APPENDIX A

TABLE #1 **SAMPLE SIZE DETERMINATIONS**

The CPC study was designed based on the assumption that studying the associations between many possible variables is of primary interest. For example, the subjects can be cross-classified according to presence or absence of a given symptom, such as pain exceeding a certain threshold, and presence or absence of a laboratory-based marker such as elevated white count in EPS. The variable of interest can be a risk factor *(e.g.* alcohol consumption), another symptom (*e.g.* pain during urination), or the same symptom at a later point in time. The table below illustrates this cross-classification.

	ANY VARIABLE		
SYMPTOM	R_1 (present)	R_2 (absent)	
S_1 (present)	$p_{1\|1}$	$p_{2\|1}$	n_1
S_2 (absent)	$p_{1\|2}$	$p_{2\|2}$	n_2

Notation

Let the first subscript in $p_{i|j}$ represent the level of the column variable, and the second subscript represent the level of the row variable. That is, let $p_{1|1}$ represent the probability that the variable of interest is present, given that the symptom is present, and $p_{1|2}$ represent the probability that the variable of interest is present, given that the symptom is absent. Let n_1 represent the number of subjects with the symptom present, and n_2 represent the number of subjects with the symptom absent. Finally, let θ represent the true underlying odds ratio.

Assumptions
The following assumptions were made in arriving at the required overall sample size:

1. The proportion of subjects ($p_{1|2}$) with the risk factor, given the symptom is absent, is 0.5. (This estimate is conservative, because it maximizes the binomial variance).

2. At least 80% power is desired to test $\theta = 1$ against $\theta = 2.0$ and 2.5. The odds ratios correspond to the following proportions:

θ	$p_{1\|2}$	$p_{1\|1}$
1.0	0.50	0.50
2.0	0.50	0.67
2.5	0.50	0.71

3. Two-sided tests with significance level 0.05 are desired.

4. The existence of clustering due to homogeneity of patients within Clinical Centers relative to simple random sampling requires a 1.5-fold increase in the necessary sample size to adjust for the clustering.

Results

Based on the above assumptions, but ignoring attrition, the following table summarizes the overall sample size ($n_1 + n_2$) required, given the assumed distribution of the symptom prevalence.

Table 1. Sample Size Requirements for Detecting Specified Odds Ratios Under Selected Study Design Characteristics: Type I Error Rate of 5%, Power of 80%

Underlying Odds Ratio (OR)	Percent Allocation for n_1:n_2	Sample Size for Symptom Present (n_1)	Sample Size for Symptom Absent (n_2)	Total Sample Size ($n_1 + n_2$)
OR= 2.0	10:90	110	918	1,028
	20:80	123	479	602
	30:70	140	335	474
	40:60	165	242	407
	50:50	197	197	393
OR= 2.5	10:90	69	684	753
	20:80	78	320	398
	30:70	90	207	297
	40:60	105	156	261
	50:50	126	126	252

Adjusted for clustering affect within Clinical Research Centers. The original sample size was expanded by a factor of 1.5 to adjust for the clustering.

TABLE #2

Distribution of Baseline Screening Visits, Follow-up Patient Contacts and Clinical Research Center (CRC) Workload by Study Months Under Specified Assumptions* (50 new patients/year/CRC)

Budget Year	Study Months	Baseline Screening	Follow-up Patient Contacts at Selected Months**						CRC Workload***			ANNUAL TOTALS
			6 (TI)	12 (CV)	18 (TI)	24 (CV)	30 (TI)	36 (CV)	Clinic Visits	Telephone Interviews	Total Contact	
2	1-3	12.50							25.00	0.00	25.00	
	4-6	12.50							25.00	0.00	25.00	
	7-9	12.50	11.25						25.00	11.25	36.25	
	10-12	12.50	11.25						25.00	11.25	36.25	122.50
3	13-15	12.50	11.25	10.13					35.13	11.25	46.38	
	16-18	12.50	11.25	10.13					35.13	11.25	46.38	
	19-21	12.50	11.25	10.13	9.11				35.13	20.36	55.49	
	22-24	12.50	11.25	10.13	9.11				35.13	20.36	55.49	203.73
4	25-27	12.50	11.25	10.13	9.11	8.20			43.33	20.36	63.69	
	28-30	12.50	11.25	10.13	9.11	8.20			43.33	20.36	63.69	
	31-33	12.50	11.25	10.13	9.11	8.20	7.38		43.33	27.74	71.07	
	34-36	12.50	11.25	10.13	9.11	8.20	7.38		43.33	27.74	71.07	269.52
5	37-39		11.25	10.13	9.11	8.20	7.38	6.64	24.97	27.74	52.71	
	40-42		11.25	10.13	9.11	8.20	7.38	6.64	24.97	27.74	52.71	
	43-45			10.13	9.11	8.20	7.38	6.64	24.97	16.49	41.46	
	46-48			10.13	9.11	8.20	7.38	6.64	24.97	16.49	41.46	188.35
	CRC Total	150.00	135.00	121.50	91.13	65.61	44.29	26.57	513.68	270.41	784.09	
	Combined (6 CRCs)	900.00	810.00	729.00	546.75	393.66	265.72	159.43	3082.09	1622.47	4704.56	

