

Patient Registry for Primary Pulmonary Hypertension

MANUAL OF OPERATIONS AND PROCEDURES

VERSION 1 REVISION 0 PROJECT YEAR 1982 - 1.0(1982) -

-Applies to PPH forms labelled VERSION 1.0 or VERSION 1.0(1982)-

INSTITUTIONAL CODE LIST

IDENTIFICATION AND DEMOGRAPHIC DATA

PRESENT MEDICAL HISTORY

PAST MEDICAL HISTORY

FAMILY HISTORY AND FAMILY SCREENING RESULTS

PHYSICAL EXAMINATION RESULTS

LABORATORY TEST RESULTS

ETIOLOGY - ADDITIONAL INFORMATION ON DEFINED SUBSETS

HEMODYNAMIC DATA AND HEMODYNAMIC MEASUREMENTS

SAMPLE HEMODYNAMIC MEASUREMENT FORM - PANEL I & II

APPENDICES

DRUG THERAPY WITH VASODILATOR TYPE AGENTS

ALTITUDES OF MAJOR U.S. CITIES

April 6, 1982

UPDATE

MANUAL OF OPERATIONS AND PROCEDURES

1. Due to an inadvertent deletion we ask that those investigators who fill out Question #9 in the Laboratory Testing Section of the BASELINE REPORTING FORM answer the following as part D:

9.D Is there evidence for right-to-left shunt

- 1 () No
- 2 () Yes

2. In perusing the protocol, MOOP and forms note that we request clinical investigators to save the following items for possible future testing or studies:

- 1) All chest x-rays
- 2) All electrocardiograms
- 3) All lung scans
- 4) Blood samples from serial visits

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The initial reporting form is divided into eight sections. The entire form may be completed at one time, or section by section, whichever is more convenient.

For any procedure or question in the data forms which you DO NOT PERFORM, please leave the answer spaces BLANK. For any other questions which you perform, and for which you do not find an appropriate response, enter DK (for Don't Know) in the appropriate space. If you still are unsure please call the Project Coordinator.

+-----+
| 1. IDENTIFICATION: |
+-----+

At the top of each section is a place for a patient I.D. number. This is comprised of a center number (which will be assigned to you by the DCC, and will be the same for every patient), a patient number which you will assign to each patient seen at your institution, beginning with 001, and an alphabetical acrostic comprised of the first initial of the first name, first initial of the middle name, and the first three initials of the last name.

EXAMPLE: John W. Smith would be JWSMI

For patients who have no middle initial, or a last name shorter than three letters, substitute any letter where one would be missing.

EXAMPLE: George Lu would GXLUY

It is critical that the I.D. number given to a patient be kept constant and accurate throughout the study in order to allow identification of individual patients.

+-----+
| 2. DATE PATIENT WAS FIRST SEEN: |
+-----+

Date patient was first seen by you.

+-----+
| 3. DATE FORM COMPLETED: |
+-----+

Date this Form I was completed in its entirety.

+-----+
| 4. DATE OF BIRTH: |
+-----+

Birthdate of patient.

+-----+
| 5. AGE: |
+-----+

Indicate age of patient.

+-----+
| 6. SEX: |
+-----+

Check appropriate sex.

+-----+
| 7. RACE: |
+-----+

Check appropriate answer. Indicate mixed races and other
races where specified.

+-----+
| 8. MARITAL STATUS; |
+-----+

Check appropriate answer.

+-----+
| 9. PRESENT OCCUPATION: |
+-----+

Indicate present occupation. If unemployed, state so.

+-----+
| 10. HEIGHT (CHECK UNITS): |
+-----+

List in either centimeters or inches and indicate the
units.

+-----+
| 11. WEIGHT (CHECK UNITS): |
+-----+

List in kilograms or pounds and indicate the units.

+-----+
| 12. SIGNATURES: |
+-----+

At the bottom of this section is a place for the signatures of the person completing and reviewing the forms. At some institutions this may be the same person. In all cases, the reviewer should be the principal investigator for that institution. The person completing SECTION I should be the same person completing all sections for a given patient.

1. PREDOMINANT SYMPTOMS: ENTER THE NUMBER CORRESPONDING TO THE CHRONOLOGICAL ORDER OF APPEARANCE OF THE SYMPTOM.

Check asymptomatic if the patient is currently symptom free. Enter a number next to a given symptom in the order that the patient became aware of it. If a patient states that two symptoms appeared at the same time, a number can be used twice.

EXAMPLE: A patient states that two years ago, he began to notice some dyspnea on exertion. Over the past two months however, he began to develop palpitations and ankle edema. Place #1 next to "dyspnea on exertion" and #2 next to "palpitations" and "edema". Next to edema, write the word "ankle".

