Conferece Summary

Metered-Dose Inhalers and Dry Powder Inhalers in Aerosol Therapy

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Summary

Inhaled drug delivery is an important part of the armamentarium of clinicians caring for patients with pulmonary disease. An increasing variety of metered-dose inhalers and dry powder inhalers are becoming available. This has been driven by the development of new formulations and the impending ban on chlorofluorocarbon propellants. The result is a proliferation of devices, resulting in a confusing number of choices for the clinician, as well as confusion for patients trying to use these devices correctly. The presenters at this conference included many of the world’s authorities on metered-dose inhalers and dry powder inhalers, and were an appropriate mix of academic aerosol scientists, clinician researchers with an interest in aerosol therapy, and aerosol scientists working for industry. Improper inhaler technique is common among patients. One of the important take-home messages of this conference is the importance of clinicians knowledgeable in the use of aerosol delivery devices and clinicians’ ability to teach patients how to use these devices correctly. Respiratory therapists are uniquely positioned to provide this service, and there is evidence that respiratory therapists may do this better than others. The proceedings of this conference provide the current state of the art of metered-dose inhalers and dry powder inhalers. Key words: metered-dose inhaler, MDI, dry powder inhaler, DPI, aerosol, drug delivery. [Respir Care 2005;50(10):1376–1383. © 2005 Daedalus Enterprises]

Introduction

Inhaled drug delivery is an important part of the armamentarium of clinicians caring for patients with pulmonary disease. The use of inhaled aerosols allows selective treatment of the lungs by achieving high drug concentrations in the airway and reducing systemic adverse effects. Not only is aerosol therapy used to treat lung disease, but increasingly inhalation is being explored as a method for systemic drug delivery (eg, inhaled insulin and inhaled narcotics). Moreover, inhaled drug delivery is used to treat not only airway disease and pulmonary infection, but also to treat pulmonary vascular disease (eg, iloprost). The effectiveness of inhaled drugs depends not only on the formulation, but perhaps even more on the delivery device and the patient’s ability to use the device correctly. A less-than-optimal technique results in decreased drug delivery and potentially reduced efficacy. An important disadvantage of inhaled drug delivery is that specific techniques are necessary for the proper use of inhaler devices.
The American Respiratory Care Foundation sponsored a conference on liquid nebulization in 2002, and I was fortunate to be invited to summarize that conference. A logical extension of that conference is this one entitled, “Metered-Dose Inhalers and Dry Powder Inhalers in Aerosol Therapy.” An increasing variety of metered-dose inhalers (MDIs) and dry powder inhalers (DPIs) are becoming available. This has been driven in large part by the development of new formulations and the impending ban on chlorofluorocarbon (CFC) propellants. The result is a proliferation of devices, resulting in a confusing number of choices for the health-care provider, as well as confusion for patients trying to use these devices correctly.

The presenters at this conference included many of the world’s authorities on MDIs and DPIs. The presenters were an appropriate mix of academic aerosol scientists, clinician researchers with an interest in aerosol therapy, and aerosol scientists working for industry. The result was a rigorous discussion of the science of MDI and DPI, with a distinctly clinical bent. The readers of Respiratory Care should be able to translate this wealth of information to the care of their patients. I am flattered to have been asked to summarize the conference proceedings.

**Overview**

The conference started with a fascinating presentation by Paula Anderson on the history of aerosol therapy. Anderson provided an historical perspective of aerosol therapy, dating to 2000 BC. I have captured some of her presentation in a timeline (Fig. 1). Anderson has been a collector of aerosol therapy antiquities for many years, and some of the slides of historical devices that she showed are of devices from her personal collection. She also referred to a Web site that features many pictures from the history of aerosol therapy (http://www.inhalatorium.com). She finished her presentation by discussing major influences on modern inhaled drug delivery: theoretical models and predictions, indirect measures of lung deposition, particle sizing and in vitro measurements, scintigraphy, pharmacokinetics and pharmacodynamics, and the Montreal Protocol. This set the stage nicely for the remainder of the conference.

