SOP Spirometry

1. General considerations

Spirometry serves as a physiological test to quantify pulmonary disease severity and to assess clinical change in respiratory function over time. Standard spirometric measures will include dynamic lung function parameters as forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and mean (mid-) expiratory flow (MEF 25-75). Spirometry will be performed at baseline and at follow up visits according to the corresponding study protocol.

	Definition	**Unit**
FVC	**Forced vital capacity:** maximal volume of air exhaled with maximally forced effort from a maximal inspiration.	l (liter) at BTPS[1]
FEV1	**Forced expiratory volume in one second:** maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration.	l (liter)* at BTPS
MEF 25-75	**Mean forced expiratory flow:** mean expiratory flow between 25% an 75% of the FVC	l/s

Tab.1: lung function parameters for interventional trials.

The following has been adapted from the ATS/ERS-guideline on spirometry ("ATS/ERS-TASK FORCE: Standardisation of Lung Function"). For more detailed information please refer to:
http://www.thoracic.org/statements/resources/pft/PFT2.pdf

Various studies show, that pulmonary function testing in preschool-aged infants (4y +) produces acceptable and repeatable spirometry results [1-3]. In this study spirometry will be performed in all (non ventilated) patient from age 4 on.
All technicians involved in pulmonary function testing of children should be specifically trained to deal with such a situation. A pleasant, age-appropriate atmosphere is important in making children feel at ease. Detailed but simple instructions, encouragement and visual feedback in the teaching are important in helping children to perform the manoeuvre. Even if unsuccessful at the first session, children will learn to be less intimidated and may perform far better in a subsequent session.

It is recommended that patients should not be tested within 1 month of a myocardial infarction (contraindication). Patients with any of the conditions listed in table 2 are unlikely to achieve optimal or repeatable results.

Chest or abdominal pain of any cause (e.g. surgery)
Oral or facial pain exacerbated by a mouthpiece
Stress incontinence
Confusional state

Tab.2: Conditions potentially causing suboptimal lung function results.

[1] BTPS: body temperature and ambient pressure with water vapour

All measures recommended by the ATS/ERS Task Force to prevent transmission of infection to patients and/or staff during pulmonary function testing are applying to spirometric testing within this study (see http://www.thoracic.org/statements/resources/pft/PFT1.pdf "HYGIENE AND INFECTION CONTROL").

2. Equipment performance criteria and equipment validation

To provide accurate spirometry data ATS/ERS recommendations on equipment and calibration procedures should be followed. Potential study centres have to send in a detailed description of their spirometry equipment, which will be evaluated by the study coordinating team. Only if minimal requirements are met the respective center can participate in the study.

Detailed information on minimal technical requirements and calibration procedure for spirometer are listed here:
http://www.thoracic.org/statements/resources/pft/PFT2.pdf

3. Equipment quality control

Quality-control procedures are essential to validate spirometric equipment within calibration limits. Key aspects of equipment quality control are summarised in table 3. Calibration checks for volume accuracy and system leaks have to be undertaken at least daily before spirometry testing. If a device fails to meet the accuracy requirement (table 3), a new calibration procedure or equipment maintenance is required.

A log of following parameters must be kept (will be reviewed by auditing team):

- log of calibration results and calibration checks (see also table 2).
- documentation of repairs or other alterations of the equipment.
- dates of computer software and hardware updates or changes.

Test	**Minimum interval**	**Action**	**Accuracy requirement**
Volume	Daily	check with a 3 l syringe	accuracy of measured volume must be in **+/-3,5%** of the true
Leak	Daily	3 cmH2O (0.3 kPa) constant pressure for 1 min	volume loss must be **< 30 mL** after 1 min
Flow linearity	Weekly	test at least three different flow ranges (triple test)	accuracy of measured volume at these 3 flows must be in **+/-3,5%** of the true
Volume linearity	Quarterly	1 l increments with a calibrating syringe measured over entire volume range	accuracy of measured volume must be in **+/-3,5%** of the true for all volumes tested
Time	Quarterly	mechanical recorder check with stopwatch	accuracy of **+/-2%**
Software	Specified by manufacturer	install latest software available	

Tab. 3: summary of equipment quality control.