2. REFERRING TO QUESTION 1 ABOVE: APPROXIMATELY HOW MANY YEARS HAS THE FIRST SYMPTOM BEEN PRESENT:

List, if known, how long the patient has been symptomatic.

3. FUNCTIONAL CAPACITY (NEW YORK HEART ASS'N CLASSIFICATION):

Circle your estimation of the patient's current functional class according to the New York Heart Association criteria.

4. IS THERE EVIDENCE FOR RAYNAUD'S PHENOMENA:

Indicate the presence or absence of evidence for disease.

5. IS PATIENT CURRENTLY TAKING ANY MEDICATIONS:

Please list current medications, total daily dose, and the appropriate units (e.g. mgs, grains, etc.). Please list all types of medications, including vitamins and antacids, etc.

-----+
| 6. DIET OR DRUG HISTORY: |
-----+

If there is reason to believe that the patient has had chronic ingestion of specific drug, or diet, that may in some way be causally related to the presence of the pulmonary hypertension, please specify and provide pertinent details. Please note that appetite suppressant type drugs have been implicated in the occurrence of PPH and should be noted here.

1. WAS PATIENT EVER TOLD HE/SHE HAD THE DIAGNOSIS OF
PULMONARY HYPERTENSION:

If a patient was told that they have pulmonary hypertension prior to seeing you, please note the date when they were so informed. For all patients referred to you with the suspected diagnosis of PPH the answer should be yes.

2. PRIOR TO THE DIAGNOSIS OF PUL. HTN. DID THE PATIENT
EVER HAVE AN EKG/CHEST X-RAY DOCUMENTED:

For some patients the old records will be available to you. Some other patients will know definitely when they had prior tests and the results. The purpose of this question is to see if it can be established at what point the patient developed pulmonary hypertension. You may include data obtained from a phoned report, or from the patient himself if they are certain of the test, date, and results. (This applies to this question only).

EXAMPLE: Previous records on your patient shows that an EKG was performed every three years. The reports show that the EKG was normal in 1972 and 1975, but there was right axis deviation in 1978. The most recent normal EKG would be 1975 (question 2A). The first abnormal EKG would be 1978, with the abnormality "right axis deviation" (question 2B).

3. TO YOUR KNOWLEDGE, IS THERE ANY EVIDENCE THAT THE
PATIENT HAS EVER HAD ANY OF THE FOLLOWING:
- A. CONGENITAL DIAPHRAGMATIC HERNIA:
 - B. CONGENITAL HEART DISEASE:
 - C. RESPIRATORY DISTRESS SYNDROME AS AN INFANT:
 - D. PULMONARY DISEASE:
 - E. DEEP VEIN THROMBOSIS:
 - F. PULMONARY EMBOLI:
 - G. HISTORY OF TRAUMA AND/OR BONE FRACTURE:

Check the correct answer for the different illnesses listed. Under congenital heart disease, list the type. Under pulmonary disease, list chronic conditions. Do not list acute pneumonias that have resolved. If there is more than one pulmonary disease, list the one that is most clinically important. Under deep vein thrombosis and pulmonary emboli, if there were multiple occurrences, list the most recent one. Specify the bone(s) involved if there is a history of fractures or trauma.

-----+
| 4. MAJOR OPERATIONS: |
-----+

List all major operations and dates.

-----+
| 5. OBSTETRIC HISTORY: |
-----+

For female patients only. List the gravida, parity, and number of abortions that the patient has had. Also, note if the patient is currently pregnant. List the complications that may have occurred during any of the patient's past pregnancies. Use the space provided if some other complication has occurred that may have some relevance to the patient's pulmonary hypertension.

-----+
| 6. HAS THE PATIENT USED ORAL CONTRACEPTIVES: |
-----+

Note any history of their usage.

-----+
| 7. SMOKING HISTORY: |
-----+

Please inquire if the patient has any history of inhalation of any smoked plant or drug. Check "current" or "former" for patient who smoked on somewhat of a regular basis. A patient who tried marijuana one time should be marked as "never". For current or former users, please fill in the dates, as best known of when the patient started and stopped smoking. Also, list the average number of packs smoked per day by the patient.

+-----+
| 8. HIGH ALTITUDE LIVING: |

- | A. HAS THE PATIENT RESIDED AT AN ALTITUDE OTHER THAN SEA |
-
- | LEVEL FOR ANY LENGTH OF TIME: |
-
- +-----+

If relevant, please complete this as much as possible. The exact altitude of many cities may not be known. By "other than sea level" we mean locations that are truly elevated. Do not include cities that are 50 feet above sea level, for example. Please see the APPENDIX to the MOOP labeled 'ALTITUDES OF MAJOR U.S. CITIES' as a guide to answering the question.

