Nebulisers are not always appropriately used in France. Some patients who ought to be treated with them are not prescribed the treatment and many others are incorrectly treated.

The Groupe AérosolThérapie (GAT) of the Société de Pneumologie de Langue Française (SPLF) therefore reviewed the recommendations of the first nebulisation experts meeting held in 1997.

The proposals put forward in 2007 remain a compromise; they are in fact based on what it would seem reasonable to do in view of the state of the art and current constraints.

These best practice guidelines do not concern the use of MDIs or DPIs.

The best practice proposals below are not exhaustive. It is particularly important in all cases to refer to the instructions given by the pharmaceutical companies that market the drugs and the manufacturers of the medical devices.

1. Scope of application of the nebulisation best practice guidelines

1.1 These best practice guidelines are designed for health care personnel, physicians and any person who implements an aerosol treatment using a nebuliser in a hospital setting, a health care centre or at home.

1.2 This document does not cover best nebulisation practices for the purposes of diagnosis (ventilation scintigraphy, bronchial provocation tests) or nebulisers used to treat patients under mechanical ventilation, even if many of the principles apply equally in these cases.

2. The nebulisation system

2.1 A nebulisation system is a medical device and must therefore bear the CE medical device approval label
and its performances must be stated in the documents enclosed in its packaging in compliance with standard EN 13544.

2.2 Nebulisation systems are made up of: a generator, a nebuliser and a patient interface; they may also include complementary functions.

2.3 The 3 types of aerosol generator currently available are:

### GLOSSARY

**Aerosol:** Stable suspension of solid or liquid particles in a gas (fall under 0.5 m/sec).

**Nebulisation therapy:** Treatment by an active principle delivered in an aerosol.

**Delivery circuit:** Set of accessories placed between the nebuliser’s reservoir and the entrance to the patient’s airways.

**CE:** Logo showing that a medical device has been manufactured in compliance with the specifications stipulated by the European Union. A nebulisation system that carries the CE sign must also bear the number of the notified certification body.

**Disinfection:** Procedure aimed at eliminating infectious agents for a limited period of time (on the contrary to sterilization which aims at making sure that there are no germs for the period indicated on the packaging).

**Medical device:** Equipment or item, considered alone or combined with others, which the manufacturer has designed to be used for the diagnosis, prevention, treatment or mitigation of a medical condition.

**Health care provider:** Physical person or moral entity that makes the nebulisation system available to the carer or the patient.

**Complementary functions:** Series of functions added to the nebulisation function.

**Manufacturer:** Physical person or moral entity that ensures that all or part of a nebulisation system is in good working order, even if it does not manufacture the system.

**Interface:** Part of the aerosol delivery circuit that is directly in contact with the patient.

**MMAD:** Mass median aerodynamic diameter of an aerosol, measured in pre-defined conditions.

**Nebulisation:** Creating an aerosol from a liquid preparation.

**Single patient:** A single-patient device is dedicated to the use of only one patient. The maximum duration of use after opening the packaging is indicated by the manufacturer.

**Preparation:** Medication(s) and the diluent liquid placed in the nebuliser’s reservoir.

**Nebulisation system:** Set of equipment designed to produce an aerosol by nebulisation.

**Single use/disposable:** A disposable device is a device that can only be used once for one session on one patient. It cannot be disinfected nor reconditioned.

2.3.1 Compressed air generators in which the medicated preparation is nebulised by compressed gas (Bernoulli effect). The gas propellant can be stored under pressure (in a gas tank or from a supply line in hospital) or produced by a compressor.

2.3.2 Ultrasonic generators in which the medicated preparation is nebulised by ultrasounds (cavitation effect). Generators can be equipped with single or double reservoirs. They can also be equipped with a power actuator to adjust the output of the nebuliser.

2.3.3 Mesh generators in which the medicated preparation is nebulised by high throughput, high frequency vibrations through the micro-pores of a membrane or mesh.

2.4 The nebuliser is connected to the generator by a length of tube (this is included into the device for the ultrasound and vibrating mesh models) and a reservoir into which the medicated preparation is poured. The patient interface is connected up to this tube.

