

Newsletter - January 2006

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Jack summarises the key points in the new joint ATS/ERS Guideline for Standardization of Spirometry

*Jack Wanger has worked in the field of respiratory medicine for over 35 years at establishments of world-renown such as UCLA (Los Angeles, California, USA) and National Jewish Medical and Research Center (Denver, Colorado, USA). Jack is a member of the American Thoracic Society Proficiency and Standards for Clinical Pulmonary Function Laboratories Committee and was a member of **ATS/ERS Task Force** that developed the new joint ATS/ERS pulmonary function guidelines. He was the lead writer for the joint ATS/ERS Guideline on the Measurement of Lung Volumes. For the last 4 years he has also provided his expert knowledge in a consultancy capacity to Vitalograph specifically in the area of clinical trials and in organizing for Vitalograph a team of experts who provide **QA review of all spirometry tests** transmitted within a centralized spirometry environment. In this short review Jack shares some key thoughts on the new joint **ATS/ERS Standardization of Spirometry** Guideline.*

In 2005, the European Respiratory Society (**ERS**) and American Thoracic Society (**ATS**) finalized and published joint guidelines on standardizing pulmonary function tests. These guidelines represent a consensus of a task force consisting of 19 scientists with recognized expertise in pulmonary function testing. They reflect the current knowledge in the field and provide a guide for good clinical practice.

The need for **global guidelines** became more apparent as global initiatives were undertaken for the diagnosis and treatment of pulmonary diseases. Additionally, pulmonary function testing instrumentation varied considerably in the worldwide market.

Of particular interest to the pharmaceutical clinical trial arena is the Standardization of Spirometry Guideline (Miller MR, et al., [Eur Respir J. 2005](#)). It is a cleaner and more user-friendly document compared to earlier ATS and ERS guidelines. The forced vital capacity (FVC) maneuver section describes instrumentation requirements and quality control issues including volume accuracy checks. Calibration checks should be done daily and the accuracy of the known-volume syringe must be considered. For devices using disposable flow sensors, a new sensor from the supply used for patient tests should be checked each day of use.

The within-maneuver acceptability criteria are similar to earlier spirometry guidelines. However, the **between-maneuver criteria** (repeatability) have been tightened. In earlier guidelines it was recommended that the two highest FVC and forced expiratory volume in 1 second (FEV₁) values from acceptable maneuvers agree within 0.200 L. In the new ATS/ERS Guideline, this has been changed to **0.150 L**. This should improve within-subject variability.

In most respiratory research trials a determination of airflow-limitation reversibility is common. The new Guideline describes this procedure mostly from a clinical perspective; however, the recommendations can also be applied to research. One suggestion is to administer 4 separate doses (puffs) of albuterol/salbutamol using a valved spacer. Each breath is then held for 5 to 10 seconds before the subject exhales, and separated by about 30 seconds. This dose ensures that the response is high on the albuterol dose-response curve. The Guideline also notes that a lower dose can be used if there is a concern about any effect on the subject's heart rate or tremor.

Also included in the Guideline are recommendations for measuring vital capacity (VC), **inspiratory capacity (IC)**, and peak expiratory flow (PEF). These measurements are common endpoints in respiratory trials and have lacked detailed performance recommendations in the past. The measurement of IC has taken on increased interest in **COPD clinical trials** because it is a surrogate for the measurement of lung hyperinflation and has been shown to be a good predictor of lung function improvement. When performing the IC maneuver, the Guideline suggests the patient be relaxed (shoulders down and relaxed) and asked to breathe regularly for several breaths (at least 3) to establish a stable end-expiratory lung volume. The patient should be urged to then take a full inspiration with no hesitation. While there is insufficient evidence regarding optimal recommendations for the repeatability criteria of IC, the Standardization of Spirometry Guideline recommends that the average of at least three IC maneuvers be reported.

The interpretation of pulmonary function data including spirometry is usually based on the comparison of measured data in an individual patient with **reference (predicted) values**. In clinical trials we use reference values to define the study population. The reference values used should be obtained from studies of healthy subjects with the same anthropometric and ethnic characteristics as the patient being tested. The ATS/ERS Interpretative Strategies Guideline (Pellegrino R, et al., Eur Respir J, 2005) suggests that **in the USA**, the ethnically appropriate **NHANES III reference equations** (Hankinson J, et al., Am J Respir Crit Care Med 1999) for those 8 to 80 years of age. For children under age 8, the equations of **Wang et al** (Wang X, et al., Pediatr Pulmonol, 1993) are recommended. However, the Guideline also notes that other reference equations may be used if there are valid reasons for the choice. In Europe, the combined reference equations published by the ERS in 1993 (Quanjer PH, et al. Eur Respir J, 1993) are often used for those 18 to 70 years of age, and the reference equations from Quanjer et al (Quanjer P, et al., Eur Respir J, 1989) for children 6 to 18 years of age. However, the **Guideline did not make recommendations for use of specific equations in Europe**, and suggests the need for a new Europe-wide study to derive updated reference equations for lung function.

While the Standardization of Spirometry Guideline, as well as the other joint ATS/ERS pulmonary function test guidelines represent a significant step forward in the development of global guidelines for pulmonary function testing, they are not perfect. Inevitably new scientific evidence and technology will lead to changes and updates in the future.



Expert QA Review



Site Spirometry



Patient Diary



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Contacts

Email: pharma@vitalograph.co.uk

Vitalograph USA - tel: +1 913-888-4221
Vitalograph UK/International - tel: +44 (0) 1280 827120
Vitalograph Germany - tel: +49 (0) 40 547391-0
Vitalograph Ireland - tel: +353 (0) 65 686 4100
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