1. PLEASE COMPLETE FOR EACH MEMBER OF THE PATIENT'S
IMMEDIATE FAMILY (PARENTS, SIBLINGS, CHILDREN):

Please list all blood-related immediate family members (not adopted family or relatives by marriage). List multiple siblings and offspring as sister #1, sister #2, etc. If the patient, referring physician, or you know of a family member that has a definite diagnosis of unexplained pulmonary hypertension answer YES in the appropriate column.

We are asking that the immediate family members of all patients be screened for the possibility of silent pulmonary hypertension, if they are available and willing. Although the literature documents that familial cases exist, the extent of this has never been explored prospectively. We are recommending that the family members have a physical exam, chest x-ray, and electrocardiogram as screening for the possibility of pulmonary hypertension. Please note all the family members that have been screened, and the method(s) used in the screening, in the appropriate column. If a family member has recently had a chest x-ray or EKG elsewhere, you may use that test for your screening. However, all patients screened should be examined by the investigator.

2. REFERRING TO QUESTION 1 ABOVE, LIST FAMILY MEMBERS YOU
HAVE SCREENED WITH FINDINGS SUGGESTIVE OF PUL. HTN.:

List all the family members who had one or more test that suggested pulmonary hypertension from the screening. Check the test (s) that revealed an abnormality. Please note if this person is already in the registry.

EXAMPLE: You screen the family of a patient and find an enlarged pulmonary artery on the x-ray of brother #2. You would enter "brother #2" and check column 2 under "chest x-ray". If you pursue a work-up of brother #2 and also find primary pulmonary hypertension you may want to enter him into the registry as well. If brother #2 has been entered into the registry by some other investigator, please indicate so in the space provided.

+-----+
| 1. VITAL SIGNS: |
+-----+

Please enter the Heart rate, Blood pressure, and Respiratory rate in the spaces provided.

+-----+
| 2. CHEST EXAM: |
| A. ABNORMAL BREATH SOUNDS: |
+-----+

Check appropriate answers if there are any abnormal breath sounds.

+-----+
| 3. CARDIAC EXAM: |
| A. JUGULAR VENOUS PRESSURE: |
| B. CAROTID PULSE: |
| C. LEFT VENTRICULAR IMPULSE: |
| D. RIGHT VENTRICULAR IMPULSE: |
| E. IS PULMONIC CLOSURE PALPABLE: |
| F. HEART SOUNDS: |
| G. EXTRA SOUNDS (CLICKS, RUBS, ETC.): |
| H. MURMURS: |
+-----+

Enter the appropriate findings of the cardiac exam.

- A. Jugular venous pressure should be estimated referable to the level of the right atrium.
- B. Specify any unusual features of the carotid pulse.
- C. Characterize the left ventricular impulse.
- D. Characterize the right ventricular impulse.
- E. Note if pulmonic closure is palpable.
- F. Check the appropriate answers about the heart sounds.
- G. Specify any unusual extra heart sounds.
- H. Describe any murmurs that are present.

4. ESTIMATE THE LIVER SPAN:

Estimate the liver span by percussion, in centimeters.

- A. Note if there are systolic pulsations characteristic of tricuspid insufficiency.

5. EXTREMITIES:

- A. PERIPHERAL EDEMA:
B. CYANOSIS:
C. CLUBBING:

Note any abnormal findings. Cyanosis refers to cyanosis at rest.

6. IS THERE ANY CLINICAL EVIDENCE FOR:

- A. TRICUSPID REGURGITATION:
B. MITRAL REGURGITATION:
C. PULMONIC INSUFFICIENCY:
D. RIGHT-TO-LEFT SHUNTING:

If there is any clinical evidence, either based on your physical exam, non-invasive tests, or cath data, to suggest the presence of tricuspid regurgitation, mitral regurgitation, pulmonic insufficiency, or right-to-left shunting, please indicate so.

1. CHEST X-RAY:
- A. CARDIOTHORACIC RATIO:
 - B. PULMONARY VASCULATURE:
 - C. LUNG FIELDS:
 - D. PLEURAL EFFUSION:
 - E. ADDITIONAL PERTINENT FINDINGS:

Please save all chest x-rays taken of this patient. Some institutions no longer keep x-rays that are more than a few years old. It would probably be best if you could keep your own private file for these patients with primary pulmonary hypertension.