2.4.1 The patient interface can be:
- a mouth-piece,
- a face mask covering the nose and mouth,
- nostril-pieces,
- a tracheal connector.

2.4.2 The delivery circuit can either be closed or include air inlets to admit extra air (Venturi effect). The main air inlet and the additional inlets may also include a one-way valves to stop the aerosol from escaping from the delivery circuit during the expiratory phase.

2.4.3 The delivery circuit may also include an expiratory circuit, with or without a valve and may also include a filter to collect the particles exhaled or produced during expiration.

2.5 The following complementary functions may also be included into the generators and the delivery circuits or proposed as accessories:

2.5.1 Manually operated, breath actuated or ventilator dependent devices to control aerosol production and/or delivery;

2.5.2 Dose-measurement systems to measure the amount of medicated preparation delivered at each breath and the number of breaths taken;

2.5.3 Some nebulisers produce sound vibrations at around 100 Hz (sonic effect), the sonic effect is designed to enhance the aerosol’s penetration into the sinuses;

2.5.4 Others combine sound vibrations with pressure waves (manosonic effect); the manosonic effect is designed to enhance particle deposition in the sinuses and the Eustachian tubes;

2.5.5 There are also devices who include an extra airflow system (fan) to pick up the aerosol that has been generated, especially useful in continuous humidification;

2.5.6 Liquids that are nebulised to humidify the air can be warmed (but this never applies to drug preparations);
2.5.7 There are models that display the patient’s inspiratory rate;
2.5.8 They may also be fitted with a timing system, with or without an alarm;
2.5.9 Many devices also include a sound alarm or a and warning in case of malfunction.
2.5.10 Somes devices include a module to record nebulisation courses.
2.6 Nebulisation systems are classified in 3 categories according to the target site where the active ingredient is to be deposited in the upper or lower airways:
2.6.1 Nebulisers designed to deposit medicated preparations in the upper airways produce large particle aerosols; most of the aerosol is carried in particles of over 5 µm in diameter (N.B. The best particle size for preparations to be deposited in the sinuses is unknown and must be assessed);
2.6.2 Systems designed to deposit preparations in the trachea and bronchi produce an aerosol which is mainly carried in 2 to 5 µm particles;
2.6.3 Systems designed to deposit preparations deep in the lungs produce an aerosol which is mainly carried in 0.5 to 2 µm particles;
2.6.4 The use of a pictogram is recommended to clearly identify each of these 3 categories (appendix 1).
2.7 It is important to make sure that the nebulisation system is compatible with the medication prescribed and suitable for its stability; the characteristics of the aerosol produced must be checked, using a procedure based on validated results (standard EN 13544-1, summary of product characteristics published by French agency for medications (AFSSAPS), publications and/or expert opinions).
2.7.1 The written results of the tests can be issued from:
– the pharmaceutical company that markets the drug which is licensed to be used in aerosols and recommends the use of one or several nebulisation systems for this purpose,
– the manufacturer of the nebuliser,
– the regulations,
– a knowledgeable society,
– the scientific literature.
2.7.2 An active ingredient should not be used in any nebulisation system(s) unless the system has been tested for this purpose.
2.7.3 The pharmaceutical company must be able to produce the results of measurements made using the drugs they manufacture in each of the 3 types of nebuliser (compressed air, ultrasound, mesh) and prove that they meet the specifications of standard EN 13544.1.

These measurements will either prove that the drug behaves in a similar way to sodium fluoride (used to apply the European standard) or characterize the differences.

If the results are not satisfactory, further measurements must be made before authorising the use of the aerosol generator, which must meet the requirements of the nebulisation principle stipulated for the drug it is approved for use with.

2.8 The energy source used to operate a compressed air generator can be either a compressor or a source of pre-stored compressed gas.
2.8.1 It is important to respect the pressure and the flow-rates advised for the nebuliser reservoir, otherwise the particle size may change. The relevant information must be provided on the instructions delivered with each nebuliser.
2.8.2 When a compressed gas is used to supply the pressure and input to the nebuliser’s reservoir, unless otherwise prescribed the gas should always be compressed air.
2.8.3 Medical oxygen cannot be considered as a simple propellant gas. It must only be used on special medical prescription if medically required, having checked that it is compatible with the product to be nebulised and made sure that the patient treated has no contraindication to high-velocity oxygen treatment.
2.9 The leaflet containing the instructions for use in French should include all the information listed in the main requirements* n°13 (Appendix I of decree 95-292 of the 16 March 1996 and in standard EN 13544-1).

