

Chapter 55. Quality Control of Pulmonary Function Tests

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55.1 Introduction

Characterization of pulmonary function at or time of entry into the PVDOMICS study is an important aspect of the project. Clinical Centers will forward pulmonary function data (spirometry, lung volumes, diffusing capacity to PVDOMICS as PDF files of the screen shots taken during testing and reports generated upon completion of the test as well as completed PVDOMICS forms: Form 270 (Pulmonary Function Testing Form). Historical PFT data will be submitted in the same fashion using Form 271 (Historical Pulmonary Function Testing Form).

The forms and PDF files will be reviewed for adherence to ATS/ERS Guidelines by the Pulmonary Function Core using a spreadsheet designed to log the evaluation of every effort. A final data quality designation will be assigned to each pulmonary function test. The data will be rated as Acceptable, Usable, Unacceptable or Unable to Rate.

Data Evaluation:

55.2 Forced Spirometry Measurement Quality Grades Quality Control Grades

1. Acceptable Forced Spirometry Measurement Received
A forced spirometry measurement that was transferred to the PVDOMICS database that meets the ATS/ERS Guidelines for acceptability and repeatability with the current Best effort of Acceptable quality as outlined below.
2. Borderline Acceptable Forced Spirometry Measurement Received
A forced spirometry measurement that was transferred to the PVDOMICS database meets the ATS/ERS Guidelines and the study specific criteria for acceptability but not repeatability or meets the ATS/ERS Guidelines and the study specific criteria for usable data with the current Best effort of Acceptable quality as outlined below.
3. Unacceptable Forced Spirometry Measurement Received A forced spirometry measurement that was transferred to the PVDOMICS database where the Current Best effort does not meet the ATS/ERS Guidelines and the study specific criteria for usable measurement as outlined below.
4. Unable to Rate
A forced spirometry measurement that was transferred to the PVDOMICS database without sufficient information or documentation to evaluate the adherence to the ATS/ERS Guidelines and the study-specific criteria.

Acceptability and Repeatability Criteria

When reviewing individual efforts to determine their quality, the PVDOMICS PFT Overreader will be guided by the following criteria for acceptability and repeatability from the ATS/ERS document in accordance with their best clinical judgment:

- Criteria for Acceptability:
 - Start of test criteria:
 - Back extrapolated Volume within acceptable limits

- Back extrapolated volume < 5% of FVC or 150 ml whichever is greater.
 - Or Back extrapolated volume < 5% of FVC > 100 ml whichever is greater when FVC is $\leq$ 1 L.
 - Time to Peak Expiratory Flow is < 120 ms.
 - Absence of artifact or cough within the 1st second.
- End of Effort Criteria
 - Exhalation $\geq$ 6 seconds (no abrupt termination of flow) or 1 second plateau.
- Lack of Technical problems during effort (e.g., baseline drift)
- Criteria for Repeatability
 - Will be based on the Best effort (highest) compared to next Best effort (second highest) based upon FVC and FEV1 values to be
 - $\pm$ 150 ml or
 - $\pm$ 100 ml when FVC < 1L.

- **Forced Spirometry Overall Statements**

The following section lists the specific statements that will be generated by the Overreader during the QC process as explained below.

- **Forced Spirometry All Efforts**
 - Measurement doesn't meet ATS/ERS standards; however Technician's note acceptably explains why measurement does not meet ATS/ERS criteria.
 - QC Report statement: "Measurement does not meet ATS/ERS 2005 standards; however technician provided an adequate explanation why." This will be commented only if there is a technician's note explaining why the measurement does not meet ATS/ERS/study specific criteria and the OverReader determines this is an adequate reason for the measurement to be non ATS/ERS/study specific.
 - Pneumotach reversed.
 - QC Report statement: "All Efforts: Subject breathing on wrong side of pneumotach."
 - Comment made if on all efforts the subject is breathing on the wrong side of the pneumotach (Upside down loops).
 - Baseline drift.
 - Report statement: "All Efforts: Baseline drift."
 - Comment made if on all efforts there is significant baseline drift that in the judgment of the Overreader could affect the measurement.
 - Poor subject effort on all efforts.
 - QC Report statement: "All Efforts: Poor subject effort."
 - Comment made if in the judgment of the Overreader all of the efforts represent a poor subject effort when no other statement could be used to describe the measurements
 - Late time to peak flow
 - QC Report statement: "All Efforts: Poor start of effort, late time to peak flow ($\geq$ 120 ms)".
 - Comment made if on all efforts the time to peak flow is $\geq$ 120 ms.
 - Hesitation during start of forced exhalation, back extrapolated volume is greater than

- 5% of the total FVC or >150 ml whichever is greater. Or > 100 ml when FVC is < 1 L.
 - QC Report statement: “All Efforts: Hesitation during start of forced exhalation,
 - Back extrapolated volume is out of acceptable range.”
 - Comment made if on all efforts the back extrapolated volume is greater than 5% of the total FVC or >150 ml whichever is greater or >100 ml when FVC is < 1 L.
 - Only two acceptable efforts performed.
 - QC Report statement: “All Efforts: Only two acceptable efforts performed.”
 - Comment made if the “Best” effort for FEV1 and FVC are from the effort that meets the acceptability criteria and there is another effort that meets the acceptability criteria or the “Best” FEV1 and FVC come from 2 separate efforts and both efforts meet the acceptability criteria
 - Only one acceptable effort performed.
 - QC Report statement: “All efforts: Only one acceptable effort performed”.
 - Comment made if the “Best” effort for FEV1 and FVC come from the same effort and that effort that meets the acceptability criteria
 - Artifact/Cough during all efforts.
 - QC Report statement: “All Efforts: Artifact/Cough during all efforts.”
 - Comment if there is Artifact/Cough before FEV1 on all efforts or there is Artifact/Cough on all efforts that in the clinical judgment of the OverReader affect the measurement.
 - No efforts available for analysis
 - QC Report Statement: “All Efforts: No efforts available for analysis.”
 - Comment made when there no efforts or values visible for analysis for a measurement.
 - Unable to rate test
 - QC Report Statement: “All Efforts: insufficient data forwarded to rate the quality of the test.”
 - Comment made when there is insufficient data available to rate the quality of the test.
- **Forced Spirometry Best FEV1**
 - Pneumotach reversed.
 - QC Report statement: “Best FEV1: Subject breathing on wrong side of pneumotach, effort should have been deselected.”
 - Comment made if the Best FEV1 effort has the pneumotach reversed (upside down loop) and there is another effort that meets the acceptability criteria with the subject breathing on thePVDOMICS correct side of the pneumotach.
 - QC Report statement: “Best FEV1: Subject breathing on wrong side of pneumotach with no other acceptable efforts performed.”
 - Comment made if the Best FEV1 effort has the pneumotach reversed (upside down loop) and there are no other efforts that meets the acceptability criteria with the subject breathing on the correct side of the pneumotach.
 - Baseline drift.
 - QC Report statement: “Best FEV1: Baseline drift, effort should have been deselected.
 - Comment made if the Best FEV1 effort has a baseline drift and there is another effort that meets the acceptability criteria