4. Test Procedure

A. Test Preperation

- Anthropometric Data

The patient's age, height and weight (wearing indoor clothes without shoes) are recorded for use in the calculation of reference values. Height is measured using an accurate measuring device without shoes, with the feet together, standing as tall as possible with the eyes level and looking straight ahead. Age is expressed in years. Height and weight are recorded in meter (m) and kilogram (kg).

- Therapy

Type, dosage and last intake of any (inhaled or oral) medication that may alter lung function are recorded. Long- and short-acting bronchodilators must not be administered before testing (SABA/SAMA: 3 hours; LABA/LAMA: 8 hours before testing).

- Position

Sitting is preferable for safety reasons in order to avoid falling due to syncope. If testing is performed in standing individuals, the test manoeuvre has to be performed with slightly elevated head. The use of a nose clip or manual occlusion of the nares is recommended. Posture and noseclip use should be recorded and reported.

- Instructions and demonstration by technician

Before performing the test technician demonstrate the appropriate technique described below. Instruction should be detailed but simple and age-appropriate (see also above). In between tests instructions should be repeated if necessary.

B. Breathing Manoeuvre (closed circuit method)

The FVC manoeuvre consists of three distinct phases 1) maximal inspiration; 2) a "blast" of exhalation; and 3) continued complete exhalation to the end of test.

- **Have subject assume the correct position.**

- **Attach nose clip, place mouthpiece in mouth and close lips around the mouthpiece:** the breathing tube should be inserted into the patient's mouth, making sure the lips are sealed around the mouthpiece and that the tongue does not occlude it.

- **Inhale completely and rapidly with a pause of < 1 s at total lung capacity (TLC):** Patients should inhale rapidly and completely from

functional residual capacity (FRC) to total lung capacity (TLC). The following exhalation manoeuvre should be begun without pause.

- **Maximal exhalation until no more air can be expelled while maintaining an upright posture:** The subject should be prompted to fully exhale. Throughout the manoeuvre, enthusiastic coaching of the subject using body language and phrases, such as "keep going" are required. If a manoeuvre has an obviously hesitant start, the technician may terminate the trial early to avoid an unnecessary prolonged effort (see also start of test criteria). The exhalation manoeuver should be continued until end of test criteria are fulfilled (see below).

- **Repeat for a minimum of three valid manoeuvres.** Manoeuvres that do not meet test quality criteria should not be used to satisfy the requirement of three acceptable manoeuvres.

D. Test Quality Criteria

Within-manoeuvre quality criteria are a satisfactory start of test and a satisfactory end of test (EOT), i.e. a plateau in the volume–time curve. In addition, the technician should observe that the subject understood the instructions and performed the manoeuvre with a maximum inspiration, a good start, a smooth continuous exhalation and maximal effort (see table 4).
It is recommended to use computer-based system for rapid feedback to the technician when in manoeuver criteria are not met.

Only test manoeuvers, which meet all within-manoeuvre quality criteria can be used for determination of lung function parameters.

