.

_____
Print Participant's Name

_____ _____ _____
Signature of Participant Time Date

_____
Print Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date

OPTIONAL SUB-STUDY

You may choose not to donate your blood and urine samples for future research studies while still participating in the main study. 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.

However, if you agree, your blood cells will be put through a process that will 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

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will be kept anonymous. The information about uses and disclosures of your health information for the main study also applies to your blood samples.

Please initial the options with which you agree.

(A)_____I give my permission to have my DNA isolated. 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.

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.

_____ 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.

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.

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Print Participant's Name

Signature of Participant | Time | Date

Print Name of Person Obtaining Consent

Signature of Person Obtaining Consent | Date

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University of Kansas Relative Consent Form

CRISP III Study Flowsheets

Emory University Flow-Sheets

ACTSI-CIS DAY TO DAY ORDERS
EMORY UNIVERSITY SCHOOL OF MEDICINE

TITLE: CRISP III STUDY
INPATIENT STAY (at year 10 and 12)
Study E52434 (version date: 04-15-2011)

Admission Date:
Patient Name:
Medical Record No:
Investigators: Arlene Chapman, M.D. (PIC # 10162, home # 404-373-6085); Frederic Rahbari Oskoui, MD (PIC#17680)
Amirali Masoumi, MD (PIC#20503)
Coordinators: Stacie Hitchcock (2-1235); Yoosun Han (PIC# 13695)

Day 0:_____; Date: _____

Initials

_____ 1. Admit to ACTSI-CIS.

_____ 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. Rahbari (PIC#17680) or Dr. Chapman (PIC 10162) or Dr. Masoumi (PIC 20503).

_____ 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.

Day 0:_____; Date: _____ (continued)

_____**8.** Check **medication list.** Patient may take own medication during in-patient stay unless specified by Dr. Masoumi, Dr. Rahbari,

Principal Investigator's Signature
Arlene Chapman MD PIC # 10162

Variances & Actions:	RN Signature:	Initials:

or Dr. Chapman. Verify if patient has recently taken following medications or has any of the following symptoms. If the answer is yes, notify Dr. Masoumi, Dr. Rahbari or Dr. Chapman.

☐Trimethoprim/Sulfa Antibiotics
☐Cephalosporin Antibiotics
☐H-2 Blockers/Antacids
☐Unusual Headache/Neurological symptoms
☐Cloudy urine
☐Fever and/or chills
☐Hematuria/Dysuria
☐potential nephrotoxicity (**NSAIDs, antibiotics**)
☐altering serum creatinine independent of GFR (**trimethoprim [Bactrim], cimetidine**)
☐ altering renal hemodynamics (**nausea/vomiting, diarrhea, dizziness/lighheadedness**)

* However, participants taking low dose aspirin (81 or 325 mg once daily) will be allowed to continue on this dose throughout the study.

_____ **9.** Subject can take own medications during in-patient stay except antihypertensives. ***Subjects not to take medication in the mornings until after GFR and MR complete. Continue fluid intake ≥ 2500 cc/day. No smoking, caffeinated beverages.***

_____ 10. Send urine to EUH Lab for ☐qualitative pregnancy test for all women (except those with hysterectomies/ women with tubal ligations will still have a pregnancy test)

- Have results on the chart before the end of the day.
- Call coordinator if she is pregnant. The patient needs to be rescheduled.

_____ 11. **Begin 12-hour urine collection**. Instruct patient to void completely and ring the bell. Record exact time of first void: _____am/pm

_____12. Regular diet for dinner.

_____13. Between 9 p.m. and 11 p.m., give subject 4 x 8 oz glasses of water (may have more if desire). **If 12 hour total urine volume is less than 1.5 liter, give 2 x 8 oz glasses of water.*

_____14. Have the patient in bed. **NPO except water after 11pm.** **The subject cannot have meals until after the GFR test and MRI is complete in the morning. Continue fluid intake ≥ 2500 cc/day.*

Day 1: _____ Date:_____

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Initials

_____**1.** Wake subject at 6:45a.m. Have the patient empty bladder. Have the patient ring a bell at the completion of 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 A-CTSI CIS core lab.** ****Urine collection should be kept on ice throughout this process.***

1) **to Emory CIS core lab** for □future RNA/ DNA retrieval, and □six 5 mL urine aliquots. The rest of urine remains at Emory **CIS core** lab as a back-up for 5 days.
2) to Emory University Hospital **(EUH) Lab** for □**urine albumin** and □**urine creatinine.**

_____3. **Complete 12-hour urine collection** exactly 12 hours after it was started. Have patient ring bell when finished voiding.
Record exact time of final void: _____: _____ AM / PM

Record Total urine volume for 12 hours: _____ml
Send the entire urine collection to CIS core Lab.