- without the baseline drift.
- QC Report statement: “Best FEV1: Baseline drift with no other acceptable efforts performed.”
- Comment made if the Best FEV1 effort has a baseline drift and there are no other efforts that meets the acceptability criteria
- Poor subject effort on effort with “Best FEV1”.
 - QC Report statement: “Best FEV1: Poor subject effort, effort should have been deselected.”
 - Comment made if the Best FEV1 is poor subject effort and there is another effort that meets the acceptability criteria when no other statement could be used to describe the measurement.
This should be made based on ATS/ERS criteria and the judgment of the PVDOMICS Overreader.
 - QC Report statement: “Best FEV1: Poor subject effort with no other acceptable efforts performed”.
 - Comment made if the Best FEV1 is poor subject effort and there are no other efforts that meet the acceptability criteria when no other statement could be used to describe the measurement.
This should be made based on ATS/ERS criteria and the judgment of the PVDOMICS Overreader.
- Late time to Peak
 - QC Report statement: “Best FEV1: Poor start of effort, late time to peak flow (≥ 120 ms), effort should have been deselected.”
 - Comment made if the Best effort for FEV1 has a time to peak ≥ 120 ms and there is another effort that meets the acceptability criteria in section 8.1.2.
 - QC Report statement: “Best FEV1: Poor start of effort, late time to peak flow (≥ 120 ms) with no other acceptable efforts performed.
 - Comment made if the Best effort for FEV1 has a time to peak ≥ 120 ms and there are no other efforts that meet the acceptability criteria in section 8.1.2.
- Hesitation during start of forced exhalation on the effort chosen as Best, back extrapolated volume is greater than 5% of the total FVC or >150 ml whichever is greater (or > 100 ml when FVC < 1 L).
 - QC Report statement: “Best FEV1: Hesitation during start of forced exhalation, back extrapolated volume is out of acceptable range, effort should have been deselected.”
 - Comment made if the Best effort for FEV1 has a back extrapolated volume that is greater than 5% of the total FVC or >150 ml whichever is greater (or > 100 ml when FVC < 1) and there is another effort that meets the acceptability criteria.
 - QC Report statement: “Best FEV1: Hesitation during start of forced exhalation, back extrapolated volume is out of acceptable range with no other acceptable efforts performed.”
 - Comment made if the Best effort for FEV1 has a back extrapolated volume that is greater than 5% of the total FVC or >150 ml whichever is greater (or > 100 ml when FVC < 1) and there are no other efforts that meet the acceptability criteria
- Artifact/Cough during measurement that was used as best: effort should have been deselected.
 - QC Report statement: “Best FEV1: Artifact/Cough during effort; effort should have been deselected.”
 - Comment made if the Best effort for FEV1 has an Artifact/Cough prior

- to FEV1 and there is another effort that meets the acceptability criteria.
 - QC Report statement: “Best FEV1: Cough during effort with no other acceptable efforts performed.”
 - Comment made if the Best effort for FEV1 has an Artifact/Cough prior to FEV1) and there are no other efforts that meet the acceptability criteria.
- Best two FEV1s not repeatable: not within 150 ml.
 - QC Report statement: “Best two FEV1s not repeatable: not within 150 ml.”
 - Comment made if the two highest FEV1 are not within 150 ml and the Best FEV1 effort meets the acceptability criteria.
- Best FEV1: Abrupt end of exhalation.
 - QC Report statement: “Abrupt end of exhalation at or around 1 second.”
 -
- **Forced Spirometry Best FVC**

If the errors listed below in this section are found for the effort marked as, “Best FVC” within a measurement then the “QC Report Statement” listed under the error will be generated.

 - Pneumotach reversed.
 - QC Report statement: “Best FVC: Subject breathing on wrong side of pneumotach, effort should have been deselected.
 - Comment made if the Best FVC effort is separate from the Best FEV1 and has the pneumotach reversed (upside down loop) and there is another effort that meets the acceptability with the subject breathing on the correct side of the pneumotach.
 - QC Report statement: “Best FVC: Subject breathing on wrong side of pneumotach with no other acceptable FVC performed.”
 - Comment made if the Best FVC effort separate from the Best FEV1 and has the pneumotach reversed (upside down loop) and there are no other efforts that meets the acceptability criteria with the subject breathing on the correct side of the pneumotach.
 - Baseline drift.
 - QC Report statement: “Best FVC: Baseline drift, effort should be deselected.”
 - Comment made if the Best FVC effort is separate from the Best FEV1, has a baseline drift and there is another effort that meets the acceptability criteria without the baseline drift.
 - QC Report statement: “Best FVC: Baseline drift with no other acceptable FVC performed.”
 - Comment made if the Best FVC effort separate from the Best FEV1 and has a baseline drift and there are no other efforts that meets the acceptability criteria.
 - Poor subject effort on effort with Best FVC.
 - QC Report statement: “Best FVC: Poor subject effort, effort should have been deselected.”
 - Comment made if the “Best FVC effort is separate from the Best FEV1 effort, shows poor subject effort and there is another effort that meets the acceptability criteria when no other statement could be used to describe the measurement.
 - This should be made based on ATS/ERS criteria and the judgment of the PVDOMICS Overreader.
 - QC Report statement: “Best FVC: Poor subject effort with no other acceptable FVC performed.”
 - Comment made if the “Best FVC effort is separate from the Best FEV1, is poor subject effort and there are no other efforts that meet the acceptability criteria when no other statement