Criteria	Definition
Start of test	defines the start of timed measurements (time 0). To achieve an accurate time 0 and assure the FEV1 comes from a maximal effort curve, the EV (back extrapolated volume) must be < 5% of the FVC or < 0.150 L, whichever is greater. Rapid computerized feedback to the technician when the start criteria are not met is strongly recommended.
End of test	EOT criteria are used to identify a reasonable FVC effort (one or more). I) The subject cannot or should not continue further exhalation. Although subjects should be encouraged to achieve their maximal effort, they should be allowed to terminate the manoeuvre on their own at any time, especially if they are experiencing discomfort. II) Plateau on time volume curve. The volume–time curve shows no change in volume (< 0.025l) for ≥1 s, and the subject has tried to exhale for ≥3s in children aged <10 years and for ≥6 s in subjects aged ≥10 years.
Free from artefacts	Artefacts interfere with the measurement of accurate results: • Cough during the first second of exhalation; • Glottis closure or hesitation during the manoeuver that causes a cessation of the airflow; • Leak at mouthpiece or obstruction of mouthpiece (e.g. tongue) • Early termination or cut-off, extra breathing • Effort that is not maximal throughout

Tab. 4: summary of within-manoeuvre quality criteria.

Between-manoeuvre quality criteria define repeatability of conducted test manoeuvre. A valid test requires a minimum of three acceptable FVC manoeuvres. Acceptable repeatability is achieved when the difference between the largest and the next largest FVC is ≤0.15 l and the difference between the largest and next largest FEV1 is ≤0.15 l (resp. ≤0.1 l for FVC of <1.0 l; both measures).
If both of these criteria are met, the test session may be concluded. If these criteria are not met in three manoeuvres, additional trials should be attempted, up to a maximum of eight manoeuvres.

5. Test Result Selection

FVC and FEV1 should be measured from a series of at least three forced expiratory curves that meet all quality criteria described above.
The *largest* FVC and the *largest* FEV1 should be recorded after examining the data from all of the usable curves, even if they do not come from the same curve. MEF 25-75 is taken from the blow with the largest sum of FEV1 and FVC (see also figure 1).

All measures have to be reported in absolute numbers (l;l/s).

If only a single satisfactory manoeuver is recorded, then these results should not be excluded simply because of poor repeatability. The number of technically satisfactory maneuvers and the repeatability results should always be reported.

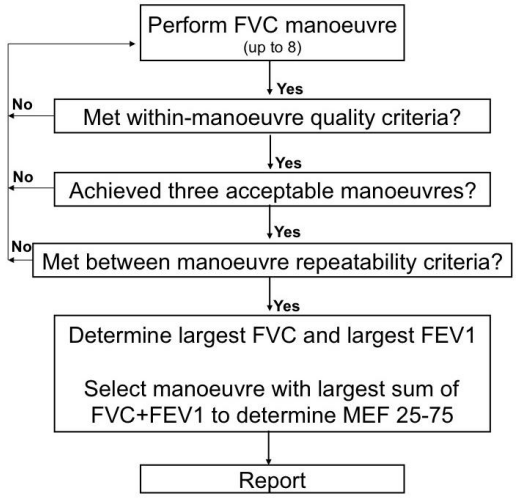

Fig. 1: application of quality criteria and test result selection.

6. Reference Values

Relative values will be calculated using spirometric prediction equations, which have been provided by the European Respiratory Society Global Lung Function Initiative (adjusted for age range, sex and ethnicity) [4].

7. Overview of recorded measures

Measure	Unit	
FVC	l	
FEV1	l	
MEF 25-75	l/s	
sex		male/female
age	years	
weight	kg	
height	m	
posture when performing test		sitting/standing
occlusion of the nares		yes/no
number of technically satisfactory manoeuvres	n	

1. Loeb, J.S., et al., *Acceptability and repeatability of spirometry in children using updated ATS/ERS criteria.* Pediatr Pulmonol, 2008. **43**(10): p. 1020-4.
2. Gaffin, J.M., et al., *Clinically useful spirometry in preschool-aged children: evaluation of the 2007 American Thoracic Society Guidelines.* J Asthma. **47**(7): p. 762-7.
3. Aurora, P., et al., *Quality control for spirometry in preschool children with and without lung disease.* Am J Respir Crit Care Med, 2004. **169**(10): p. 1152-9.
4. Quanjer PH., et al., *Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations.* Eur Respir J, 2012. **40**(6): p.1324-43.