The next presentation, by Gerald Smaldone, was titled, “Assessing New Technologies: Patient-Device Interactions and Deposition.” Smaldone presented a classification of aerosol delivery systems based on inertia. He classified the MDI as a high-inertia system; the use of a valved holding chamber or spacer converts the MDI from high inertia to low inertia. The nebulizer is a low-inertia system, and the DPI is a moderate-inertia system. Smaldone challenged the group to consider dose and response (eg, move away from the bronchodilator mentality). He then challenged us not only to consider new devices, but to take a new look at old devices. As an example, aerosol delivery via face mask was discussed. Face masks are used for aerosol delivery with nebulizers, valved holding chambers, and non-invasive ventilation. However, the nuances of the effects of the face mask are not commonly appreciated. He also challenged us to consider the role of breathing pattern on aerosol delivery, suggesting that it is important either to control the breathing pattern or to adapt the aerosol device output to the breathing pattern. There may not be a breath-
ing pattern that is ideal for all patients and all diseases. This raised a provocative question during the discussion: should scintigraphy be used to determine the best breathing pattern for inhaled drug delivery for a specific patient? With the discussion of methods to improve delivery, we were reminded that “more is not always better,” in that it has the potential to result in toxicity.

“The Expanding Role of Aerosols in Systemic Drug Delivery, Gene Therapy, and Vaccination” was presented by Beth Laube. She began her presentation with a discussion of the use of the inhalation route for systemic drug delivery (eg, insulin and narcotics). A major advantage of the inhalation route is that it avoids the unwanted effects of drug delivery via injection (ie, no needles). The challenge is to develop appropriate inhalation devices and formulations. As she described, devices and formulations of inhaled insulin are in various stages of development. Laube also discussed issues related to aerosolized gene vectors. The greatest clinical and academic interest for aerosolized gene therapy is in cystic fibrosis (inhaled cystic fibrosis transmembrane regulator vectors). Gene transfer via inhalation has not achieved clinical benefit to date, but remains a subject of intense interest. There is also interest in the delivery of vaccines via aerosol (eg, measles, influenza, and measles/mumps/rubella). As an example, Laube described the World Health Organization Measles Aerosol Project.

The Metered-Dose Inhaler

Stephen Newman began the discussion on the MDI with his presentation, “Principles of Metered-Dose Inhaler Design.” It was noted that we are approaching the 50th anniversary of the introduction of the MDI. In a short time frame, unheard of today, the Medihaler-Epi and Medihaler-Iso were approved by the Food and Drug Administration in March 1956, and marketing of these products began in May 1956. Although more than 400 million MDIs are produced annually, these devices have been called the most complex dosage form in medicine. The components of the MDI include the container (usually aluminum), the propellant (CFC or hydrofluoroalkane [HFA]), the formulation (suspension in the case of CFC or solution in the case of HFA), the metering valve, and the actuator (press-and-breathe or breath-actuated). It was noted that the actuator nozzle is a key determinant of aerosol characteristics, and the quality of the aerosol is related to nozzle size, cleanliness, and the presence of moisture. Dose counters are currently not incorporated in the design of the MDI, but can be added from third-party vendors. In the future, a dose counter may be a requirement in the design of the MDI. Newman also described the design of devices that modify the aerosol emitted from the MDI. These include velocity modifiers and spacers. Spacers can be classified as tube extensions to the inhaler mouthpiece (eg, Azmacort), holding chambers (eg, Aerochamber), and reverse-flow devices (eg, InspirEase, Optihaler). The spacer places time and distance between the patient and the MDI, reduces oropharyngeal deposition, increases lung deposition, reduces the need for coordination, and reduces the “cold-Freon” effect. Aerosol retention and emitted dose depends on the size and shape of the spacer, static charge on the inner walls of plastic spacers, and dead volume for children. In addition, valves in the spacer must open easily, and ideally there should be an inspiratory flow rate signal.

“Optimizing Aerosol Delivery by Pressurized Metered-Dose Inhalers” was addressed by Bruce Rubin. Rubin pointed out that there are numerous limitations of CFC MDIs, including limited formulations, priming requirements, inconsistent dosing, tail-off as the canister approaches empty, lack of dose counter, decreased dose when cold, high plume flow, and high oropharyngeal deposition. Some of these limitations of traditional press-and-breathe MDIs are overcome with the breath-actuated MDI. There are also improvements with HFA MDIs, including less oropharyngeal deposition and greater lung deposition, decreased requirement for priming, and less tail-off when the canister approaches empty. Although holding chambers are commonly used with the MDI, Rubin pointed out a number of potential issues, including mask fit and seal in children; crying and asynchrony in children; dead volume in children; electrostatic charge; multiple actuations into the chamber, which decreases dose delivery; and delay between actuation into the chamber and inhaling the dose. It was also pointed out that dose delivery can be affected in some designs if the boot on the device does not fit the MDI. The issue of whether or not to lower the dose when the MDI is used with children was discussed, and the group did not reach consensus on this issue. There were several memorable quotes from Rubin’s presentation, including, “Even if we had foolproof devices, we do not have foolproof patients,” and “Patients may use what they like best . . . they will not use a device they don’t like . . . they might not even use a device that they like.”