_____ **4.** Using the same scale as admission, **weight without shoes** in kg (to 0.1 kg) _____ . __ **kg**

****Patient should be NPO except water before labs and until the completion of GFR test and MR exam. No smoking, no caffeinated beverages. No medications until after labs drawn.***

Start of GFR test:
(Hydration):

_____5. **Right after 6:45am** urine void, have the **patient drink** 6 x 8 oz glasses of **water** in preparation for the Iothalamate clearance determination.

_____6 Instruct the patient that she or he can urinate, if the patient can not 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 determine 60 minute urine void. If the patient needs to urinate in 55 minutes, use it as 60 minute urine void.

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Urination flow check:

_____ 7. **At 7:45am**, 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 Flow rate _____ ml/min (volume/time)
(*Have the **patient drink** another 4 x 8 oz glasses of **water in the preparation of GFR test if the flow rate is <2.5ml/min.)**

Blood draws:

_____ 8 **Around 8:15am,** place **heplock** in **forearm;** use **0.9% saline** for **flushes.**

_____ 9. **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 (70120007) and ☐ Blood Count, Auto Diff (70170663) to EUH Lab
(Check each box after placing order)

Send 3 x 10ml Red/Gray top tubes to the **CIS Core Lab:** (1 tube for Cleveland Clinic and 2 tubes for NIDDK repository)
and 2 x 8 ml Green/Gray top tubes to the **CIS Core Lab** for NIDDK repository.

****Send the blood samples IMMEDIATELY to the CIS Core Lab for processing. CIS 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. *****

(UO and Iothalamate Injection):

_____10. Prepare Iothalamate injection immediately before 9:15 injection:
Dose: **0.5 ml Iothalamate** (300 mg) mixed with **0.5 ml sterile Bacteriostatic Water.**
NOTE: All patients over 40 kg receive the same dose of Iothalamate.

_____11. **At 9:15am**, 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
Time between 7:45am urine void and 9:15 UO: ____ min. Flow rate: _____ ml/min (volume/time)
(*If the flow rate is < 2.5ml/min, page Dr. Rahbari at PIC # 17680.)

_____12. **Inject Iothalamate meglumine subcutaneously IMMEDIATELY after completing urine void.**

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Inject by the deltoid in the arm opposite where the heplock is placed.
Record exact **time** of injection: _____am/pm

_____13. Aliquot **5 ml** of **urine** into tube labeled UO. Store **UO** tube with urine in the clear door refrigerator at Emory CIS lab.

_____14. Have the patient drink 2 x 8 oz glasses of water. If total volume of 12 hour urine is less than 1.5 liter, give extra fluid.

_____15. **PAGE Dr. Rahbari (PIC# 17680) by 9:15 to notify of UE ultrasound of bladder at 10am.**

(UE & P1):

_____16. **At 10:15am,** have the patient urinate completely again (**Ask the patient* to *double void*: ask the patient to try to urinate again after urination to ensure complete urine void), 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.

_____17. **Bladder ultrasound** determines if the bladder is completely empty. This needs to be done **WITHIN 1-2 MINUTES.** Do ultrasound reading of bladder x 1, and record. **Bladder volume:** _____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. **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. After determining the total volume of UE urine, discard urine.
Time between UO &UE: _____min

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Flow rate: _____ml/min (volume/time) (*Urine void flow rate must be ≥ 3 ml/min.)

_____18. **Within 5 minutes** of UE voiding draw **4 ml** of **blood (P1)** in sodium heparin **green top** plasma tube from the **heplock (DO NOT DRAW the blood if the bladder volume is > 20 ml)** (***DO NOT use light green top tube!**).
Time of blood draw _____am/pm (circle one)

_____19. Send 4 ml of blood (P1) plasma tube to **Emory CIS Core 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.

_____ 20. Discard UE (equilibration urine) urine specimen, after making sure that the bladder volume was < 20 ml.

_____ 21. Have the **patient** drink 1-2 x 8 oz glasses of **water**. ***If 12 hour total urine volume is less than 1.5 liter, give extra fluid.***

_____ 22. Instruct the patient that she or he can urinate, if the patient can not 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.