- could be used to describe the measurement.
 - This should be made based on ATS/ERS criteria and the judgment of the PVDOMICS Overreader.
- Artifact/Cough during measurement that was used as Best, effort should have been deselected.
 - QC Report statement: “Best FVC: Artifact/Cough during effort, effort should have been deselected.”
 - Comment made if the Best effort for FVC is separate from the Best FEV1, has an Artifact/Cough that in the clinical judgment of the PVDOMICS Overreader affects the FVC values and there is another effort that meets the acceptability criteria.
 - QC Report statement: “Best FVC: Artifact/Cough during effort with no other acceptable FVC performed.”
 - Comment made if the Best effort for FVC is separate from the Best FEV1 and has an Artifact/Cough that in the clinical judgment of the PVDOMICS Overreader affects the FVC values and there are no other better efforts or FEV1 and FVC are coming from the same effort with an Artifact/Cough that in the clinical judgment of the PVDOMICS Overreader affects the FVC values.
- Subject did not reach plateau at end exhalation, FVC may be underestimated.
 - QC Report statement: “Best FVC: Subject did not reach plateau at end exhalation, FVC may be underestimated.”
 - Comment made only if in the opinion of the PVDOMICS Overreader, the “no plateau” has had a significant effect on the FVC.
- Subject did not exhale for longer than 6 seconds.
 - QC Report statement: “Best FVC: Subject did not exhale for longer than 6 seconds FVC may be underestimated.”
 - Comment made if the expiratory time is <6 seconds on the Best FVC effort and there is no plateau of the end expiratory arm regardless if the FVC and FEV come from the same effort.
If the expiratory time <6 seconds and there is a plateau on the end expiratory arm this comment will not be generated.
- Best two FVC not repeatable: not within 150 ml.
 - QC Report statement: “Best two FVC not repeatable: not within 150 ml.”
 - Comment made if the two highest FVC are not within 150 ml and the Best FVC effort meets the acceptability criteria .
- Best FVC: Abrupt end of exhalation.
 - QC Report statement: “Abrupt end of exhalation; FVC likely to be understated.”
 - Comment made when on the Best FVC effort there is significant drop in the flow rate at the end of the exhalation with a very sharp angle on the volume time curve.

• **Forced Spirometry QC Grade**

After the QC statements are generated a grade will then be assigned based on Quality Control Statements generated during the Quality Control of the measurement. These grades will be:

- Acceptable.
 - Borderline Acceptable.
 - Unacceptable.
- The following is a list of statements generated and the QC grade that would be assigned to a measurement after the QC statements have been generated.

- **Acceptable Forced Spirometry measurement received.**
 - No QC statement indicating less than optimal quality

- ≥ 3 efforts including the current best that meets the acceptability outlined above.
- **Borderline Acceptable Forced Spirometry measurement received.**
 - Data does not meet ATS/ERS 2005 standards; however technician provided
 - an adequate explanation why.
 - All Efforts: Only one acceptable effort performed.
 - With no QC error code generated and the current “Best” meets the acceptability criteria outlined above.
 - All Efforts: Only two acceptable efforts performed.
 - With no other error code generated and the current “Best” meets the acceptability criteria outlined above.
 - Best FEV1: Best two FEV1 not repeatable: not within 150 ml
 - With 2 or more loops including the current best that meets the acceptability criteria outlined above.
 - Best FVC: Best two FVC not repeatable: not within 150 ml.
 - With 2 or more loops including the current best that meets the acceptability criteria.
 - Best FVC: Subject did not reach plateau at end exhalation, FVC may be underestimated.
 - With no other error code generated and the current best meets the acceptability criteria outlined above.
 - Best FVC: Subject did not exhale for longer than 6 seconds, FVC may be underestimated.
 - With no other error code generated and current best meets the acceptability criteria outlined above.
 - Best FVC: Artifact/Cough during effort, with no other acceptable FVC performed.
 - When the Best FEV1 and Best FVC are coming from the same effort this will be graded as Borderline Acceptable when the Artifact/Cough occurs after the first second.
 - When FEV1 and FVC are on different efforts this will be Borderline Acceptable when there are no other errors affecting FEV1.
 - Best FVC: Artifact/Cough, effort should have been deselected.
 - When an artifact or cough is present that seems to have artifactually added volume to the FVC
 - Best FVC: Abrupt end of exhalation.
 - This will be graded as Borderline Acceptable data when the FEV1 and FVC do not equal each other.
 - If the FEV1 and FVC equal each other this will be graded as Unacceptable data.
 - Best FVC: Poor subject effort, effort should have been deselected.
 - This will be graded as Unacceptable the subject’s efforts appears to be poor or inconsistent with the performance of a forced vital capacity maneuver.
 - Best FVC: Poor subject effort with no other acceptable FVC performed
 - The will be graded as Borderline acceptable if the best FEV1 is acceptable.
 - Best FVC: Drift in baseline, effort should have been deselected.
 - Best FVC: Subject breathing on wrong side of pneumotach effort should have been deselected.
- **Unacceptable Forced Spirometry measurement received.**
 - All Efforts: Subject breathing on wrong side of pneumotach.
 - All Efforts: Baseline drift.
 - All Efforts: Poor subject effort.