“The CFC to HFA Transition and Its Impact on Pulmonary Drug Development” was discussed by Chet Leach. We were reminded that the ozone layer of the atmosphere reduces the amount of ultraviolet radiation reaching the earth and CFC depletes atmospheric ozone. The Montreal Protocol on Substances That Deplete the Ozone Layer (which came into force in January 1989) set a timetable for elimination of CFC use. There are exemptions for essential uses (eg, MDIs and the space shuttle) until at least 2008. Obviously, no one advocates destruction of the ozone layer. HFA-134a does not deplete the ozone layer and has a low order of toxicity, thus making it an attractive alternative to CFC propellants in the MDI. However, HFA has posed a variety of pharmaceutical challenges to industry, with the goal to match dose delivery to an existing CFC product. Interestingly, use of an HFA propellant is able to over-
come some of the issues with CFC MDIs, including priming, temperature effects, tail-off, and plume geometry. However, a breath-hold is more important with use of an HFA propellant. A concern related to HFAs is that they are greenhouse gases. But in a memorable quote, Leach stated, “One cow contributes more greenhouse gas per day than 10 asthmatics each inhaling 2 puffs of Proventil-HFA 4 times a day.” It remains to be seen whether there may be a move to ban HFA in the future.

The Dry Powder Inhaler

Anthony Hickey addressed “Dry Powder Inhaler Formulation.” Particle characteristics are determined by their shape and structure. Processing of particles includes blending and controlled aggregation. Flow and dispersion are important dynamic properties of powders. We also learned that the DPI requires 3 elements for functionality: a formulation, a metering system, and a dispersion mechanism. Hickey made the point that, “There is no generic dry powder inhaler.” Although this statement is correct in North America today, that might change in the future.

“Issues in Drug Delivery: Concepts and Practice” was presented by Ted Martonen. This was largely the work that Martonen has been doing on in silico modeling of the human lungs (mathematical modeling simulations). Martonen first introduced his work related to models of the lower respiratory tract to the respiratory care community at a previous Respiratory Care Journal Conference. Since that publication he has further validated this model. He is now developing models of the upper respiratory tract. He presented some impressive images of these models and, in particular, how they are relevant to delivery of MDI and DPI aerosols through the upper airway. These models demonstrate the importance of the tongue and upper airway on aerosol delivery. Martonen now has the nose, mouth, larynx, and lower respiratory tract modeled in 3 dimensions (“lips to alveolus”). He suggested that the use of such models might allow customized targeted drug delivery from magnetic resonance images from a specific patient. This fascinating idea has potential but requires clinical validation.

“Dry Powder Inhalers: An Overview” was presented by Paul Atkins. Atkins began his presentation by telling us that the production of an aerosol requires energy. In the case of a MDI, this energy comes from propellants; in the case of the DPI, the energy comes from the patient. The first-generation DPIs were single-dose and required insertion of a drug capsule. The second-generation DPIs are multi-dose and have dose counters. It was stated that 120 million of the Diskus DPI are made each year. DPIs are either passive or active devices. Although DPIs used in North America today are passive devices, in which a mechanism in the device disperses the powder, will be available in the near future. Although the device/formulation is packaged as a unit today, in the future there may be DPI devices that use generic drugs. In this presentation and others throughout the conference, it was pointed out that there is no short-acting bronchodilator (eg, albuterol) DPI formulation in the United States. There are a number of DPIs available in the United States, including the Diskus, Aerolizer, Diskhaler, Handihaler, and Turbuhaler. These devices tend to be complex, with multiple steps required for dose administration and differences between device designs. This can result in considerable confusion for patients and clinicians.