- A. Measure the cardi thoracic ratio.
- B. Describe the pulmonary vasculature. Please give your estimate of the size, (whether normal, increased, or decreased), of the specific vessels listed. Also, indicate whether there is evidence for apical redistribution of blood flow, or peripheral pruning of the vessels. Specify any other pertinent abnormalities in the space provided.
- C. Note the character of the lung fields. If there are any opacities, specify the type and indicate as to whether their location is predominantly local or diffuse.
- D. Indicate if there is a pleural effusion.
- E. Please note any other pertinent findings.

2. ELECTROCARDIOGRAM:
PLEASE SEE INSTRUCTION BOOKLET. PLEASE SEND COPY WITH REPORT.
- A. RHYTHM:
 - B. RATE (VENTRICULAR):
 - C. P-R INTERVAL, QRS, Q-T:
 - D. QRS AXIS SPECIFY:
 - E. MAXIMUM HEIGHT OF P WAVE:
 - F. RIGHT VENTRICULAR HYPERTROPHY:
 - G. RIGHT BUNDLE BRANCH BLOCK PATTERN:
 - H. RIGHT VENTRICULAR STRAIN PATTERN:
 - I. S1, S2, S3 PATTERN:
 - J. OTHER ABNORMALITIES:

Please save a copy (photocopied is acceptable) of the patient's current EKG with this completed report. It may be used for future studies.

- A. Note the cardiac rhythm.
- B. Note the heart rate (ventricular).
- C. Note the appropriate intervals.
- D. Measure the QRS axis. Indicate whether it is positive or negative, and the amount of degrees.
- E. Measure the maximum vertical height of the P wave and indicate which limb lead was used.
- F. Note whether there is evidence for right ventricular hypertrophy. In those cases where it is unclear, mark "uncertain".
- G. Note if there is a complete right bundle branch block pattern.
- H. Note the presence of a right ventricular strain pattern. (T wave inversion in the right precordial leads.)
- I. Note if there is an S1, S2, S3 pattern.
- J. Please note any other unusual findings.

3. HEMATOLOGY:

- A. HEMOBLOBIN:
- B. HEMATOCRIT:
- C. LEUKOCYTE COUNT:
- D. DIFFERENTIAL COUNT:
- E. PLATELETS:
- F. PROTHROBIN TIME:
- G. ESR:

Please report the results of the CBC, prothrombin time and sedimentation rate.

4. RESPIRATORY FUNCTION TESTS:

- A. TLC:
- B. FVC:
- C. FRC/FRC TECHNIQUE:
- D. VE: FEQ:
- E. FEV1:
- F. FEV3:
- G. PEF 25-75:
- H. DLCO (HB CORRECTED):
DLCO TECHNIQUE:
- I. DLCO/VA:
- J. PAO:
- K. PACO:
- L. pH:

Please report the results of volumes in liters, uncorrected for BSA. It will be corrected for BSA at the DCC.

- A. Total lung capacity.
- B. Forced vital capacity.
- C. Functional residual capacity. Please note the technique used to measure.
- D. Minute ventilation, and respiratory frequency.
- E. Forced expiratory volume in one second.
- F. Forced expiratory volume in three seconds.
- G. Forced expiratory flow rate in mid expiration (may substitute MMFR or similar parameter).
- H. Diffusing capacity, hemoglobin corrected. Please state technique used.
- I. Diffusing capacity corrected for alveolar volume.
- J. pO₂ of arterial blood at room air.
- K. pCO₂ of arterial blood at room air.
- L. pH of arterial blood at room air.

5. BIOCHEMISTRY:

- A. BUN:
- B. CREATININE:
- C. TOTAL BILIRUBIN:
- D. ALKALINE PHOSPHATASE:
- E. SGOT:
- F. LDH:
- G. PLEASE CHECK IF A PLASMA SAMPLE WAS FROZEN
AND STORED FOR POSSIBLE FUTURE TESTS:

Please provide the results for the indicated biochemical tests. For the alkaline phosphatase, SGOT, and LDH, a numerator and denominator is provided. In the space for the numerator, write in the results for your patient. In the space for the denominator, fill in the upper limits of normal for your hospital's laboratory.

EXAMPLE: The patient has an LDH of 320. The upper limit of normal for your laboratory is 220. Write in :
320/220.

NOTE: Please keep one plasma sample frozen and stored, with the patient name, number, and date. This may be used at a future date for testing.

6. PLASMA PROTEIN ELECTROPHORESIS:

Please give the results of the electrophoresis in the spaces provided.

7. ANTINUCLEAR ANTIBODY TITRE:

- A. RHEUMATOID FACTOR:
- B. LE CELLS:

Note results, and if an LE prep was done.