*Baseline Screening of 12.5 new CPPS patients per quarter (50 per year) for 3 years of recruitment.

**TI: Telephone Interviews at 6,18,30 months; CV: Clinic Visit at 12,24,36 months.

Total Clinic Visit workload includes 2 baseline screening visits for each new CPC patient

TABLE #3

Distribution of Baseline Screening Visits, Follow-up Patient Contacts and Clinical Research Center (CRC) Workload by Study Months Under Specified Assumptions* (40 new patients/year/CRC)

Budget Year	Study Months	Baseline Screening	Follow-up Patient Contacts at Selected Months**						CRC Workload***			ANNUAL TOTALS
			6 (TI)	12 (CV)	18 (TI)	24 (CV)	30 (TI)	36 (CV)	Clinic Visits	Telephone Interviews	Total Contacts	
2	1-3	10.00							20.00	0.00	20.00	
	4-6	10.00							20.00	0.00	20.00	
	7-9	10.00	9.00						20.00	9.00	29.00	
	10-12	10.00	9.00						20.00	9.00	29.00	98.00
3	13-15	10.00	9.00	8.10					28.10	9.00	37.10	
	16-18	10.00	9.00	8.10					28.10	9.00	37.10	
	19-21	10.00	9.00	8.10	7.29				28.10	16.29	44.39	
	22-24	10.00	9.00	8.10	7.29				28.10	16.29	44.39	162.98
4	25-27	10.00	9.00	8.10	7.29	6.56			34.66	16.29	50.95	
	28-30	10.00	9.00	8.10	7.29	6.56			34.66	16.29	50.95	
	31-33	10.00	9.00	8.10	7.29	6.56	5.90		34.66	22.19	56.86	
	34-36	10.00	9.00	8.10	7.29	6.56	5.90		34.66	22.19	56.86	215.61
5	37-39		9.00	8.10	7.29	6.56	5.90	5.31	19.98	22.19	42.17	
	40-42		9.00	8.10	7.29	6.56	5.90	5.31	19.98	22.19	42.17	
	43-45			8.10	7.29	6.56	5.90	5.31	19.98	13.19	33.17	
	46-48			8.10	7.29	6.56	5.90	5.31	19.98	13.19	33.17	150.68
	CRC Total	120.00	108.00	97.20	72.90	52.49	35.43	21.26	410.95	216.33	627.28	
	Combined (6 CRCs)	720.00	648.00	583.20	437.40	314.93	212.58	127.55	2465.67	1297.98	3763.65	

*Baseline Screening of 10.0 new CPPS patients per quarter (40 per year) for 3 years of recruitment.

**TI: Telephone Interviews at 6,18,30 months; CV: Clinic Visit at 12,24,36 months.

Total Clinic Visit workload includes 2 baseline screening visits for each new CPC patient.

TABLE #4

Distribution of Baseline Screening Visits, Follow-up Patient Contacts and Clinical Research Center (CRC) Workload by Study Months Under Specified Assumptions* (32 new patients/year/CRC)