Clinical Applications

David Geller presented “Comparing Clinical Features of the Nebulizer, Metered-Dose Inhaler, and Dry Powder Inhaler.” He pointed out that there are limitations of drug/device combinations. For example, there are no short-acting bronchodilators available in DPIs, no steroid formulations available in breath-actuated MDIs, and no long-acting bronchodilators available in MDIs. He reminded us that there is no perfect aerosol delivery device; each device has advantages and disadvantages. The MDI is most difficult to teach, and many patients do not use a spacer, even if they know they should. DPIs are many and complex. Geller reminded us that there is still a role for the nebulizer and stated that the Aerosol Consensus Conference published in Respiratory Care journal in 2000 was “anti-nebulizer.”

Having been a member of the writing committee for that document, I agree with his assessment. He listed a number of problems with studies that compared aerosol-delivery devices. They are boring, biased, underpowered, have many design flaws and oversights, and many have unknown relevance to inhaled corticosteroids. It was pointed out that patients are more variable than devices and that patient errors are common with all devices. Geller referred to recently published evidence-based guidelines, which state that, “… each of the devices … can work equally well … in patients who can use them appropriately.”

Richard Ahrens discussed “The Role of the MDI and DPI in Pediatric Patients: Children Are Not Just Miniature Adults.” For those of us who spend most of our practice caring for adult patients, it was good to be reminded again that children are not just miniature adults. There are a number of diseases of children that can be treated with aerosols, including lung disease of prematurity, bronchopulmonary dysplasia, bronchitis, croup, cystic fibrosis, and asthma. Many inhaled drugs and devices used with infants and children are used off-label. Ahrens stated that breath-actuated MDIs and DPIs are not much different from the patient’s perspective. I agree with this, although I had not previously thought about it in this way. Issues related to
aerosol delivery in children were grouped by Ahrens according to age. For the adolescent (13–18 years old), aerosol delivery is similar to adults. For the young child (5–12 years old) the Food and Drug Administration has approved aerosol delivery is similar to adults. For the young child (5–12 years old) as the “orphan age group” because there is a lack of available approved inhaled drugs for this age group. It was also pointed out that the effect of inhaled steroids on growth is real, but often unrecognized. However, the long-term effect is not sustained if an appropriate drug and dose are used. A memorable phrase from Ahrens’s presentation was, “Inhaled medication Chinese-restaurant style,” which was used to describe the matching of drug to delivery device. He pointed out that there are many ways to fail to deliver inhaled drug to children, including crying, untreated electrostatic charge in the holding chamber, poor mask seal, low tidal volume, poor adherence, multiple puffs into the holding chamber, time delay between actuation into the holding chamber and inhalation, and a wrong choice of the combination of MDI and holding chamber.

“Inhalation Therapy With Metered-Dose Inhalers and Dry Powder Inhalers in Mechanically Ventilated Patients” was addressed by Rajiv Dhand. DPIs that can be used in the ventilator circuit are not available in the United States. Interestingly, it was pointed out that future MDI canisters may not be removable from the dose counter for use in the ventilator circuit. Regarding aerosol-generation, spacers in the ventilator circuit are better than in-line adapters, the humidity and density of the carrier gas affects aerosol delivery, and it is important to synchronize MDI actuation with the start of inhalation. Regarding breathing pattern, slow inspiratory flow is better, there may be differences in aerosol delivery between volume-controlled ventilation and pressure-controlled ventilation for the nebulizer (but not the MDI), and a breath-hold and large tidal volume are not important for MDI delivery into the ventilator circuit. Regarding the formulation, there are issues related to matching MDI and spacer, and differences between β agonists and steroids. Regarding dosing, there may be little difference between 4 puffs, 8 puffs, and 16 puffs—at least for stable, mechanically ventilated patients with chronic obstructive pulmonary disease. Regarding airway geometry, there is similar delivery of MDI bronchodilators in mechanically ventilated patients and normal control subjects. Dhand also pointed out the importance of monitoring response to inhaled bronchodilators in mechanically ventilated patients, including measures of airway resistance, intrinsic positive end-expiratory pressure, heart rate, and clinical assessment.

“Determinants of Patient Adherence to an Aerosol Regimen” was presented by Joseph Rau. He introduced us to measures of adherence such as biochemical assays, device monitors, direct observation, medical and pharmacy records, doses remaining in the canister, provider judgment, and patient self-report. He also discussed factors that affect adherence, such as device understanding, complexity of the treatment regimen, oral versus inhaled drug delivery, type of medication, sociocultural factors, patient beliefs, and patient knowledge. Rau pointed out that patients cannot use the DPI much better than the MDI, that there is a lower adherence with greater prescribed frequency, that there is better adherence with combination therapy, and that an adequately prepared health-care provider is important to improve adherence.