3. Choice of a nebulisation system

3.1 Choice of the interface between the nebuliser and the patient.
3.1.1 Nasal masks, nostril pieces or face masks (closely fitting the nose and mouth) should be used to treat young infants except in special cases and only when justified to do so.
3.1.2 For bronchial and pulmonary indications a mouth piece should be used, unless there is any constraint or special indication that warrants not doing so; face masks must only be used be used for bronchial and pulmonary disorders/infections* in young children and if a mouth-piece is not a more effective option.
3.1.3 In very young children (under the age of five), use a face-mask, which must be properly applied to the child’s face throughout the treatment.
3.1.4 When using a drug that is potentially dangerous for people around the nebuliser, such as pentamidine, some antibiotics or iloprost, the delivery circuit must be equipped with a closed interface and an expiratory circuit with a filter with an efficiency of at least 99% of the particles exhaled over 1µm in diameter.
3.1.5 If the patient is tracheotomised the interface should be a mask or a tracheal connection-piece.
3.2 The choice of a nebulisation system depends on:
3.2.1 The current recommendations concerning the pharmaceutical form of the drug to be nebulised;
3.2.2 The deposition site: E.N.T., bronchi or lungs;
3.2.3 The volume to be nebulised: the duration of the aerosol treatment, a preparation should not be nebulised for more than 10 minutes in children and 20 minutes in adults, except in special cases;
3.2.4 the patient and his/her capacity to adapt to the nebuliser (using the system, hygiene procedures);
3.2.5. Environmental and economic factors related to the nebuliser or the drug.

4. Products used in a nebuliser

4.1 The products administered using a nebuliser may be:
– drug preparations licensed to be administered by this route;
– products recognised as being effective by this route of administration, whether their action is mainly pharmacological or physical (isotonic saline solution).

4.2 It is inadvisable to nebulise:
– oily products that are likely to cause lipidic lung disorders;
– pure water and hypotonic preparations, particularly distilled water;
– preparations containing excipients or preservatives that are potentially dangerous (such as sulphides).

4.3 Products that are not designed for administration in an aerosol must not be used in nebulisers.

4.4 A preparation to be nebulised must be made up with sterile fluids.

4.5 The instructions for using drugs in a nebuliser must give details of:
– the physical nature of the active ingredient (solution or suspension);
– its possible sensitivity to heating;
– the stability of the product if it is diluted.

4.6 Products that are licensed for nebulisation are usually ready for use and do not require diluting.

5. The indications for nebulisation

5.1 Asthma and hyper-reactive bronchial conditions in other bronchial disorders.

5.1.1 On-going anti-inflammatory treatment of moderate, persistent allergic asthma: cromoglycate, according to the licensed recommendations. (N.B. this drug is not advised as a first-line treatment in the international recommendations).

5.1.2 On-going anti-inflammatory treatment of moderate, persistent juvenile allergic asthma when other treatments have failed: budesonide or beclomethasone according to the licensing recommendations.

5.1.3 Symptomatic treatment of severe acute asthma according to the licensing recommendations and of asthma that does not respond to the standard treatment: terbutaline, salbutamol, ipratropium bromide.

5.2 Cystic fibrosis.

5.2.1 To fluidify the bronchial secretions in patients over the age of 5 with an FVC > 40% of the mean predicted value: rh-DNase according to the licensing recommendations; 7% hypertonic saline solution in some indications.

5.2.2 Antibiotic treatment for chronic *Pseudomonas aeruginosa* infection using the standard rationales or as a substitute for systemic treatment: aminosides, i.e tobramycin or colimycine.