(U1 &P2):

_____23. **At 11am**, have the **patient urinate** completely (**Ask the patient* to *double void*: ask the patient to try to urinate again after urination to ensure complete urine void), 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))

_____ 24. Bladder ultrasound is to assess the completion of bladder emptying. This needs to be done **within 1-2 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)

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**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))

_____25. **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)

_____26. After P2 blood draw, remove the heplock.

_____27. **Send** 4 ml of blood **(P2)** plasma tube to **Emory CIS Core Lab** 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 shippe

_____28. Nurse will aliquot **5 ml** of **urine** into **U1** tube. **Store** the **U1** tube in a clear-door refrigerator at **Emory CIS Core lab.**

_____29. 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 CIS Core Laboratory. From Emory CIS Core lab, call coordinator at 2-1235 to ship the specimens on the same day before 1:30pm or earliest working business day.)

Start of BP measurement:

_____**30.** 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.)

_____**31. Non-dominant** arm (in terms of handedness) (circle one). **Right** **Left**

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_____**32.** Cuff size (Circle one.) **Child** (17-22 cm) **Adult** (22-32 cm) **Large** (33-42 cm)

_____**33.1)** 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

_____**34.** 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** _____

_____**35.** 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 intervals.**

Time_____:_____BP#1_____ HR#1_____ bpm

Time_____:_____BP#2_____ HR#2_____ bpm

Time_____:_____BP#3_____ HR#3_____ bpm

_____**36.** 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.)

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Time_____:_____BP#4_____ HR#4_____ bpm

Time_____:_____BP#5_____ HR#5_____ bpm

_____ 37. 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

MR exam:

_____ 38. Coordinator will escort the patient to **MRI/MRA** at the scheduled time. _____**am**. This should take approximately 30 minutes.

_____39. Patient can have a meal and medications after GFR test and MR exam.

_____40. Patient can be discharged with instructions to follow up with primary care physician.

_____41. Make copies of completed day to day order and H&P and put in basket.

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Variances & Actions:	RN Signature:	Initials:

University of Alabama-Birmingham Flow-Sheets

CRU Protocol #: 2128
IRB #: F110901006

Title: "RENAL IMAGING TO ASSESS PROGRESSION IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD): EXTENSION (CRISP III)"

STUDY VISIT WORKSHEET

DATE: _____ PATIENT CRISP ID: _____

PATIENT:_____VISIT YEAR: FV10 or FV12 **(circle one)**

DOB: _____ UAB-Medical Records #: _____

PRINCIPAL INVESTIGATOR (Admitting MD.)	Dr. Michal Mrug, MD.	UAB Pager: 7739 - Office phone: 934-9509
RESEARCH NURSE COORDINATOR	Teresa Chacana, RN, BSN.	UAB Pager: 6193 - Office phone: 934-7649 Fax: 975-0814
RADIOLOGIST:	Dr. Mark Lockhart, MD.	UAB Pager: 3489 - Office phone: 934-7130
MRI:	Phone: 975-3771 (6th floor), 934-2796 or 934-3069	
Outreach Lab:	Phone: 975-8100 (Contact person is Kathy Hamilton: 975-8103)	

Time of arrival _____:_____a.m.

V/S: B.P. _____/_____; **Pulse** _____; **Respirations** _____; **Temperature**_____
(Use the Dinemap / Critikon BP monitor)

Weight (without shoes in kg (to 0.1 kg): _____ **kg**. (1kg = 2.2 lb.)

Height (without shoes in cm (to 0.1 cm): _____ **cm**. (2.54cm = 1 inch)

ON THE DAY BEFORE TO STUDY VISIT DAY:

- The BP meds, **previous to the study visit day**, whether am or pm **are to be taken as usual**.
- The Participant must drink at least 32-48 ounces of water-at room temperature- between 21:00 and 22:00 pm last evening (prior to study visit day). The amount of water may be less if the Participant is under physician orders to restrict fluid intake.
- **NPO except for water after 10:00 PM.**

ON THE DAY OF THE STUDY VISIT:

- **Blood pressure medication** is to be **held the morning of the testing only** until visit (with MRI and GFR) is completed.
- Subject should bring and take own medications during study stay.
- Review patient's medication list and disallowed medications list. Call Research Nurse Coordinator if disallowed medications are included.
- **Do not give Participant cold water at any time during this study visit due to vasoconstriction.**
- **Participant remains fasting, caffeine and smoking free.**

Allergy to Iodine (circle one): Yes No

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 canceling the test.