- All Efforts: Poor start of effort, late time to peak flow (≥ 120 ms).
- All Efforts: Hesitation during start of forced exhalation, back extrapolated volume out of acceptable range.
- All Efforts: Artifact/Cough during all efforts.
- All Efforts: No efforts available for analysis.
- Best FEV1: Subject breathing on wrong side of pneumotach effort should have been deselected.
- Best FEV1: Subject breathing on wrong side of pneumotach with no other acceptable efforts performed.
- Best FEV1: Baseline drift, effort should have been deselected.
- Best FEV1: Baseline drift with no other acceptable efforts performed.
- Best FEV1: Poor subject effort, effort should have been deselected.
- Best FEV1: Poor subject effort with no other acceptable efforts performed.
- Best FEV1: Poor start of effort, late time to peak flow (≥ 120 ms), effort should have been deselected.
- Best FEV1: Poor start of effort, late time to peak flow (≥ 120 ms) with no other acceptable efforts performed.
- Best FEV1: Hesitation during start of forced exhalation, back extrapolated volume is out of acceptable range, effort should have been deselected.
- Best FEV1: Hesitation during start of forced exhalation, back extrapolated volume is out of acceptable range with no other acceptable efforts performed.
- Best FEV1: Artifact/Cough during effort; effort should have been deselected.
- Best FEV1: Artifact/Cough during effort with no other acceptable efforts performed.
- Best FEV1: Abrupt end of exhalation.
- Best FVC: Subject breathing on wrong side of pneumotach effort should have been deselected.
- Best FVC: Subject breathing on wrong side of pneumotach with no other acceptable FVC performed.
- Best FVC: Baseline drift: effort should have been deselected.
- Best FVC: Baseline drift with no other acceptable FVC performed.
- Best FVC: Poor subject effort, effort should have been deselected.
- Best FVC: Poor subject effort with no other acceptable FVC performed.
- Best FVC: Artifact/Cough, effort should have been deselected.
- Best FVC: Artifact/Cough during effort with no other acceptable FVC performed.

55.3 Lung Volumes by Plethysmography Measurement Quality Grades Quality Control Grades

1. **Acceptable Lung Volume by Plethysmography Measurement Received**
A lung volume by plethysmography measurement that was transferred to the PVDOMICS database that meets the ATS/ERS Guidelines for acceptability and repeatability with the current Best effort of Acceptable quality as outlined below.
2. **Borderline Acceptable Lung Volume by Plethysmography Measurement Received**
A Lung Volume by Plethysmography Measurement that was transferred to the PVDOMICS database meets the ATS/ERS Guidelines and the study specific criteria for acceptability but not repeatability or meets the ATS/ERS Guidelines and the study specific criteria for usable data with the current Best effort of Acceptable quality as outlined below.
3. **Unacceptable Forced Spirometry Measurement Received**
A Lung Volume by Plethysmography Measurement that was transferred to the PVDOMICS database where the Current Best effort does not meet the ATS/ERS

Guidelines and the study specific criteria for usable measurement as outlined below.

4. Unable to Rate

A Lung Volume by Plethysmography Measurement that was received without sufficient documentation to allow a QC rating to be assigned.

How the Quality Control Checks are performed:

- Plethysmography measurements will be performed according to the ATS/ERS 2005 recommendations (ERJ 2005; 26(3):511-22). The measurement phase will be reviewed:
 - Thoracic Gas Volume (FRC PLETH) determination
 - Tidal breathing is recorded for at least 30s and a stable end-expiratory lung volume (EELV) is observed for 3 to 5 breathings before activating the shutter.
 - Proceeding to the TGV phase, while still panting, during closure of the shutter, an artifact free Volume shift/Mouth pressure curve should be observed.
 - After opening of the shutter, the subject should perform no more than one or two tidal breaths followed by:
 - a full inspiration to TLC and then a complete, unforced expiration to RV
 - a complete, unforced expiration to RV followed by a complete inspiration to TLC.
 - SVC values $\leq 0.150\text{L}$ difference between the largest and smallest SVC's.
- The “Best” values from the FRC PLETH measurement are calculated from the selected recordings as follows:
 - TLC: RV + largest VC
 - ERV: Average of ERVs from technically acceptable efforts.
 - FRC PLETH: Average of repeatable and technical acceptable FRC PLETH efforts.
 - RV: FRCpleth - VC
 - IC: TLC -FRC PLETH
 - VC (or SVC): the largest VC from an acceptable effort.
 - Comments which were entered by the site personnel are considered when reviewing and grading the measurements.
- PVDOMICS Overreader will choose one QC statement for the specific grade for each FRC PLETH effort that was performed.
 - If there are no errors on an effort then the comment “OK” will be chosen for that effort.
- PVDOMICS PFT Overreader will only report those errors that in their best clinical judgment were due to technical, subject or operator error and have a significant impact on the results.
 - The QC statements for lung volume determination are grouped by all efforts and each individual effort.
 - If there is an error on a particular effort, a statement will be chosen from the statements for that effort.
 - For example: 4 FRC PLETH efforts were collected and the FRC PLETH line of effort 1 had a significant artifact, and efforts 2, 3 and 4 were OK, the Overreader will choose a statement from the effort 1 list for artifact and will chose OK for effort 2,3 and 4.
 - If the error is found on all effort then the statement will be chosen from the all efforts category.