James Fink presented the final topic at the conference, “Problems With Inhaler Use: A Call for Improved Clinician and Patient Education.” He reminded us that management of chronic disease is “10% drug and 90% education.” It was sobering to learn that between one third and two thirds of nurses, physicians, and respiratory therapists (RTs) are unable to use these devices correctly. Thus, education is as important for the clinician as for the patient. Although there are multiple sources of information related to the correct use of MDIs and DPIs, they may be incorrect, too confusing, and may be ignored by many clinicians. For patient education, simplicity and repetition are important. There are multiple problems encountered in patient education, including low literacy rate, poor attention span, inadequate time to learn, inadequate information, inadequate follow-up, patient hesitation to ask questions, and limited financial incentives for education. Differences between device types create confusion and unique education challenges. For example, there are numerous differences between MDI and DPI use (Table 1). This can result in considerable confusion for the patient, who may use an MDI for their quick-relief medication and a DPI for their controller medication.

What Is a Clinician to Do?

With the ever-increasing number of aerosol delivery device options, how does the clinician decide which to
prescribe? Is one device better than another? This was addressed in a recently published systematic review with evidence-based guidelines. The results of this systematic review were essentially the same in each of the clinical settings that were reviewed. None of the pooled meta-analyses showed a significant difference between devices in any efficacy outcome in any patient group. Each of the devices studied can work equally well in patients who can use them appropriately. This is a powerful statement, given that the selection of device is often based on the bias of the clinician that one device is superior to another. The same guidelines recommend the following considerations when selecting an aerosol delivery device:

- In what devices is the desired drug available?
- What device can the patient use properly?
- For which device is reimbursement available?
- Which device is least costly?
- Can all types of prescribed inhaled drugs be delivered with the same type of device?
- Which device is most convenient for the patient or family or medical staff?
- Does the patient or clinician have a specific device preference?
- Proper patient education is critical
- Physicians, RTs, and nurses caring for patients with respiratory diseases should be familiar with correct device technique

Improper inhaler technique is common among patients. Considerable confusion can occur when the patient is prescribed multiple aerosol-delivery devices. It is easy for patients to become confused about the correct technique and dosing strategy for each device and formulation. Moreover, patients can be confused between their oral and inhalation drugs. The unintentional oral administration of Foradil and Spiriva capsules has recently been reported and stemmed from the fact that these capsules resemble those typically taken orally. The Food and Drug Administration has received 30 cases concerning the inadvertent oral administration of Foradil and two concerning Spiriva. Issues with proper use of inhaler devices is likely to increase as the population ages, related to the cognitive and psychomotor deficits that can occur with the aging process.

One of the important take-home messages of this conference is the importance of clinicians being knowledgeable in the use of aerosol delivery devices and able to teach patients how to use these devices correctly. All who care for patients with respiratory disease share this responsibility. Studies have reported lack of physician, nurse, and RT knowledge of device use. RTs are uniquely positioned to provide this service, and there is evidence that RTs may do this better than others. This is the core of our practice and derives from the genesis of our profession. In fact, an early moniker of the profession was “inha- lation therapy.”

Admittedly, it is difficult to remember the correct steps for the use of each of the MDIs and DPIs currently available in the United States. Some time ago I assembled a quick reference for my personal use when instructing the use of these devices. I share this in the Appendix in hopes that it may be useful for clinicians and their patients.

Summary

The proceedings of this conference provide the current state of the art of MDI and DPI. With the previously published state-of-the-art conference on nebulizers, these issues of Respiratory Care Journal provide a comprehensive reference for all aspects of aerosol delivery.

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APPENDIX

Technique for Use of MDI and DPI

Technique for Use of MDI
Hold the MDI in your hand to warm it.
Remove the mouthpiece cover.
Inspect the mouthpiece for foreign objects.
Hold the MDI in a vertical position.
Shake the MDI.
If the MDI is new or has not been used recently, prime it by shaking
and pressing the canister to deliver a dose into the room. Repeat
several times.
Breathe out normally.
Open your mouth and keep your tongue from obstructing the
mouthpiece.
Hold the MDI in a vertical position, with the mouthpiece aimed at
your mouth.
Place the mouthpiece between your lips or position it 2 finger-
widths from your mouth.
Breathe in slowly and press the MDI canister down once at the
beginning of inhalation.
Continue to inhale until your lungs are full.
Move the mouthpiece away from your mouth and hold your breath for
10 seconds (or as long as you comfortably can).
Wait at least 15 seconds between doses.
Repeat for the prescribed number of doses.
Recap the mouthpiece.
Rinse your mouth if using inhaled steroids.
Keep a diary of the number of uses so that you know when the canister is empty.