Childbearing women: On arrival to unit do a urine PREGNANCY TEST using a **CRU test kit.**
If Pregnancy test is positive, notify Dr. Michal Mrug and **STOP** study visit.

PREGNANCY TEST (circle one): Done by:_____

Positive Negative Witness of result_____

You can use remaining urine to send urine sample for Outreach Lab; see below.

07:15 AM: Please ask Participant to hold void the longer he/she can (waiting for the CRU lab to be open).
If Participant to void before the CRU lab is open, save urine for THE OUTREACH LAB sample ONLY.

If void:
Voiding time _____:_____ a.m. **Total volume voided _____ ml**

Collect urine sample for **Outreach Lab** (if not done before): Send at least 10 ml to Outreach Lab (urine albumin, urine creatinine, urine albumin/creatinine ratio).

Collect urine sample for **CRU Lab**: Send at least 35 ml to CRU Lab (place tubes on ice). **Urine must be processed in less than 30 minutes**. Do not save rest of this urine.

Complete **initial BP assessment** for CRISP III: To determine what arm **will be used** on sitting and standing BP readings.

INITIAL BP ASSESSMENT FOR CRISP III: Obtain after patient **rested** for 30 min. The Participant is to have abstained from smoking and caffeine for at least 30 min prior to readings Use the Dinemap / Critikon BP monitor.
Measure the upper arm circumference (both arms) to determine cuff size

Right Arm_____cm **Cuff size_____**

Left Arm _____cm **Cuff size_____**

Thigh cuff [>41 cm]
Adult cuff [24->33 cm]
Large cuff [33-41 cm]
Child cuff [<24 cm]

NON DOMINANT ARM (in terms of handedness) RIGHT arm LEFT arm **(Circle one)**

CRISP III will use the **non- dominant arm (in terms of handedness)** for sitting and standing BP readings. **BUT, IF** on 3 consecutive measurements there is a **difference in systolic BP of 20 mm Hg or more between arms**, the arm with the higher blood pressure will be used to check sitting and standing BP's regardless of which arm is the non-dominant (in terms of handedness).
BP's are to be taken 3 times at least 30 seconds apart in both arms.

Right arm (use appropriate cuff)			
Time	Systolic / Diastolic	Heart Rate	BPM
_____	_____/_____	_____	_____
_____	_____/_____	_____	_____
_____	_____/_____	_____	_____

Left arm (use appropriate cuff)			
Time	Systolic / Diastolic	Hearst Rate	BPM
_____	_____/_____	_____	_____
_____	_____/_____	_____	_____
_____	_____/_____	_____	_____

Use this non- dominant arm and this cuff size to obtain CRISP II sitting and standing BP readings

NON- DOMINANT ARM is **(circle one)** Right arm Left arm CUFF_____

07:30 AM: Call MRI at 4-2796 to make sure they are ready for the Participant.
Patient may void between now and 9:00 a.m. (time when patient starts drinking water).

07:40 AM. Blood Pressure Assessment: Obtain BPs after patient rest for at least 30 min.
No caffeine or smoking 30 minutes prior to Blood Pressure readings. **Use the non-dominant arm and cuff determinated early.**
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 in NON Dominant arm.

Three SITTING B/Ps on the Non Dominant Arm:

Time: ___:___ am pm; (sitting) ____/ ____ (mm Hg) Heart Rate: _____ MAP: _____

Time: ___:___ am pm; (sitting) ____/ ____ (mm Hg) Heart Rate: _____ MAP: _____

Time: ___:___ am pm; (sitting) ____/ ____ (mm Hg) Heart 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) Heart Rate: _____ MAP: _____

Time: ___:___ am pm; (sitting) ____/ ____ (mm Hg) Heart Rate: _____ MAP: _____

Have Participant to stand up for 3 minutes with arm supported at heart level and obtain:

One STANDING BP on the NON Dominant Arm:

Time: ___:___ am / pm (standing) ____/ ____ (mm Hg) Heart Rate: _____ MAP: _____

08:00 AM: **MRI** on the MRI research machine at ____:____ a.m **Return from** MRI at ____:____am
Keep Participant NPO (may drink water moderately with **no ice**).