8. PREGNANCY TEST (IF APPROPRIATE):

If appropriate. Do not assume lack of pregnancy in age bearing women.

9. LUNG VENTILATION/PERFUSION SCANS:
(PLEASE SAVE A COPY)
A. VENTILATION SCAN:
B. PERFUSION SCAN:
C. PROBABILITY OF PULMONARY EMBOLISM:

Please save a copy of the ventilation and perfusion scans for your patients. These may be used for future studies.

- A. Note if the ventilation scan was normal or abnormal.
- B. Note if the perfusion scan was normal or abnormal. If abnormal, specify the type of defects present.
- C. List the probability for the presence of pulmonary emboli by lung scan.
- D. Note if there is evidence for right-to-left shunting. Right-to-left shunting can often be detected from a lung scan by uptake in the kidneys. Your radiologist can check for this during the routine perfusion scan if he is informed ahead of time.

10. WAS AN OPEN LUNG BIOPSY PERFORMED:

Note if an open lung biopsy was performed. Please refer to the section in this manual on lung biopsies.

11. TREADMILL EXERCISE TEST:
A. LIST PROTOCOL USED:
B. CONTROL (STANDING):
C. MAXIMAL EXERCISE ATTAINED:
D. DURATION OF EXERCISE:
E. REASON FOR STOPPING:
F. TOTAL METS ACHIEVED:
G. WORKLOAD:

Treadmill tests can be useful in following the effort tolerance in these patients. There is an increased risk in testing these patients, particularly if stressed too much. We are recommending that the treadmill test be terminated at the point where the patient feels that they would ordinarily stop, and not as a test of maximal stress. The test should begin at a low level of exercise (2 METs), and progress gradually from stage to stage (two, and preferably three minutes/stage). Please note the protocol used in your lab. Please indicate the heart rate and blood pressure before and during exercise, the duration of the test and the reason for stopping. If METS are estimated in your laboratory, indicate the work achieved. If the work-load is measured in watts, indicate so in the space provided.

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| 12. ECHOCARDIOGRAMS (PLEASE SAVE COPIES): |
| A. M-MODE: |
| B. 2-D STUDY (SEE INSTRUCTION BOOKLET): |
|-----+-----|

A. M-MODE:

Please save copies of all m-mode echocardiograms done on your patients. All measurements should be made according to the American Society of Echocardiography guidelines.

1. MEASUREMENTS:

- 1) Left atrium.
- 2) Aortic root.
- 3) Left ventricular internal dimension at end diastole.
- 4) Left ventricular internal dimension at end systole.
- 5) Right ventricular internal dimension at end diastole.
- 6) Intraventricular septal thickness at end diastole.
- 7) Left ventricular posterior wall thickness at end diastole.

2. CHECK FOR:

Note appropriate findings if present. 'B' hump on tricuspid valve refers to the same hump that is often seen

on the mitral valve in patients with left ventricular dysfunction.

3. NOTE any other pertinent findings.

B. TWO-DIMENSIONAL STUDY.

1. Note the presence of tricuspid regurgitation using saline contrast (define as contrast visualized in the IVC and hepatic veins during ventricular systole).
2. Note the presence of right-to-left shunting by saline contrast.
3. Please note any other remarkable findings.

13. SPECIFIC TESTS PERFORMED IN THE WORK-UP
OF PRIMARY PULMONARY HYPERTENSION:
- A. PLEASE CHECK METHOD(S) USED TO EXCLUDE UNDERLYING
LEFT TO RIGHT SHUNT:
 - B. WAS A PULMONARY ANGIOGRAM PERFORMED AS
PART OF THE WORK-UP:

- A. Please indicate the method used to exclude the presence of an underlying left-to-right shunt as the cause of the pulmonary hypertension in this patient.
- B. Please note if a pulmonary angiogram was performed in the evaluation of this patient to exclude pulmonary emboli. If so, please note if there were any adverse effects of the procedure.

The following section pertains to patients who, in addition to having primary pulmonary hypertension, also have a history of either cirrhosis, or collagen vascular disorder.

Please look over this section and see if your patient applies. If so fill out the appropriate questions. If not, indicate so and go on to section VIII (HEMODYNAMICS).

1. HEPATIC CIRRHOSIS:
A. COMPLICATIONS:
B. TYPE OF CIRRHOSIS:

For any patient who has a history of cirrhosis please fill out the following:

- A. Complications of the cirrhosis, such as esophageal varices, hepatic encephalopathy, ascites, etc.
- B. Type of cirrhosis. Please check the type of cirrhosis.