Detailed Description of Errors Reported

- During the QC process each individual FRC PLETH effort that was performed will be commented on.
- “Best” values for TLC, FRC PLETH, RV and IC are calculated as;
 - Reported FRC PLETH is the mean of at least 3 acceptable FRC PLETH values in Liters.
 - Reported ERV is the mean of all ERVs from acceptable VC maneuvers
 - Reported VC is the largest of all acceptable VC maneuvers
 - Reported RV is the difference between the mean FRC PLETH and the mean ERV
 - TLC is the sum of the largest VC and the reported RV

QC statements for all FRC PLETH Efforts:

1. OK
2. Irregular breathing.
 - a. QC Report Statement: “All Efforts: Irregular breathing.”
3. Baseline drift.
 - a. QC Report Statement: “All Efforts: Baseline drift.”
4. Artifacts/leak during shutter maneuver.
 - a. QC Report Statement: “All Efforts: Artifact/leak during shutter maneuver.”
5. Only one or two acceptable FRC PLETH maneuvers performed.
 - a. QC Report Statement: “All Efforts: Only 1 or 2 acceptable FRC PLETH maneuvers performed.”
6. Less than 3 tidal breaths before shutter maneuver.
 - a. QC Report Statement: “All Efforts: < 3 tidal breaths prior to shutter maneuver.”
7. Respiratory Rate > 30 breaths per minute prior to shutter closure.
 - a. QC Report Statement: “All Efforts: > 30 breaths per minute prior to shutter closure.”
8. Efforts during shutter closure > 60 efforts per minute.
 - a. QC Report Statement: “All Efforts: > 60 efforts per minute during shutter closure.”
9. Improper procedure after shutter maneuver.
 - a. QC Report Statement: “All Efforts: Improper procedure after shutter maneuver.”
10. No VC performed after shutter maneuver.
 - a. QC Report Statement: “All Efforts: No VC performed after shutter maneuver.”
11. FRC PLETH is not repeatable ($\Delta > 5\%$).
 - a. QC Report Statement: “FRC PLETH not repeatable within 5%.”
12. SVC not repeatable within .0150L.
 - a. QC Report Statement: SVC not repeatable within 0.150L.
13. No valid lung volume efforts performed
 - a. QC Report Statement: “All Efforts: No valid lung volume efforts performed.”
14. No stable baseline prior to shutter maneuver
 - a. QC Report Statement: “All Efforts: No stable baseline prior to shutter maneuver.”

Individual FRC PLETH Efforts:

In order to save space each individual effort error code list will not be listed in this section. These will be listed in Appendix B of this document. For this section the phrase of Individual Effort will be used to represent the phrase Effort 1, Effort 2 etc. for each effort.

QC statements for FRC PLETH Effort x:

- OK.
- 2. Baseline drift. a. QC Report Statement: “Individual effort X: Baseline drift.”
- 3. No stable baseline prior to shutter maneuver.
 - a. QC Report Statement: “Individual effort X: No stable baseline prior to shutter maneuver.”

4. Less than 3 breaths before shutter maneuver.
 - a. QC Report Statement: "Individual effort X: < 3 breaths before shutter maneuver."
5. Artifact/Leak detected during shutter maneuver.
 - a. QC Report Statement: "Individual effort X: Leak detected during shutter maneuver."
6. VC maneuver not performed.
 - a. QC Report Statement: "Individual effort X: VC maneuver not performed."
7. Start of VC maneuver not within 20 s after shutter opened.
 - a. QC Report Statement: "Individual effort X: Start of VC maneuver not within 20 s after shutter opened."
8. Improper VC maneuver performed.
 - a. QC Report Statement: "Individual effort X: Improper VC maneuver performed."
9. No valid lung volume effort.
 - a. QC Report Statement: "Individual effort X: No valid lung volume effort."
10. Resting Respiratory Rate > 30 breaths per minute prior to shutter closure.
 - a. QC Report Statement: "Individual effort X: > 30 breaths per minute prior to shutter closure."
12. Efforts during shutter closure > 90 per minute.
 - a. QC Report Statement: "Individual effort X: > 90 efforts during shutter closure."
13. FRC Pleth is not repeatable
 - a. QC Report Statement: "Individual effort X: FRC Pleth is not repeatable".

Body Plethysmography Lung Volumes QC Grade

Each test set will be assigned a grade based on Quality Control Statements generated during the Quality Control of the data. These grades will be:

- Acceptable lung volume data.
- Borderline Acceptable lung volume data.
- Unacceptable lung volume data.

1. Acceptable FRC PLETH data received:
 - a. No QC statements other than OK.
2. Borderline Acceptable FRC PLETH data received:
 - a. Only 2 valid FRC PLETH maneuvers with no additional individual effort error.
 - b. SVC not repeatable; not within 0.150L.
 - c. FRC PLETH not repeatable > 5% but within 10%.
3. Unacceptable FRC PLETH data received:
 - a. ≤ 1 valid FRC PLETH maneuver.
 - b. All Efforts: Baseline drift.
 - c. Individual Effort: Baseline drift
 - d. All Efforts: No VC performed after shutter maneuver.
 - e. Individual Effort: No VC performed after shutter maneuver.
 - f. All Efforts: Start of VC not within 20 s after shutter opened.
 - g. Individual Effort: Start of VC not within 20 s after shutter opened.
 - h. All Efforts: Resting Respiratory Rate > 30 breaths per minute prior to shutter closure.
 - i. Individual Effort: Resting Respiratory Rate > 30 breaths per minute prior to shutter closure.
 - j. All Efforts: Efforts during shutter closure > 60 efforts per minute.
 - k. Individual Effort: Efforts during shutter closure > 60 efforts per minute.
 - l. All Efforts: FRC variability exceeds variability limit of 10%.
 - m. Individual effort: FRC exceeds variability limit of 10%.
 - n. All Efforts: Artifact/Leak detected during shutter maneuver.
 - o. Individual effort: Artifact/Leak detected during shutter maneuver.
 - p. All Efforts: Less than 3 breaths before shutter maneuver.
 - q. Individual effort: Less than 3 breaths before shutter maneuver.