Between 9:00 and 10:00 AM the Participant **should drink 32-48 ounces of water** (960-1440 ml). Participant may have more if desire in preparation for the GFR test. If possible, **the Participant must not void during this time (until 09:55 a.m).**

09:15 AM: Start Saline lock to be used for blood samples and GFR test samples.
Collect a total of four 10 ml tiger tubes and two 8 ml green tubes. Plus **Possible** 3 yellow tubes (the research Nurse Coordinator will let you know).

Times of blood sample collection: _____:_____ a.m.

Send one tiger tube (10 ml) to Outreach Lab for: TOTAL ELECTROLYTE PANEL – sodium, potassium, chloride, total CO2, LIPID PANEL – Total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol, SERUM CREATININE (for "local sample").
Send three tiger tubes (10 ml each) and two green tubes (8 ml each) to CRU Lab. Invert SST tubes (tiger top) 6 times and PST tubes (green top) 8-10 times.

Complete Appendix C GFR Checklist: **This form must be completed and returned with specimens.**

GFR RENAL GUIDELINES: **Name of Nurse performing GFR**: _____

- **Measure and save all the urine. Ask the Research Coordinator when to discard urine. We will collect a sample from some of the voids.**
- Urinary catheter is not approved for this Study
- 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 of < 10% of voided volume is acceptable, PROVIDED residual volume is < 50 ml.

Time at the end of drinking water: _____:_____ a.m. **Amount of water taken** _____ ml

09:55 AM: Have Participant empty bladder to begin GFR Test. **This will be U0 sample.**

U0 - Time Void ENDED (U0): ____:____ a.m. (record the time participant returns after voiding). If more than one void, urine must be pooled. The collection time will be the time of last void and the sample will be from the total sample.

U0 Collection Volume: _____ ml ***(Save 5 ml the urine for U0 sample. Take sample to CRU lab)***

10:00 AM: Injection of Iothalamate (Conray® 60%), with a 1-ml Tuberculin Syringe, draw up 0.5 ml of Iothalamate. Add 0.5 ml of sterile Bacteriostatic Water. Inject SQ (subcutaneous) into the OPPOSITE arm that is selected for blood drawing. INJECTION SITE: _____
Iothalamate Vials are for single dose use ONLY. Discard unused VIAL portion.
Iothalamate Lot# _____ Expiration Date_____
Sterile Water Lot# _____ Expiration Date_____

Between 10:00 and 11:00 AM, Participant should drink **10-20 ounces of water** (300-600mls) now. Do not void until 60 minutes after injection.

Time at the end of drinking water: _____:_____ a.m. **Amount of water taken** _____ ml

11:00 AM: Have Participant empty bladder. This is **Ue**: **Urine collected 60 minutes (+ or – 5 min.) after Iothalamate Injection**. **Discard this urine, no aliquot at this time.**

BLADDER scan to be done AFTER Ue and U1.

NOTE: Have Participant empty bladder as completely as possible. Participant may need to go bathroom more than one time, please accurately record all urine volumes & times void ended (if urine is pooled from more than one void).
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 scan- it should be done within 1 – 2 minutes after voiding

Time Void	Scan #1	Scan #2	Scan #3		Residual

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.

Ue Total Volume _____ **(ml)** **Flow (ml/min)** _____.___
(DO NOT save urine sample) *Flow is rounded to 2 places behind the decimal

11:05 AM: Plasma 1, **(P1)**, collected **immediately after collecting Ue**
Do P1 within 5 minutes maximum of the time the Ue void ended at (Ue collection time).

If used, tourniquet time MUST be LESS than 1 min. Blood draw from opposite arm of Iothalamate Injection.