2. ASSOCIATED COLLAGEN VASCULAR DISEASES:

Note that Raynaud's phenomena refers to the syndrome that is associated with a specific disease. Raynaud's disease is the syndrome, in the absence of any other related disease. Check any co-existing collagen vascular disease, or immune related disease.

+-----+
| 1. Data acquired from another investigator/institution: |
+-----+

All prospective data on patients entered into the registry must come from the participating clinical center. However, a patient may have been referred to you that previously had a catheterization at another institution. If you wish to provide that data to the registry, indicate in the space provided the date that this data was obtained. This data is to be entered in test panel "A" only and only as "control" data.

+-----+
| 2. Hemoglobin: |
+-----+

At the time of catheterization

+-----+
| 3. Method of O2 Content Determination: |
+-----+

Check the method used in this study.

+-----+
| 4. Method of Cardiac Output Determination: |
+-----+

Specify the technique used in this study. If two techniques are used, specify the second.

+-----+
| 5. Second method of Cardiac Output Determination: |
+-----++-----+
| 6. Chronic Drug Therapy: |
+-----+

If the patient is currently taking chronic oral medications for treatment of their PPH prior to the control measurements being established, please list the drug, daily dosage, and duration of the medical therapy.

+-----+
| Hemodynamic Data: |
+-----+

There are eight sections, numbered 'TEST A', 'TEST B', through 'TEST H'. Each of these is divided into two panels, labelled 'PANEL I' and 'PANEL II'. The eight sections allow reporting of up to eight separate hemodynamic 'tests'. This has been done to allow reporting of measurements from tests which might be made on successive days, or might be made in the lab at one time. These sections are to be filled out for one hospitalization only. (On page -8.3- of the BASELINE REPORTING FORM is a list of the abbreviations which are used in the measurement reporting sections.)

PANEL I (questions 1-8)

1. The date of the study.
2. The time that a drug was administered, if the study is to test drug effects. Please only use MILITARY TIME.
3. The time that the hemodynamic measurements were made. This will then provide knowledge as to how long after the drug was given the measurements were made, or exercise was performed.
4. If this is a study for control data, indicate so.
5. If a drug is being studied, indicate so and provide the name, dose, and route of administration. If more than one drug is administered at the same time, list the second drug in the space provided at the end of panel II under "additional comments". If two drugs are being studied and evaluated at same time, but they are administered at different times, use a second panel to note the time of administration and measurement of the second drug.
6. If the patient is exercised, note the duration, work load, and units of work that the patient performed.
7. Indicate the purpose of the hemodynamic testing.
8. Fill in the hemodynamic measurements in the appropriate spaces.

PANEL II (questions 9-12)

9. List the premedication, if any, that was used in this patient prior to the cath study, and note how long prior to the time reported as "time of measurement" (question 3.) it was given.
10. Deleterious effects of the catheterization. Please note if there were any untoward effects that you determine to be related to the performing of the catheterization procedure (and not from drugs that were given or exercise performed).
11. Deleterious effects of drug testing. Please note if there were any untoward effects that you relate to the administration of the drug that was tested. Indicate (under "C"), if these effects occurred during the procedure, within 24 hours, or before discharge from the hospital.
12. Space is provided for additional comments. It is possible that some centers will be studying patients in a fashion that makes it difficult to report the results on this form. Please use this space to report any information necessary.

EXAMPLE.

(Please refer to the sample form provided for your perusal at the end of this section of the manual.) This sample is provided to help clarify how these forms should be filled out. The following description of a hypothetical case is not intended to serve as a guide to the actual testing of a patient with PPH.

PANEL I

You wish to assess the effects of hydralazine on the exercise hemodynamics of one of your patients. You have already determined the control hemodynamics, and the effects of hydralazine at rest. The date of the test is entered on line 1. The time that hydralazine was given, is indicated on line 2 (13:15 MILITARY TIME = 1:15 pm). The time interval in which the measurements were made is noted on line 3 (30 minutes later). Since this is a drug test, the appropriate space is checked after #5, and the drug hydralazine, is filled in, as well as the dose given and the route of administration. Since this is also an exercise study, the appropriate spaces are marked after #6, as well as the duration of exercise, and the workload (25 WATTS). Since the study is to assess the acute effect of the drug,

this is indicated after #7. The measurements obtained are then listed in the appropriate spaces under #8. Since only one method of cardiac output determination was done, the spaces after Qs (method 2) are left blank.

PANEL II

The patient was given 10 mg valium as premedication 30 minutes before hydralazine was given, and thus 60 minutes before the measurements were given. Thus, valium is noted after question #9, with the dose and time prior to the measurements noted as 60 minutes. There were no deleterious effects noted from the catheterization procedure and this is indicated in #10. However, one hour following the exercise period the patient became hypotensive and required fluids for a short period of time until an adequate blood pressure was restored. This is noted in #11.