Clean the Metered-Dose Inhaler Once a Week and as Needed
Look at the hole where the medicine sprays out from your inhaler.
Clean the inhaler if you see powder in or around the hole.
Remove the metal canister from the mouthpiece.
Set the canister aside so it does not get wet.
Rinse the mouthpiece and cap in warm water and dry overnight.
Put the canister back inside the mouthpiece and replace the cap.

Technique for Use of Breath-Actuated MDI (Autohaler)
Priming Procedure (if new MDI or not used recently)
Remove mouthpiece cover.
Point the mouthpiece away from yourself.
Push the lever so that it stays up.
Push the white test fire slide on the bottom of the mouthpiece to
release a priming spray.
To release the second priming spray, return the lever to its down
position and repeat previous steps.
Return the lever to its down position.

Using the Autohaler
Hold the MDI in your hand to warm it.
Remove the mouthpiece cover.
Inspect the mouthpiece for foreign objects.
Hold the Autohaler upright; the arrows should point up; do not block
the air vents.
Raise the lever so that it snaps into place.
Shake the Autohaler.
Breathe out normally.
Open your mouth and keep your tongue from obstructing the
mouthpiece.
Seal your lips tightly around the mouthpiece.
Inhale deeply through the mouthpiece with steady moderate force.
You will hear a click and feel a soft puff when the device triggers the
release of medicine.
Continue to inhale until your lungs are full.
Remove the mouthpiece from your mouth and hold your breath for 10
seconds (or as long as you comfortably can).
Hold the Autohaler upright and lower the lever after each inhalation.
Repeat for the prescribed number of doses.
Recap the mouthpiece.
Make sure the lever is down.
Keep a diary of the number of uses so that you know when the
canister is empty.

Clean the Autohaler Once a Week and As Needed
Remove the mouthpiece cover.
Turn the Autohaler upside-down.
Wipe the mouthpiece with a clean dry cloth.
Gently tap the back of Autohaler so the flap comes down and the
spray hole can be seen.
Clean the surface of the flap with a dry cotton swab.
Recap the mouthpiece and make sure the lever is down.

Technique for Use of MDI With Spacer or Valved Holding Chamber
Hold the MDI in your hand to warm it.
Assemble the apparatus and check for foreign objects.
Remove the mouthpiece cover.
Shake the MDI.
If the MDI is new or has not been used recently, prime the device by
shaking it and pressing the canister to deliver a dose into the room.
Repeat several times.
Hold the canister in a vertical position.
Breathe out normally.
Open your mouth and keep your tongue from obstructing the
mouthpiece.
Place the mouthpiece into your mouth (or place the mask completely
over your nose and mouth).
Breathe in slowly through your mouth and press the MDI canister once
at the beginning of inspiration.
If the device produces a “whistle,” your inspiration is too rapid.
Allow 15 seconds between puffs.
Move the mouthpiece away from your mouth and hold your breath for
10 seconds (or as long as you comfortably can).
The technique is slightly different for a device with a collapsible bag:
Open the bag to its full size.
Remove the canister from the MDI mouthpiece and insert it into
the mouthpiece attached to the collapsible bag.
Press the MDI canister immediately before inhalation and inhale
until the bag is completely collapsed (if you have difficulty
emptying the bag, you can breathe in and out of the bag several
times to evacuate the medication).
Rinse your mouth if using inhaled steroids.

Clean the Holding Chamber Every Two Weeks and As Needed
Chamber device:
Disassemble the device for cleaning.
Wash in clean warm soapy water; rinsing is optional.
Drip dry over night. Do not towel dry the spacer as this will reduce dose delivery because of static charge. Reassemble the spacer after it is dry.

Collapsible bag device:
Disassemble the device for cleaning.
Remove the plastic bag assembly from the mouthpiece.
The mouthpiece can be washed with warm water.
Drip dry over night.
Reassemble the device after it is dry.
The plastic bag should not be cleaned, but should be replaced every 4 weeks or as needed.