Tourniquet used ___yes ___no **Time left on** ____:____ Seconds

P1 collection Time: _____:_____a.m. (*3 ml blood –into a 5 ml green-top tube. Take tube to CRU lab*)

Participant should **drink 10-20 ounces of water** (300-600ml). **Do not void until 45 minutes after Ue.**

Time at the end of drinking water: _____:_____ a.m. **Amount of water taken** _____ ml

11:45 AM: U1=All urine collected for at least 45 minutes (but no more than 90 minutes) after Ue.
It should be at least 100 ml. (5 ml of urine into screw-top polypropylene tube). Take tube to CRU lab.
NOTE: Have Participant empty bladder as completely as possible. Participant may need to go bathroom more than one time, please accurately record all urine volumes & times void ended (if urine is pooled from more than one void).

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 total U1 collection time to a 90 minutes maximum 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 scan- it should be done within 1 – 2 minutes after voiding

Time Void	Scan #1	Scan #2	Scan #3		Residual

U1 Collection time _____:_____ a.m. (record the time Participant returns after voiding). If more than one void, urine must be pooled. The collection time will be the time of last void and the sample will be from the total sample.

U1 Collection Volume: _____ ml **U1 Flow (ml/min) _____._____**
(Save 5 ml the urine for U1 sample. Take sample to CRU lab) * rounded to 2 places behind the decimal

U1 COLLECTION DURATION= _____minutes. This is the time difference, in minutes, from Ue to U1.

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.

11:50 AM: Plasma 2 (**P2**), 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

P2 collection Time: _____:_____a.m. *(3 ml blood –into a 5 ml green-top tube. Take tube to CRU lab)*

12:00: After GFR test complete, discontinue saline lock and serve lunch. Caffeine is allowed at lunch
Dismissal from CRU before 15:00.

V.S.: Respirations: _____ B.P. _____/_____ Pulse _____ Time of discharge: _____:_____p.m.

University of Kansas Flow-Sheets

PROTOCOL #171 CRISP III
FV10/FV12 & 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 – 49460728

Ht (cm) _____ (in) _____ Wt (kg) _____ (lb) _____

Must remove shoes & heavy clothing

Temp (C) _____ P _____ R _____

Sitting BPs ***Wait 30 seconds between BPs***

COMPLETE FORM 11

_____
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 SUPPLIES

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 (for GFR to MAYO)
1 – IV needle
1 – IV Prep Kit
1 – IV Cap

9– 5ml Cryovials
1-2ml white cryovial
1 – 50ml Falcon tube

1 - TB syringe
1 – Iothalamate Vile
1 – Sterile Water Vile

3 – Vacutainer /Adaptor / blunt needle
3 – 3cc syringe / blunt needle
3 – 10cc saline syringe / blunt needle

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

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____ 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

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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 # 49460728 *** 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# 88506

____ Fax Shipment Alert Form to MML Fax# 1-507-284-1790
(fax from KUKI office)

Beth office x87609
cell 913-302-0493
Marilyn office x 83985
Cell 913-980-8883

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

CRISP III Study Address Directory

Consortium for Radiologic Imaging Studies of
Polycystic Kidney Disease

CRISP III STUDY

ADDRESS DIRECTORY

September 2011

Prepared by:
Data Coordinating Image Analysis Center
University of Pittsburgh
Pittsburgh, PA 15213
(412) 641-2328

DIRECTORY TABLE OF CONTENTS

National Institute of Diabetes and Digestive and Kidney Diseases
Bethesda, Maryland

FLESSNER, Michael F., MD, PhD Telephone: (301) 451-4901
Director, Inflammatory Renal Disease Programs
KUH, NIH – NIDDK Fax: (301) 480-3510
2 Democracy Plaza – Room 641 email: flessnermf@niddk.nih.gov
6707 Democracy Boulevard Rm 641
Bethesda, MD 20892-5458

External Expert Group (EEG)
Consortium for Radiological Imaging Studies of Polycystic Kidney Disease, Phase III

Bluemke, David A., MD, PhD
Clinical Director, MRI
Russel H. Morgan Dept. of Radiology
Johns Hopkins Medical Institutions
Bethesda, MD 21287
NIH: Radiology and Imaging Sciences
Bethesda, MD
Telephone:(410) 955-4062
Fax:(410) 955-9799
email:dbluemke@jhmi.edu

SEDOR, John R., MD
MetroHealth Research Endowment Professor
Kidney Disease Research Center
Departments of Medicine and Physiology and Biophysics
Case Western Reserve University
Cleveland, OH
Telephone:(215) 898-0901
Fax:(215) 898-0643
email:njones@cceb.med.ipenn.edu