Budget Year	Study Months	Baseline Screening	Follow-up Patient Contacts at Selected Months**						CRC Workload***			ANNUAL TOTALS
			6 (TI)	12 (CV)	18 (TI)	24 (CV)	30 (TI)	36 (CV)	Clinic Visits	Telephone Interviews	Total Contacts	
2	1-3	8.00							16.00	0.00	16.00	
	4-6	8.00							16.00	0.00	16.00	
	7-9	8.00	7.20						16.00	7.20	23.20	
	10-12	8.00	7.20						16.00	7.20	23.20	78.40
3	13-15	8.00	7.20	6.48					22.48	7.20	29.68	
	16-18	8.00	7.20	6.48					22.48	7.20	29.68	
	19-21	8.00	7.20	6.48	5.83				22.48	13.03	35.51	
	22-24	8.00	7.20	6.48	5.83				22.48	13.03	35.51	130.38
4	25-27	8.00	7.20	6.48	5.83	5.25			27.73	13.03	40.76	
	28-30	8.00	7.20	6.48	5.83	5.25			27.73	13.03	40.76	
	31-33	8.00	7.20	6.48	5.83	5.25	4.72		27.73	17.76	45.48	
	34-36	8.00	7.20	6.48	5.83	5.25	4.72		27.73	17.76	45.48	172.49
5	37-39		7.20	6.48	5.83	5.25	4.72	4.25	15.98	17.76	33.74	
	40-42		7.20	6.48	5.83	5.25	4.72	4.25	15.98	17.76	33.74	
	43-45			6.48	5.83	5.25	4.72	4.25	15.98	10.56	26.54	
	46-48			6.48	5.83	5.25	4.72	4.25	15.98	10.56	26.54	120.54
	CRC Total	96.00	86.40	77.76	58.32	41.99	28.34	17.01	328.76	173.06	501.82	
	Combined (6 CRCs)	576.00	518.40	466.56	349.92	251.94	170.06	102.04	1972.54	1038.38	3010.92	

*Baseline Screening of 8.0 new CPPS patients per quarter (32 per year) for 3 years of recruitment.

**TI: Telephone Interviews at 6,18,30 months; CV: Clinic Visit at 12,24,36 months.

***Total Clinic Visit workload includes 2 baseline screening visits for each new CPC patient.

APPENDIX B

INFORMED CONSENT

(Will need to be tailored to specific institutional culture)

CONSENT FORM
CHRONIC PROSTATITIS COLLABORATIVE RESEARCH NETWORK (CPCRN)

PURPOSE

Chronic Prostatitis (CP) is a disabling condition affecting an untold number of men of all ages and ethnic origins. The symptoms are variable but usually include pelvic pain or discomfort in the absence of bacterial infection, unrelieved by antimicrobial therapy. The **Chronic Prostatitis Collaborative Research Network** (CPCRN), has been established and sponsored by the National Institutes of Health and National Institute of Diabetes, Digestive and Kidney Diseases to identify and study men with this syndrome. The purpose of the CPCRN is to develop and maintain a centralized data bank of patients with symptomatology consistent with Chronic Prostatitis (CP). Although it is hoped that such a data bank will eventually lead to refinements in the clinical methods for both diagnosing and treating CP, it is not the purpose of the CPCRN project to promote any one specific therapy or assume the financial or clinical responsibility for caring for patients with CP.

SELECTION OF PATIENTS

Any male patient presenting with symptoms of pelvic pain or discomfort which persists for at least three months will be considered a candidate for enrollment in the Chronic Prostatitis Cohort (CPC) Study. This study will be directed by six primary centers throughout the United States and Canada: Brigham and Women=s Hospital, Northwestern University, Queen=s University, Temple University, University of California at Los Angeles and University of Maryland.

GENERAL PROCEDURES

The study will be conducted until September 30, 2002. The longest duration for follow-up will be 36 months, the shortest follow-up will be 12 months or less. Blood and urine tests, as well as other relevant tests must be performed under the direction of the principal investigator at the clinical center. Fees for office visits, examinations, tests, operating room, anesthesia and surgery are considered routine and will not be paid for by the CPCRN.

SPECIFIC PROCEDURES

As part of this study, patients will be required to provide information on voiding frequency, pain and urgency symptoms, personal medical history, family medical history, prior diagnosis, treatments, medication history, dietary habits, and quality of life. This information will be used anonymously to establish vital statistics on patients suffering from CP. All patients will receive a focused physical examination, urinalysis and urine culture during the initial screening period. One small tube of blood will be drawn during the screening period. Additional tests may be ordered because of a patient=s current clinical condition; reports from these studies may be entered into the cohort study.

Specific procedures include but are not limited to:

1.) Uroflow Study (bladder function test) which measures flow during urination.
2.) EPS (expressed prostatic specimen) which involves prostate massage to obtain a small fluid sample.
3.) Urethral swab which requires a Q-tip like swab to be quickly inserted and removed from the penis to obtain a specimen.
4.) Semen sample which involves masturbating to provide a specimen.