- r. All Efforts: No stable baseline prior to shutter maneuver.
- s. Individual effort: No stable baseline prior to shutter maneuver.
- t. All Efforts: No valid lung volume efforts.
- u. Individual effort: No valid lung volume effort.
- v. All Efforts: Improper VC maneuver performed.
- w. Individual effort: Improper VC maneuver performed

Reporting of Quality Control Results

Best Test Review (BTR)

Description of Best Test Review “BTR” Process

1. During the BTR process
 - a. All measurements are reviewed.
 - b. If there is an effort with an error this effort will be deselected if:
 - i. There are other efforts present which are acceptable.
 - ii. By removing this effort the BTR grade will be Borderline Acceptable or Acceptable.
2. Unacceptable efforts will not be reactivated during the BTR process.
3. If an effort is deselected, the PVDOMICS Overreader will be required to choose a statement indicating that the effort has been deselected as well as one or more statements indicating the reason(s) for the change.
4. If the PVDOMICS Overreader does not change the data, a statement indicating that the data has not been changed will be made.

Body Plethysmography Best Test Review

This section of the document will list the BTR statements will be generated during BTR. Each test set will have one of the following statements generated during BTR.

1. Body Plethysmography data unchanged.
2. Body Plethysmography data changed.
3. Body Plethysmography original data was reactivated because BTR data changes were rejected by Principal Investigator. DO NOT REPLY TO THIS FAX.

Statements used when an effort is removed

When an effort is deselected or modified the PVDOMICS Overreader will be required to select a reason why from the list below:

FRC PLETH maneuver removed due to:

- a. No stable baseline prior to shutter maneuver.
- b. Baseline drift.
- c. Less than 3 breaths before shutter maneuver.
- d. VC maneuver not performed.
- e. Start of VC maneuver not within 20 s after shutter opened.
- f. Improper VC maneuver performed.
- g. No valid measurement.
- h. Resting Respiratory Rate > 30 breaths per minute prior to shutter closure.
- i. Efforts during shutter closure > 60 breaths per minute.
- j. Artifact/Leak during shutter maneuver.

Body Plethysmography BTR Grade

Each test set will be assigned a grade based on BTR Statements generated during the BTR of the data. This grade will be: Acceptable, Borderline Acceptable and Unacceptable. The following is a list of BTR statements and the grade that would be assigned if they were chosen.

Body Plethysmography FRC PLETH BTR Grades:

1. Acceptable FRC PLETH data after BTR.
 - a. ≥ 3 acceptable FRC PLETH efforts after BTR process demonstrating $< 5\%$ variability.
 - Borderline acceptable FRC PLETH data after BTR.
 - a. 2 acceptable FRC PLETH efforts after BTR process.
 - b. Variability of >2 acceptable FRC PLETH efforts is greater than 5% but less than 10%.
 3. Unacceptable FRC PLETH data after BTR.
 - a. ≤ 1 acceptable FRC PLETH effort after BTR process.
 - b. Variability of acceptable FRC PLETH efforts exceeds 10%.
- a) Establishing a stable EELV.

Lung Volumes by Multiple Breath Washout measurement Quality Grades

1. Quality Control Grade
 - a. Acceptable Lung Volumes by Multiple Breath Washout measurement received.
 - i. A Lung Volumes by Multiple Breath Washout measurement that was transferred to the PVDOMICS database that has all efforts that meet the Acceptability and Repeatability criteria outlined .
 - b. Borderline Acceptable Lung Volumes by Multiple Breath Washout measurement received.
 - i. A Lung Volumes by Multiple Breath Washout measurement that was transferred to the PVDOMICS database that has at least 2 efforts that meet the Acceptability criteria outlined and not the Repeatability criteria.
 - c. Unacceptable Lung Volumes by Multiple Breath Washout measurement received.
 - i. A Lung Volumes by Multiple Breath Washout measurement that was transferred to the PVDOMICS database that has ≥ 1 effort that do not meet the study specific Acceptability criteria outlined .
2. Best Test Review Grades
 - a. Acceptable Lung Volumes by Multiple Breath Washout measurement after Best Test Review
 - i. A Measurement that after BTR that has ≥ 2 efforts that meet the Acceptability and Repeatability criteria .
 - b. Borderline Acceptable Lung Volumes by Multiple Breath Washout measurement after Best Test Review
 - i. A Measurement that after BTR that has ≥ 1 efforts that meet the Acceptability criteria .
 - c. Unacceptable Lung Volumes by Multiple Breath Washout measurement after Best Test Review
 - i. A Measurement that after BTR that has 0 efforts that meet the Acceptability criteria .

Pulmonary Function Definitions

1. **Functional Residual Capacity measured by multiple breath washout of nitrogen from the lungs: FRC_{MBW} .**

The functional residual capacity is the volume of air in the lungs at the end of a normal resting expiration. This volume is set by the balance between the elastic properties of the lung and chest wall. The FRC is comprised of two volumes: the expiratory reserve volume (ERV) and the residual volume (RV).

2. Expiratory Reserve Volume: ERV

The maximum volume of air that can be voluntarily exhaled from beyond the FRC. This volume is limited by the duration of the expiratory effort of the patient and by airway closure caused increased expiratory pressure. Coaching to obtain a maximum ERV is best done by coaching for a sustained submaximal expiratory effort.

3. Inspiratory Capacity: IC

The maximum volume of air that can be inspired from FRC. This volume is limited by the inspiratory effort of the subject and can be maximized by vigorous coaching.

4. Residual Volume: RV

The volume of air left in the lungs after a maximal exhalation. The residual volume is calculated by subtracting the expiratory reserve volume (ERV) from the functional residual capacity (FRC).

5. Percent Predicted (% Predicted):

The ratio of a value to a mean predicted normal value which was calculated from a gender-specific regression equation that incorporates the subject's age and height. The regression equation is obtained from a study of subjects determined to be free of cardiopulmonary disease.

6. Total Lung Capacity: TLC

The volume of air attained in the lungs after a maximal inhalation. This value is calculated as the sum of the vital capacity (VC) and the residual volume (RV).

7. Vital Capacity: VC

The volume of air measured from a slow, complete expiration after a maximal inspiration, without a maximal forced effort. Sometimes specified as the Slow Vital Capacity (SVC). In this study, VC EX is used to designate the VC maneuver performed after the IC maneuver.