7. DISCHARGE THERAPY

Please provide the medical therapy that you discharged the patient on from the hospital in the space provided.

8. ASSESSMENT OF DISCHARGE DRUG THERAPY

This question is for your assessment of the effects of the therapy that you selected to send the patient home on. Please indicate in the appropriate spaces A. if you feel that this therapy has been beneficial to the patient, B. if there was any subjective improvements noted in the patient's symptoms. Space is provided for any other additional comments that you may have.

SAMPLE HEMODYNAMIC MEASUREMENT FORM PANEL I & II

TEST = (PANEL I)

CTR: | = | = |

PAT: | = | = | = |

ACR: | = | = | = | = |

TEST = (PANEL I)	CTR: = =	PAT: = = =	ACR: = = = =
8. Measurements			
1. DATE (M/D/Y) (0 4) (0 1) 19(8 2)	1) Heart rate	1	1 4 0
2. Time drug administered (1 3:1 5)	2) Pra (mean)	2	1 0
3. Time of measurement (1 3 :4 5)	3) Ppa (systolic)	3	_ 9 5
<u>If applicable, specify</u>	4) Ppa (diastolic)	4	_ 4 3
4. () Control	5) Ppa (mean)	5	_ 7 2
<u>If applicable, specify</u>	6) Ppcw (mean)	6	1 2
5. (X) DRUG TEST	7) Psys (systolic)	7	1 3 6
1) NAME <u>HYDRALIZINE</u>	8) Psys (diastolic)	8	_ 7 4
2) DOSE <u>15 mg</u>	9) Psys (mean)	9	_ 8 8
3) ROUTE <u>i.v.</u>	10) Qs. (method 1)	10	_ 6.0 2
<u>If applicable, specify</u>	11) Qs. (method 2)	11	_ _ _ _
6. (X) EXER. TEST	12) PaO2	12	_ 9 6
1) DURATION <u>3 min.</u>	13) PaCO2	13	_ 2 7
2) WORK-LOAD <u>25</u>	14) Sys. Art. PH	14	7.4 9 _
3) WORK-LOAD UNITS <u>watts</u>	15) SA content	15	1 9.6 _
	16) PA content	16	1 2.8 _
	17) VO2	17	4 6 5
7. Purpose(s) of this study: (Check those which apply)			
1) (X) Acute drug effectiveness			
2) () Chronic drug effectiveness			
3) () Control hemodynamics			

TEST == (PANEL I)	CTR: _ _	PAT: _ _	ACR: _ _ _ _
1. DATE (M/D/Y) (0 4) (0 1) 19(8 2)			
2. Time drug administered (1 3:1 5)			
3. Time of measurement (1 3 :4 5)			
<u>If applicable, specify</u>			
4. () Control			
<u>If applicable, specify</u>			
5. (X) DRUG TEST			
1) NAME <u>HYDRALIZINE</u>			
2) DOSE <u>15 mg</u>			
3) ROUTE <u>i.v.</u>			
<u>If applicable, specify</u>			
6. (X) EXER. TEST			
1) DURATION <u>3 min.</u>			
2) WORK-LOAD <u>25</u>			
3) WORK-LOAD UNITS <u>watts</u>			
7. Purpose(s) of this study: (Check those which apply)			
1) (X) Acute drug effectiveness			
2) () Chronic drug effectiveness			
3) () Control hemodynamics			
8. Measurements			
1) Heart rate	1	1 4 0	
2) Pra (mean)	2	1 0	
3) Ppa (systolic)	3	_ 9 5	
4) Ppa (diastolic)	4	_ 4 3	
5) Ppa (mean)	5	_ 7 2	
6) Ppcw (mean)	6	1 2	
7) Psys (systolic)	7	1 3 6	
8) Psys (diastolic)	8	_ 7 4	
9) Psys (mean)	9	_ 8 8	
10) Qs. (method 1)	10	_ 6.0 2	
11) Qs. (method 2)	11	_ _ _	
12) PaO2	12	_ 9 6	
13) PaCO2	13	_ 2 7	
14) Sys. Art. PH	14	7.4 9 _	
15) SA content	15	1 9.6 _	
16) PA content	16	1 2.8 _	
17) V02	17	4 6 5	

SAMPLE HEMODYNAMIC MEASUREMENT FORM PANEL I & II

TEST = (PANEL II)

