

Chapter 5: Adjudication and Recruitment Committee (ARC)

5.1 Overview

The Adjudication and Recruitment Committee (ARC) is tasked to review on-going recruitment, to minimizing inter-center variability with respect to WHO Group classification, assist in the difficult to discern overlap cases and adjudicate any study related events and complications. The committee membership consists of: Drs. Evelyn Horn (Chair), Robert Frantz, Jane Leopold, Stephen Mathai, Franz Rischard, Aaron Waxman and representatives from the Data Coordinating Center (DCC).

5.2 Enrollment of WHO Groups 1-5 PH Participants

While all institutions will strive for inclusion of participants in all WHO Groups there may be differences and institutional/network realignment of target population goals based on ongoing enrollment. Specifically, beyond the WHO Group 1 cohort, it is recognized that there will be some center specific strength in recruitment amongst the WHO Groups 2, 3, 4 and 5. Enrollment will be targeted to 3 – 3.5 years.

5.2.1 Primary WHO Group Diagnosis

- WHO 1: IPAH, HPAH, CTD, CHD, HIV, Portal hypertension, drug induced, PVOD, PCH, CTD (SSc, SLE, MCTD, Sjogren's, RA)
- WHO 2: HFrEF, HFpEF, VHD, RCM, HCM
- WHO 3: COPD, IPF, SSc ILD, other ILD, OHS, OSA, non-parenchymal lung diagnosis, CPFE
- WHO 4: CTEPH: surgery; non-surgical
- WHO 5: sarcoidosis, myeloproliferative disease, hemoglobinopathy (SS or Thalassemia)

WHO Group	1	2	3	4	5
Target/center	50	50	50	8-9	8-9
Target/total	300	300	300	50	50
Incident cases/total	75	75	75	12-13	12-13

5.2.2 Secondary WHO Group Diagnosis (if applicable)

Categorize under primary group and where appropriate include a secondary diagnosis utilizing same criteria for WHO Groups 1-5.

For the specific **overlap diagnosis** of WHO 2, 3 and WHO 1, 3 and possibly WHO 1, 2, 3 we will ask the center Principal Investigator (PI) to include a brief rationale to permit for quick review by committee call (3-4 ARC physician members).

The following criteria should be utilized:

WHO 2, 3: (PCW > 18, LAH, LAE, atrial fib) AND (COPD, IPF, SSC ILD, OHS, OSA, non- parenchymal restrictive lung diagnosis or CPFE);

Supporting rationale for 2 vs 3 primary diagnosis may include response to exercise or hemodynamic challenge such that acute worsening in filling pressures with exercise would prompt the primary WHO 2 diagnosis (and hence WHO 2, 3);

Acute worsening of oxygenation or only mild elevation of PCW would prompt the primary WHO 3 diagnosis (and hence WHO 3, 2);

WHO 1, 3: (features of WHO 1: i.e., autoimmune serology, positive family history) + mild (COPD, IPF, SSC ILD, OHS, OSA, non-parenchymal restrictive lung diagnosis, CPFE);

Stability and severity of hypoxemia/mild parenchymal lung disease in response to activity and/or over time with evidence of progressive PAH.

Within the primary diagnosis group, a running total of the numbers of secondary diagnosis will be maintained and included in the dashboard numbers.

5.2.3 Healthy Controls

- Target/center 16.7; Target/total = 100

5.2.4 Comparator Groups with Mild & Moderate Subclassification in Groups 2 and 3

- WHO 1: mild PH, ePAH, relative of heritable pulmonary arterial hypertension (HPAH), CTD with mild or no PH
- WHO 2: Iso-PH, no PVD
- WHO 3: mild to no PVD, mod PVD
- WHO 4: chronic PE with mild to no PVD

Target Enrollment for WHO Group Comparators

WHO Comparators	1	2 mild-none	2 moderate	3 mild-none	3 moderate	4 mild-none
Target/ctr	20	10.4	10.4	10.4	10.4	5
Target/total	120	62.5	62.5	62.5	62.5	30

5.3 Committee Responsibilities (ARC)

1. Ensure enrollment distributions across traditional groups as outlined in the protocol and in Section 5.2.1-5.2.4.
2. As long as the overall enrollment numbers are met across WHO Groups, comparators and controls, it is recognized that based on center-specific expertise each center may achieve somewhat different target group numbers. Amongst the institutions we do have strength in different areas.
 - a. Cardio-centric
 - b. Pulmonary-centric
 - c. CTEPH
 - d. CTD
3. The Committee will monitor this every 3 months, establish and share a dashboard on current enrollment based on classification groups. This will be sent to centers on a regular basis and will be incorporated into the recruitment reports provided by the DCC.
4. The active dashboard will address deficiencies in a timely matter.
5. The ARC will ensure consistency across centers for WHO Group classification and classification of the mixed disease participants, incident vs prevalent disease, controls and comparators.
6. The ARC will specifically review participants with overlap of diagnoses (e.g., WHO Groups 2, 3 and 1, 3) with criteria as per protocol and outlined above.
7. The ARC will review difficult cases as requested by the center PI.
8. It is recommended that the ARC review all difficult cases for the first 6 months.
9. The ARC will adjudicate any complications that occur during the study evaluations.