8. Tidal Volume: VT or TV

The volume of air the subject breaths during relaxed, resting breathing. No coaching should be done during the collection of tidal breathing to prevent the subject from consciously varying the size of the breath or the rate of respiration.

Best Test Review

1. All study subjects will have their measurements reviewed for BTR on a continuing basis in a second step after QC has been performed for a given measurement. Internal Data Review

55.4 Diffusion Capacity Test (DLCO)

Quality Control

1. The following will be evaluated on the DLCO measurement:
 - a. Phase 1 tidal breathing
 - b. Phase 2: the ERV maneuver and has a plateau prior to inhaling the gas mixture.
 - c. Phase 3: quick and deep inhalation after the ERV maneuver.
 - d. Phase 4: a stable breath hold without an increase in mouth pressure.
 - e. Phase 5: after the breath hold an exhalation of minimal 1.5 L.

How are the Quality Control Checks Performed:

1. The DLCO data will first be analyzed by computer algorithms based on the ATS/ERS 2005 criteria for single breath diffusion testing (ERJ 2005; 26: 720–735).
2. When reviewing a measurement, the CHRS Clinical OverRead Specialist will be guided by the following criteria in accordance with their clinical judgment:
 - a. Complete exhalation to RV and plateau.
 - b. Breath hold at TLC for 10 seconds.
 - c. Artifacts / Morphology.
 - d. Technical errors.
 - e. Procedural errors.
3. Comments which were entered by the site personnel are considered when reviewing and grading the measurements.
4. PVDOMICS Overreader will choose a QC statement for each effort that was performed and submitted for each measurement.
 - a. If there are no errors on an effort then the comment of OK will be chosen for that effort.
 - b. PVDOMICS Overreader will only report errors that in their best clinical judgment were due to technical, subject or operator error and have a significant impact on the saved results.
5. The QC statements are grouped by all efforts and each individual effort.
 - a. If there is an error on a particular effort a statement will be chosen from statements for that effort.
 - b. For example: a subject performed 4 efforts and effort 1 had an artifact/cough, and efforts 2, 3, and 4 were OK, the PVDOMICS Overreader will choose a statement from the effort 1 list for artifact/cough and will chose OK for effort 2, 3 and 4.
 - c. If the error is found on all efforts then the statement will be chosen from the all efforts category for that specific error.
6. This computer generated information along with clinical judgment will be used by the Clinical Specialist to determine if there are any errors present with data as it was received from the investigator sites.

Detailed Description of Errors Reported

During the QC process each individual effort that was performed will be commented on. This is done because average values are reported and each effort has an influence on the average.

All Efforts:

1. Baseline drift.
 - a. QC Report Statement: “All Efforts: Baseline drift.”
 - i. This comment is made when there is a drifting baseline on all efforts.
2. Only one DLCO measurement performed.
 - a. QC Report Statement: “All Efforts: Only one DLCO measurement performed.”
 - i. This comment is made when there is only 1 acceptable DLCO effort present.
- No valid measurements.
 - a. QC Report Statement: “All Efforts: No valid measurements performed.”
 - i. This comment is made when there are no valid efforts present.
4. Artifact/Cough.
 - a. QC Report statement: “All Efforts: Artifact/Cough.”
 - i. This comment is made when there all efforts show an artifact/cough that in the clinical judgment of the PVDOMICS Overreader is affecting the data. This statement will be chosen from the all efforts list.
5. Subject did not fully exhale to RV.
 - a. QC Report Statement: “All Efforts: Subject did not fully exhale to RV.”
 - i. This comment is made when the subject does not fully exhale to residual

- volume on all efforts. This may be evident due to no Plateau at RV.
6. Subject did not inhale to at least 85% of the highest VC measured at the visit (VCmax).
 - a. QC Report Statement: "All Efforts: Subject did not inhale to at least 85% of VC."
 - i. This comment is made when the subject does not meet the minimum 85% inhalation of VC on all efforts.
 7. Subject held breath for >12 seconds.
 - a. QC Report Statement: "All Efforts: Subject held breath for more than 12 seconds."
 - i. This comment is made when the subject holds their breath for more than 12 seconds from RV to TLC on all efforts.
 8. Leak detected during breath hold.
 - a. QC Report Statement: "All Efforts: Leak detected during breath hold."
 - i. This comment is made when the subject allows air to leak out around the mouthpiece at any point during the maneuver on all efforts.
 9. Increased mouth pressure during breath hold.
 - a. QC Report Statement: "All Efforts: Increased mouth pressure during breath hold."
 - i. This comment is made when the subject does not maintain a consistent mouth pressure and plateau during the 4th phase of the maneuver on all efforts.
 10. Subject did not sufficiently exhale air at the end of breath hold.
 - a. QC Report Statement: "All Efforts: Subject did not sufficiently exhale air at the end of breath hold."
 - i. This comment is made when the subject does not sufficiently exhale air at the end of the breath hold / plateau of phase 4 on all efforts.
 11. Incorrect alveolar gas analysis.
 - a. QC Report Statement: "All Efforts: Incorrect alveolar gas analysis."
 - i. This comment is made when the gas analysis curve shows an artifact or abnormality that the Overreader feels invalidates the gas analysis for that effort.
 12. DLCO not repeatable.
 - a. QC Report Statement: "DLCO not repeatable."
 - i. All values of all measurements need to be within a span of 3.0 ml/min*mmHg) of mean (Best).
 13. VA not repeatable.
 - a. QC Report Statement: "VA not repeatable."
 - i. Comment made when values of all measurements need to be within a span of 200 mL off mean (Best).

Individual Effort:

In order to save space each individual effort error code list will not be listed in this section. For this section the phrase of Individual Effort X will be used to represent the phrase for Effort 1, Effort 2 etc. of each measurement.