Pollak, Martin, MD
Beth Israel Deaconess Medical Center
Chief, Division of Nephrology, Department of Medicine
Boston, MA
Telephone: (617) 525-5840
Fax: (617) 525-5841
email: mpollak@rics.bwh.harvard.edu

HODGES, James, PhD
Associate Professor, Division of Biostatistics
University of Minnesota School of Public Health
Minneapolis, MN
Telephone: (718) 231-6704
Fax: (718) 515-8514
email: Kfreeman@montefiore.org

COX, Nabcy, PhD
Professor, Department of Medicine
Section of Genetic Medicine
The University of Chicago
Chicago, Il
Telephone: (718) 231-6704
Fax: (718) 515-8514
email: Kfreeman@montefiore.org

Watnick, Terry, MD
Professor, Department of Medicine
Johns Hopkins Univ School of Medicine
Baltimore, Maryland
Telephone: (410) 614-7590
Fax: (443) 287-7679
email: twatnick@jhmi.edu

Pendse, Shona, MD
Medical Officer
FDA
White Oak, Maryland
Telephone: (301) 796-1109
Fax:
email: shona.pendse@fda.hhs.gov

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
Douglas Landsittel, Ph.D.	(412) 864-3019	(412) 586-9672
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
Michael F. Flessner, MD, PhD	(301) 451-4901	(301) 480-3510
Michal Mrug, MD	(205) 934-9509	(205) 934-1879
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
Douglas Landsittel, Ph.D.	landsitteldp@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
Michael F. Flessner, MD, PhD	flessnermf@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
Douglas Landsittel, Ph.D.	(412) 864-3019	(412) 586-9672
Arlene B. Chapman, MD	(404) 686-8280	(404) 686-8299
Michael F. Flessner, MD, PhD	(301) 451-4901	(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
Douglas Landsittel, Ph.D.	landsitteldp@upmc.edu
Arlene B. Chapman, MD	arlene.chapman@emoryhealthcare.org
Michael F. Flessner, MD, PhD	flessnermf@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
Douglas Landsittel, Ph.D.	(412) 864-3019	(412) 586-9672
Jared J. Grantham, MD	(913) 588-7605	(913) 588- 9251
Michal Mrug, MD	(205) 934-9509	(205) 934-1879
Vicente E. Torres, MD, PhD	(507) 284-0944	(507) 266-7891

	Email Addresses
Chairman Arlene B. Chapman, MD	arlene.chapman@emoryhealthcare.org
Douglas Landsittel, Ph.D.	landsitteldp@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 Douglas Landsittel, Ph.D.	(412) 864-3019	(412) 586-9672
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 Douglas Landsittel, Ph.D.	landsitteldp@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
Stacie Hitchcock, MS	(404) 727-1235	(404) 727-5563
Vickie Kubly	(507) 266-9207	(507) 255-0770
Johana Schafer, MS	(412) 641-2328	(412) 641-2582
Marilyn Logan, RN	(913) 588-3985	(913) 588-8986

	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
Stacie Hitchcock, MS	shitch2@emory.edu
Vickie Kubly	Kubly.vickie@mayo.edu
Johana Schafer, MS	schaferj@upmc.edu
Marilyn Logan, RN	mlogan@kumc.edu

Genetics Committee

	Phone	Fax
Chairman Peter C. Harris, PhD	(507) 266-0541	(507) 266-3774
Douglas Landsittel, Ph.D.	(412) 864-3019	(412) 586-9672
Arlene B. Chapman, MD	(404) 686-8280	(404) 686-8299
Jared J. Grantham, MD	(913) 588-7605	(913) 588-9251
Michael F. Flessner, MD, PhD	(301) 451-4901	(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
Douglas Landsittel, Ph.D.	landsitteldp@upmc.edu
Arlene B. Chapman, MD	arlene.chapman@emoryhealthcare.org
Jared J. Grantham, MD	jgrantha@kumc.edu
Michael F. Flessner, MD, PhD	flessnermf@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
Pardeep K. Mittal, MD	(404) 712-1868	(404) 712-1871
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
Pardeep K. Mittal, MD	pmittal@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
Douglas Landsittel, Ph.D.	(412) 864-3019	(412) 586-9672
Arlene B. Chapman, MD	(404) 686-8280	(404) 686-8299
Jared J. Grantham, MD	(913) 588-7605	(913) 588-9251
Michael F. Flessner, MD, PhD	(301) 451-4901	(301) 480-3510