ALTERNATIVES TO PARTICIPATION

No patient who comes under the care of the investigating physician and is evaluated and managed for CP is required to enter the CPC, and similarly patients withdrawing from CPC may do so without interruption to their clinical care. Patients who are unwilling to have the specific procedures listed above or who may have had those procedures by other physicians or medical centers not listed above will not be eligible for enrollment in the CPC Study.

TIME DURATION OF THE PROCEDURES AND STUDY

The total duration of the study is at most three years. This includes a screening phase, to be conducted during the patients first and second office visit and a study phase. The study phase will be comprised of phone interviews and office interviews. Phone calls will occur every three months; office interviews will take place every twelve months. Patients will also be asked to complete surveys by mail every three to six months. Every effort will be made to coordinate the patients regular office visit follow-up with CPC interviews. Clinical information obtained during any additional office visits or hospitalizations may be entered into the CPC Study.

RISKS

Collecting blood may be uncomfortable; it requires a needle be inserted into a vein. There may be slight bruising at the needle site and there is a very remote possibility of an infection developing at the puncture site. Discomfort related to examination of the prostate, and the collection of EPS (expressed prostatic specimen) will be similar to that experienced during a normal physical examination.

BENEFITS

The major benefits to enrollment in the CPC Study is the knowledge that participation may advance the research, diagnosis and treatment of CP.

CONFIDENTIALITY

All information regarding history, voiding diaries, and quality of life questionnaires, will be available to the principal investigator. All information regarding patients will be kept in confidence except as may be required by law. For patient protection, data entry into computers for tabulation and comparison with other study centers will be done by a code which eliminates patient name. This coded information will be available to the National Institutes of Health, the CPCRN Data Coordinating Center at the University of Pennsylvania and the six clinical centers. Publication of anonymous patient profiles including symptoms, clinical test results and quality of the data is anticipated.

DISCLAIMER/WITHDRAWAL

All patients are free to decide whether or not to participate and are equally free to withdraw from the study at any time. Refusal to participate or withdrawal from the study at any time will not alter the quality of care provided to the patient. Patients should understand that they will not be paid for participation in the project and that they may withdraw from the study at any time without prejudice to their future medical care by any physician within the health care setting. This consent is not designed to release anyone involved in the study from liability due to clinical negligence.

PATIENT INJURY STATEMENT

AI understand that in the event of injury resulting from the research procedure, medical treatment in excess of that covered by third party payers will be provided without cost to me, but financial compensation is not available.@

SUBJECT RIGHTS

Patients will have the opportunity to discuss the procedures with the investigator. Patients understand that if they wish further information regarding their rights as a research subject, they may contact the Director in the Office of Research Administration at the University of Pennsylvania by telephoning (215) 898-7293.

PATIENT=S DECLARATION

AI have been given the opportunity to ask questions and they have been answered satisfactorily. I have received and read a copy of this consent form. I realize that this consent is voluntary and may be withdrawn by me at any time without prejudicing continuing care. I understand that any questions that I might have in the future will be answered verbally or, if I prefer, with a written statement. I understand the possible risks and benefits of involvement in this study and I hereby consent to being a part of it."

Patient Signature _____

Date _____

As the principal investigator, I have fully explained to _____

the nature and purpose of the above described study and the risks involved. I have answered all of the

questions to the best of my ability.

Investigator Signature _____

Date _____

Witness Signature _____

APPENDIX C

DATA FORMS AND PROCEDURES BY STUDY VISIT
OVERVIEW OF YEAR 01

Visit/Contact	*Visit 1*	*Visit 2*	*Phone*	*Clinic Visit*	*Clinic Visit*
Week	1	2	q 3 mo	q 6 mo	q 12 mo
Procedures/Data Collection	**Enrollment**	**Phase**	**Follow**	**Up**	**Phase**
Consent	X				
Inclusion/Deferral/Exclusion Criteria	X				
History/Physical Examination	X			X	X
Prior ProstatitisTests/Treatments	X				
Symptom/Impact/General Quality of Life Index	X		X *		
Four-Glass Test (Including EPS) **	X			X ♦	X ♣
Voiding Log (Send Home - Return)	X	X		X	X
Serum Sample	X				
Demographic/Epidemiologic Questionnaire		X			
Uroflow Study		X			
Urethral Swab		X			
Semen Sample		X			
Concomitant Medications		X			
Interim Health Care Events				X	

* Symptom Questions to be completed 1, 2, and 3 months post-enrollment, then every 3 months.
** Must be completed before the second visit.
♦ EPS and urine microscopy, but not culture, at 6 month visit.
♣ EPS and urine microscopy AND culture at yearly visit.