1. Baseline drift.
 - a. QC Report Statement: "Effort x: Baseline Drift."
 - i. This comment is made when there is a drifting baseline coming from one individual effort.
2. Artifact/Cough.
 - a. QC Report statement: "Effort x: Artifact/Cough."
 - i. This comment is made when the subject shows a cough/artifact that in the judgment of the PVDOMICS Overreader affects the data of one individual effort.
3. Subject did not fully exhale to RV.
 - a. QC Report Statement: "Effort x: subject did not fully exhale to RV."
 - i. This comment is made when the subject does not fully exhale to residual volume on an individual effort. This may be evident due to no Plateau at RV.
4. Subject did not inhale to at least 85% of previously measured VC.

- a. QC Report Statement: "Effort x: Subject did not inhale to at least 85% of previous VC."
 - i. This comment is made when the subject does not meet the minimum 85% inhalation of VC on an individual effort per ATS/ERS guidelines.
5. Subject did not hold breath for ≤ 12 seconds.
 - a. QC Report Statement: "Effort x: breath hold time ≥ 12 seconds."
 - i. This comment is made when the subject does not hold their breath for a minimum 12 seconds from RV to TLC on an individual effort.
6. Leak detected during breath hold.
 - a. QC Report Statement: "Effort x: Leak detected during breath hold."
 - i. This comment is made when the subject allows air to leak out around the mouthpiece at any point during the maneuver on an individual effort.
7. Increased mouth pressure during breath hold.
 - a. QC Report Statement: "Effort x: Increased mouth pressure during breath hold."
 - i. This comment is made when the subject does not maintain a consistent mouth pressure and plateau during the 4th phase of the maneuver on an individual effort.
8. Subject did not exhale enough air at the end of breath hold.
 - a. QC Report Statement: "Effort x: Subject did not sufficiently exhale air at the end of breath hold."
 - i. This comment is made when the subject does not sufficiently exhale air at the end of the breath hold / plateau of phase 4 on individual effort.
9. Incorrect alveolar gas analysis.
 - a. QC Report Statement: "Effort x: Incorrect exhaled gas analysis."
 - i. This comment is made when the Overreader determines the gas analysis for an effort has been marred by a technical problem.

QC Grade

Each test set will be assigned a grade based on Quality Control Statements generated during the Quality Control of the data. These grades will be:

- Acceptable.
 - Borderline acceptable.
 - Unacceptable Data Received: All Efforts do not meet ATS criteria. This measurement cannot be improved through Best Test Review and no data will be changed.
 - Unacceptable.
 - Unratable.
1. Acceptable DLCO data received.
 - a. No QC statement other than OK.
 2. Borderline acceptable DLCO data received.
 - a. Only one DLCO measurement performed.
 - b. DLCO not repeatable.
 3. Unacceptable DLCO Data Received: All Efforts do not meet ATS criteria. This measurement cannot be improved through Best Test Review and no data will be changed.
- Unacceptable DLCO data (selected when data can be improved by deselecting a submitted effort.
 - a. Individual Effort: Baseline Drift.
 - b. Individual Effort: Artifact/Cough.
 - c. All Efforts Subject did not fully exhale to RV.
 - d. Individual Effort: Subject did not inhale to at least 85% of previous VC.
 - e. Individual Effort: Subject did not hold breath for <12 seconds.
 - f. Individual Effort: Leak detected during breath hold.
 - g. All Effort: Increased mouth pressure during breath hold.

- h. Individual Effort: Subject did not sufficiently exhale air at the end of breath hold.
- i. Individual Effort: Incorrect alveolar gas analysis.
- 4. Unacceptable DLCO data received.
 - a. Individual Effort: Baseline Drift.
 - b. Individual Effort: Artifact/Cough.
 - c. All Efforts Subject did not fully exhale to RV.
 - d. Individual Effort: Subject did not inhale to at least 85% of previous VC.
 - e. Individual Effort: Subject did not hold breath for <12 seconds.
 - f. Individual Effort: Leak detected during breath hold.
 - g. All Effort: Increased mouth pressure during breath hold.
 - h. Individual Effort: Subject did not sufficiently exhale air at the end of breath hold.
 - i. Individual Effort: Incorrect alveolar gas analysis.

Reporting of Quality Control Results

Best Test Review

Description of Best Test Review (BTR) Process

1. During the BTR process.
 - a. All measurements are reviewed.
 - b. If there is an effort with an error this effort will be deselected if:
 - i. There are other efforts present which are acceptable.
 - ii. By removing this effort the BTR grade will be Borderline Acceptable or Acceptable.
2. If an effort is deselected, the Overreader will be required to choose a statement indicating that the effort has been deselected as well as one or more statements indicating the reason(s) for the change.
3. If the Overreader does not change the data, a statement indicating that the data has not been changed will be made.

DLCO BTR

This section of the document will list the BTR statements generated during BTR. Each test set will receive one of the following statements during BTR.

1. DLCO data unchanged.
2. DLCO data changed.

Statements used when an effort is deselected

When an effort is deselected the PVDOMICS Overreader will be required to select a reason why from the list below:

DLCO Effort removed due to:

1. Baseline drift.
2. Artifact/Cough.
3. Subject did not fully exhale to RV.
4. Subject did not inhale to at least 85% of previous VC.
5. Subject held breath for >12 seconds.
6. Leak detected during breath hold.
7. Increased mouth pressure during breath hold.
8. Subject did not sufficiently exhale air at the end of breath hold.
9. Incorrect alveolar gas analysis.
10. Technical difficulties.

DLCO BTR Grade

Each test set will be assigned a grade based on BTR Statements generated during the BTR of the data. This grade will be: Acceptable, Borderline Acceptable and Unacceptable. The following is a list of BTR statements and the grade that would be assigned if they were chosen.

DLCO BTR Grades:

1. Acceptable DLCO data after BTR.
 - ≥ 2 acceptable and repeatable DLCO efforts after BTR process.
2. Borderline acceptable DLCO data after BTR.
 - 1 acceptable DLCO effort after BTR process
 - ≥ 2 acceptable but not repeatable DLCO efforts after BTR process.
3. Unacceptable DLCO data after BTR.
 - No acceptable DLCO efforts after BTR process.