	Email Addresses
Chairman Vicente E. Torres, MD, PhD	torres.vicente@mayo.edu
Douglas Landsittel, Ph.D.	landsitteldp@upmc.edu
Arlene Chapman, MD	arlene.chapman@emoryhealthcare.org
Jared J. Grantham, MD	jgrantha@kumc.edu
Michael F. Flessner, MD, PhD	flessnermf@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

LANDSITTEL, Douglas, PhD
Investigator
University of Pittsburgh
Data Center, Center for Research on Health Care
200 Meyran Avenue, Suite 300
Pittsburgh, PA 15213
Telephone: (412) 864-3019
Fax: (412) 586-9672
email: landsitteldp@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

KAYA, Diana, MD
Research Associate
University of Pittsburgh
3362 Fifth Avenue
Pittsburgh, PA 15213
Telephone: (412) 641-2591
Fax: (412) 641-2582
email: kayad2@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

TAO, Cheng, MD
Research Associate
Telephone: (412) 641-2671
Fax: (412) 641-2582

University of Pittsburgh
3362 Fifth Avenue
Pittsburgh, PA 15213

email: taoc@upmc.edu

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

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

MITTAL, Pardeep K., MD
Department of Radiology and Imaging Sciences
Emory University Hospital
Suite BG-48
1364 Clifton Road, NE
Atlanta, GA 30322

Telephone: (404) 712-1868
Fax: (404) 712-1871
email: pmittal@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

HITCHCOCK, Stacie, MS
Study Coordinator
Emory University School of Medicine
Woodruff Memorial Research Building
Suite 338
101 Woodruff Circle
Atlanta, GA 30322

Telephone: (404) 712-1235
Fax: (404) 727-5563
email: shitch2@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

LOGAN, Marilyn, RN
Study Coordinator
University of Kansas Medical Center
MS 3002
3901 Rainbow Blvd.
Kansas City, KS 66160-7382

Telephone: (913) 588-3985
Fax: (913) 588-8986
email: mlogan@kumc.edu

CREED, Cathy, RN
Study Coordinator
University of Kansas Medical Center
MS 3002
3901 Rainbow Blvd.
Kansas City, KS 66160-7382

Telephone: (913) 588-0053
Fax: (913) 588-8986
email: ccreed@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

Participating Clinical Center
University of Alabama-Birmingham
Birmingham, Alabama

MRUG, Michal, MD Telephone: (205) 934-9509
University of Alabama at Birmingham Fax: (205) 934-1879
Kaul Building, Room 752A email: mmrug@uab.edu
1530 3rd Avenue South
Birmingham, AL 35294-0005

LOCKHART, Mark E., MD, MPH Telephone: (205) 934-7130
Department of Radiology, JTN358 Fax: (205) 975-7213
University of Alabama at Birmingham email: mlockhar@uabmc.edu
619 South 19th Street
Birmingham, AL 35294

CHACANA, Teresa, RN, BSN, CPN Telephone: (205) 934-7649
Study Coordinator Fax: (205) 975-0814
University of Alabama at Birmingham email: tchacana@uab.edu
Kaul Building, Room 705
1530 Third Avenue South
Birmingham, AL 35294-0024

CRISP III Study Electronic Mailing Lists

CRISP Steering Committee crispall@list.pitt.edu
crispsteer@list.pitt.edu
William M. Bennett
K. Ty Bae
Douglas Landsittel
Arlene B. Chapman
Jared J. Grantham
Peter C. Harris
Michael F. Flessner
Michal Mrug
Vicente E. Torres
Johana Schafer

CRISP Coordinators
crispcoord@list.pitt.edu
Teresa Chacana
Vickie Kubly
Marylin Logan
Stacie Hitchcock
Johana Schafer

CRISP Imaging Committee
crispimage@list.pitt.edu
K. Ty Bae
James F. Glockner
Bernard King
Mark Lockhart
Louis Wetzel
Cheng Tao
Jinhong Wang
Johana Schafer

CRISP Genetics Committee
crispgenetics@list.pitt.edu
Peter C. Harris
Douglas Landsittel
Arlene B. Chapman
Jared J. Grantham
Michael F. Flessner
Vicente E. Torres

All on CRISP Mailing Lists