APPENDIX D

CHRONIC PROSTATITIS COHORT STUDY - CALENDAR OF PATIENT CONTACTS
DETAILED TELEPHONE AND CLINIC VISIT SCHEDULE

	Screening Visit #1	Screening Visit #2	1 Month	2 Months	3 Months	6 Months	9 Months	12 Months
YEAR 1	C	C	T	T	T	C	T	C
					15 Months	18 Months	21 Months	24 Months
YEAR 2					T	C	T	C
					27 Months	30 Months	33 Months	36 Months
YEAR 3					T	C	T	C

T= Telephone Contact C = Clinic Visit

APPENDIX E

PATIENT INFORMATION BROCHURE

APPENDIX F

FOUR GLASS TEST - PROCEDURE

Patient Test Schedule:		
	Screening Visit #1	4 glass urine microscopy and culture
	Year 1 @ 6 months	4 glass urine microscopy
	Every 12 months	4 glass urine microscopy and culture

1. Instruct patient to retract foreskin (if uncircumcised).
2. Wipe head of penis with one alcohol pad.
3. Collect the first 10 ml sample **(VB1)** directly into sterile container. (Range 5 - 30 ml)
   Centrifuge, examine and culture as described below.*****
4. Collect midstream sample **(VB2)**.
   Dip VB2 for pH, glucose and protein. Record results
   Centrifuge, examine and culture as described below.*****
5. **EPS** - Prostatic massage
   a.) Collect EPS on a sterile surface. (Example: lid of urine cup)
   b.) Estimate volume of EPS in ΦL. (1 drop . 50 ΦL)
   c.) Examine 5 ΦL at 400X power.
   Count WBC's, RBC's, hyphae.
   d.) Place 10 ΦL on sheep blood agar (5%) of a urocult paddle and incubate at 37EC for 5 days. Record results at 48 hours and five days.
   e.) If it grows, replate colonies on MacConkey agar for identification.
   f.) Store any remaining volume of EPS in 1.0 - 1.5 ml cryovials.
   g.) Snap freeze in liquid Nitrogen for later storage at -70EC.

6. Collect first 10 ml sample post massage **(VB3)** within 30 minutes. (Range 5 - 30 ml)
   Centrifuge, examine and culture as described below.*****

***** **VB1, VB2 and VB3 SPECIMENS**

a.) Centrifuge 2-3 mls of urine for five minutes.
b.) Examine at 400X power.
c.) Count WBC's, RBC's, hyphae (average of three fields rounded to nearest whole number.)
d.) Place 100 ΦL of specimen on sheep blood agar (5%) plate and 100 ΦL of specimen on MacConkey agar plate.
e.) Culture at 37EC for 5 days. Record results at 48 hours and five days.

APPENDIX G

Serum Collection Procedure (Screening Visit #1)

1. Using sterile technique, draw one red top tube.
2. Allow to clot for 30 minutes.
3. Centrifuge for 5 minutes.
4. Aliquot serum into five 1.0 - 1.5 ml cryovials.
5. Place immediately in liquid Nitrogen for later storage at -70°C.

Uroflow Study Procedure (Screening Visit #2)

1. Instruct patient to have a full bladder for this test. A minimum volume of 150 cc's constitutes a valid test. This can be assessed by ultrasound of the bladder.
2. Record three values - Total Volume (ml)
   Peak Flow (ml/second)
   Mean Flow (ml/second)

Urethral Swab Procedure (Screening Visit #2)

1. Swab distal urethra using Calcium Alginate swab.
2. Culture specimen on sheep blood agar (5%) and MacConkey agar for 5 days.

Semen Sample Procedure (Screening Visit #2)

1. Instruct patient to remain abstinent for three days.
2. Collect specimen in a sterile urine cup.
3. Measure volume in mls.
4. Plate 100 ΦL on sheep blood agar (5%) plate and 100 ΦL on MacConkey agar. Culture at 37°C for 5 days. Record results at 48 hours and 5 days.
5. Allow sample to stand at room temperature for thirty minutes.
6. Centrifuge for five minutes.
7. Aliquot seminal plasma into 1.0 - 1.5 ml cryovials.

APPENDIX H

APPENDIX I
CASE REPORT FORMS