9. PREMEDICATION GIVEN FOR CATH STUDY.

DRUG	DOSE	TIME (MIN.) PRIOR TO STUDY
VALIUM	/ 10 mg	/ 60 min.
	/	/
	/	/

10. Deleterious effects from catheterization during procedure.

A. NoneB. Yes, check all that apply below1) Arrhythmia requiring thrapy.2) Cardiac trauma, specify: _____3) Death4) Embolic phenomena5) Hypotension requir. thrapy.6) Other, specify: _____

11. Deleterious effects of drug testing.

A. NoneB. Yes, check all apply below1) Allergic reaction2) Bradycardia3) Death4) Hypotension requir. thrapy.5) Oliguria6) Other, specify: _____

C. When were effects first noted?

1) During Cath 2) Within 24 hours3) Prior to discharge

12. Use the following space for additional comments on this test.

SAMPLE HEMODYNAMIC MEASUREMENT FORM PANEL I & II

TEST = (PANEL II)

9. PREMEDICATION GIVEN FOR CATH STUDY.		
DRUG	DOSE	TIME (MIN.) PRIOR TO STUDY
VALIUM	10 mg	60 min.
_____	_____	_____
_____	_____	_____

<p>10. Deleterious effects from catheterization during procedure.</p> <p>A. <input checked="" type="checkbox"/> None</p> <p>B. <input type="checkbox"/> Yes, check all that apply below</p> <p>1) <input type="checkbox"/> Arrhythmia requiring thrapy.</p> <p>2) <input type="checkbox"/> Cardiac trauma, specify: _____</p> <p>3) <input type="checkbox"/> Death</p> <p>4) <input type="checkbox"/> Embolic phenomena</p> <p>5) <input type="checkbox"/> Hypotension requir. thrapy.</p> <p>6) <input type="checkbox"/> Other, specify: _____</p>	<p>11. Deleterious effects of drug testing.</p> <p>A. <input type="checkbox"/> None</p> <p>B. <input checked="" type="checkbox"/> Yes, check all apply below</p> <p>1) <input type="checkbox"/> Allergic reaction</p> <p>2) <input type="checkbox"/> Bradycardia</p> <p>3) <input type="checkbox"/> Death</p> <p>4) <input checked="" type="checkbox"/> Hypotension requir. thrapy.</p> <p>5) <input type="checkbox"/> Oliguria</p> <p>6) <input type="checkbox"/> Other, specify: _____</p> <p>C. When were effects first noted?</p> <p>1) <input type="checkbox"/> During Cath 2) <input checked="" type="checkbox"/> Within 24 hours</p> <p>3) <input type="checkbox"/> Prior to discharge</p>
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<p>12. Use the following space for additional comments on this test.</p> <p>_____</p> <p>_____</p> <p>_____</p>

Drug Therapy with Vasodilator Type Agents

As a registry is not a cooperative drug trial, each individual investigator is free to choose the drug(s) and methods of drug administration to their respective patients. The registry is interested in the results of any drug therapy that may be tried, including both conventional and investigational drugs. Each institution is responsible for acquiring permission for therapies involving experimental practices.

The following list includes agents that have been tried in patients with primary pulmonary hypertension that are available without the need for IND authorization. The investigator may choose to test drugs that can be given intravenously first and then select suitable oral agents, or may empirically select oral drugs to use. In either case, the only way to document the clinical effectiveness of drug intervention is with hemodynamic measurements before and during drug therapy.

To date there has not been identified any agent that is uniformly beneficial in these patients. In addition, there is no established "correct" dosages for the individual drugs. A summary of vasodilator drug usage is given in the protocol with references in the bibliography. The investigator should feel free to use any drug or combination of drugs, in what ever dosage regimen he feels is appropriate.

It should also be pointed out that vasodilator drugs can have an adverse effect in raising pulmonary artery pressure and worsening symptoms. In addition, death following the use of some agents has been reported (particularly intravenous diazoxide). All drugs should be used with caution and patients should be monitored closely.

Vasodilator Drugs That Have Been Used In The Management
of Primary Pulmonary Hypertension

A. Intravenous Agents	Half-Life
Diazoxide	>10 hours
Hydralazine	2-7 hours
Isoproterenol	<15 min
Nitroglycerine	<1 hour
Phentolamine	1-2 hours
Tolazoline	1-4 hours
Verapamil	2-7 hours
Nitroprusside	5 min
B. Oral Agents	
Captopril	
Diazoxide	
Hydralazine	
Isoproterenol (sublingual)	
Minoxidil	
Nifedipine	
Nitroglycerine Preparations	
Phentolamine	
Phenoxybenzamine	
Prozolin	
Tolazoline	
Terbutaline	