**Technique for Use of Diskhaler**
Remove the mouthpiece cover.
Pull the tray out from device.
Place the disk on the wheel (numbers up).
Rotate the disk by sliding the tray out and in.
Lift the back of lid until fully upright so that needle pierces both sides of the blister.
Breathe out normally; do not exhale into the device.
Place the mouthpiece into your mouth and close your lips tightly around the mouthpiece.
Keep the device level while inhaling the dose with a rapid and steady flow.
Remove the mouthpiece from your mouth and hold your breath for 10 seconds (or as long as you comfortably can).
When you exhale, be sure that you are not exhaling into the device.
Store the device in a cool dry place.
Replace the disk when all of the blisters have been punctured.
Once every week, brush off any powder remaining within the device.

**Technique for Use of Diskus**
Open the device.
Slide the lever.
Breathe out normally; do not exhale into the device.
Place the mouthpiece into your mouth and close your lips tightly around the mouthpiece.
Keep device level while inhaling the dose with a rapid and steady flow.
Remove the mouthpiece from your mouth and hold your breath for 10 seconds (or as long as you comfortably can).
When you exhale, be sure that you are not exhaling into the device.
Store the device in a cool dry place.
Observe the counter for the number of doses remaining, and replace when appropriate.

**Technique for Use of Turbuhaler**
Twist and remove cap.
Hold inhaler upright (mouthpiece up).
Turn grip right, then left, until it clicks.
Breathe out normally; do not exhale into the device.
Place the mouthpiece into your mouth and close your lips tightly around the mouthpiece.
Inhale dose with a rapid and steady flow; inhaler may be held upright or horizontal during inhalation.
Remove the mouthpiece from your mouth and hold your breath for 10 seconds (or as long as you comfortably can).
When you exhale, be sure that you are not exhaling into the device.
Replace the cover and twist to close.
Store the device in a cool dry place.
When a red mark appears at the top of the dose indicator window, there are 20 doses remaining.
When the red mark reaches the bottom of the window, the Turbuhaler is empty and must be replaced.

**Technique for Use of Aerolizer**
Remove the mouthpiece cover.
Hold the base of inhaler and twist the mouthpiece counterclockwise.
Remove capsule from foil blister immediately before use; do not store the capsule in the Aerolizer.
Place the capsule in the chamber in the base of the inhaler.
Hold the base of the inhaler and turn it clockwise to close.
Simultaneously press both buttons; this pierces the capsule.
Keep your head in an upright position.
Breathe out normally; do not exhale into the device.
Hold the device horizontal, with the buttons on the left and right.
Place the mouthpiece into your mouth and close your lips tightly around the mouthpiece.
Breathe in rapidly and as deeply as possible.
Remove the mouthpiece from your mouth and hold your breath for 10 seconds (or as long as you comfortably can).
When you exhale, be sure that you are not exhaling into the device.
Open the chamber and examine the capsule; if there is powder remaining, repeat the inhalation process.
After use, remove and discard the capsule.
Close the mouthpiece and replace the cover.
Store the device in a cool dry place.

**Technique for Use of HandiHaler**
Immediately before using the HandiHaler, peel back the aluminum foil and remove a capsule; do not store capsules in the HandiHaler.
Open the dust cap by pulling it upwards.
Open the mouthpiece.
Place the capsule in the center chamber; it does not matter which end is placed in the chamber.
Close the mouthpiece firmly until you hear a click; leave the dust cap open.
Hold the HandiHaler with the mouthpiece up.
Press the piercing button once and release; this makes holes in the capsule and allows the medication to be released when you breathe in.
Exhale normally; do not exhale into the device.
Place the mouthpiece into your mouth and close your lips tightly around the mouthpiece.
Keep your head in an upright position.
Breathe in slowly, at a rate sufficient to hear the capsule vibrate, until your lungs are full.
Remove the mouthpiece from your mouth and hold your breath for 10 seconds (or as long as you comfortably can).
When you exhale, be sure that you are not exhaling into the device.
To ensure you get the full dose, repeat the inhalation from the HandiHaler.
Open the mouthpiece, tip out the used capsule, and dispose of it.
Close the mouthpiece and dust cap for storage of the HandiHaler.

**Do Not Clean the DPI**
The dry powder inhaler should not be cleaned.
It is important to keep the device dry, as moisture will decrease drug delivery.
If necessary, the mouthpiece can be wiped with a dry cloth.