5.2.3 Bronchodilators for COPD (see 5.3).

5.2.4 Steroids if the patient also has asthma.

5.3 COPD.

5.3.1 To fluidify the bronchial secretions during attacks of COPD when other treatments have failed.

5.3.2 Bronchodilation in severe forms of COPD when properly implemented treatments with MDIs or DPIs have failed: ipratropium bromide, terbutaline, salbutamol. The treatment should only be pursued for more than a month in this indication if the patient has drawn benefit from the first prescription.

5.4 Pneumocystosis.

Primary or secondary prevention after intolerance or failure of a treatment by sulfamethoxazole-trimethoprim: Pentamidine according to the licensing indications.

5.5 Treatment of primary arterial hypertension (PAH) Class III.

Iloprost according to the licensing indications.

5.6 Expectoration induced by nebulising hypertonic saline solution.

5.7 Acute or chronic inflammatory conditions of the upper airways.

Essential oil of *Melaleuca viridiflora* is the only medical preparation that is licensed for use in this case in France.

6. The implementation nebulisation

6.1 Best practice for the prescription of the treatment:
6.1.1 A prescription for nebulisation therapy should give details of:
– the active principle(s),
– the dose per session or “until the nebuliser emits no more mist”,
– dilution, if necessary (type and volume of diluent),
– the duration of the session,
– the number of sessions a day,
– schedule, if necessary,
– the number of days,
– the type of nebuliser, if relevant the type of propellant gas or at least the target site where the active ingredient should be deposited,
– the type of interface between the nebuliser and the patient,
– output adjustment if the nebuliser has an output actuator,
– how the session should be timed to fit in with any other treatments, in particular in relation to physiotherapy sessions for patients with bronchial mucus restricting the penetration of the nebulised treatment.
6.2 Best practice for the implementation of the nebulised treatment.

6.2.1 If the legal information given on the license or indicated by the prescribing physician does not give specific instructions**, the person appointed by the physician or by the pharmacist to supervise the nebulised treatment should choose the appropriate type of nebuliser: ultrasonic, compressed air or vibrating mesh system (intermittent or continuous delivery, type of patient-nebuliser interface and other functions see 2.5). The prescribing physician should be advised of the type of nebuliser selected.

6.2.2 Medical oxygen requires a special prescription (bearing details of flow-rate and duration) and should be based on the best practice in the use of medical gases.

6.2.3 When using a compressed air nebuliser the person appointed by the physician or alternatively by the pharmacist to implement the nebulised treatment, must check that:

6.2.3.1 the flow-rate rate on the prescription complies with the recommendations for use issued by the manufacturer of the nebuliser if a propellant gas is used. If no such details are given on the prescription, the recommended flow-rate should be used.

6.2.3.2 the input pressure complies with the specification of the compressor and of the nebuliser reservoir if a compressor is used.

6.2.4 Advice on how to use and maintain the system must be given in written form.

The patients and their families must be trained (informed and assessed) by a prescribing physician, a pharmacist, a physiotherapist, a nurse or a respiratory care practitioner on how to prepare, maintain and use the nebuliser and the drugs used in it.

6.2.5 The patient must be trained to inhale the aerosol properly by the prescribing physician, the pharmacist, a physiotherapist or a nurse.

6.3 The personnel appointed by the prescribing physician or by the pharmacist to implement these best practices must be trained to do so. They must be competent to carry out the instructions on the leaflets given with the different medical devices and drugs that are used in them.

6.4 The prescribing physician must check with the patient or the person in charge of operating the nebuliser that the aerosol treatment will be carried out under proper supervision and that it is complies with the prescription.

6.5 Maintenance and disinfection of the nebulisation system.

6.5.1 Disposable systems must never be re-used. They are designed to be used once only.

6.5.2 Single-patient-use or re-usable nebulisation systems must be maintained according to the instructions given in the instruction leaflet which the manufacturer must provide.

6.5.3 Extra details on the frequency and type of maintenance (disinfection, check-up) and the duration of use can be given on the prescription or via the dealer’s own internal procedures, but must never be less strict than those stipulated by the manufacturer of the medical device.
Appendix 1. Pictograms used on a nebuliser to identify the preferred target site for the saline solution or the preparation administered.
Appendix 2. Drugs licensed in France for use in a nebuliser in October 2006 (table).

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<thead>
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<th>Class</th>
<th>Brand name</th>
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