

Tips: Selecting an MDI can

Factors to consider in choosing a canister for your metered dose inhaler

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A typical MDI system includes a metal canister containing medication in the form of a pressurized aerosol. A cap containing the drug metering valve is crimped onto the mouth of the canister, and the entire system is enclosed in a plastic actuator through which the patient inhales the drug. Because canisters, unlike valves, actuators, and dose counters, have no moving parts, developers may take this component for granted. MDI cans, however, have important roles that go beyond storage of the formulation, with the potential to significantly affect product stability and shelf life, patient safety, and dosing consistency.

Since the introduction of the first metered dose inhaler (MDI) in 1956, manufacturing processes, filling technologies, and drug formulations have evolved considerably to meet changes in industry standards and regulations. In addition, many new MDI components have become available. Although the canister seems to be the simplest component in an MDI system, technological advances have led to the introduction of options that make selection increasingly more challenging.

Choosing the appropriate canister requires consideration of the number of drug doses that the MDI will deliver, the active drug substance, and the physical and chemical properties of the formulation. An inappropriate selection can result in the patient receiving less than the prescribed drug dose, a serious problem when treating life-threatening breathing problems.

Factors involved in canister selection

Canister size

Canister size depends mostly on dosing requirements and, therefore, the volume of drug formulation. The volume of each dose and the number of



doses per canister will determine the canister volume. In addition, the larger the canister, the larger the actuator will have to be, which may affect portability and ergonomics. The dimensions of the canister must also match up with the other MDI components, especially the valve, to prevent leakage.

Canisters come in a range of standard sizes, generally ranging from about 10 ml to about 30 ml. For smaller dosing requirements, manufacturers can custom make smaller canisters, or they can add a sleeve inside of a standard-sized canister to effectively reduce the volume. The latter option allows for use of the same components for MDIs of varying drug volumes, including sample versions of products.

Canister material

Most of the world's canisters are manufactured from aluminum as it is compatible with the majority of formulations. Aluminum does present several challenges; however, manufacturers have developed ways to deal with those issues. For example, aluminum may react with certain formulations, so manufacturers may add a barrier coating on the inside of the can to prevent degradation.

Also, with the switch from CFC propellants to HFA at the end of 2008, cans must now withstand higher pressures than in the past, as much as 5 times higher for HFA 134a at 20 °C than for CFC (Table 1). As a result, aluminum canisters require greater strength, so manufacturers now offer thick-walled aluminum cans. These strengthened aluminum canisters also have a stronger base and neck, making them more robust for high speed filling and crimping.

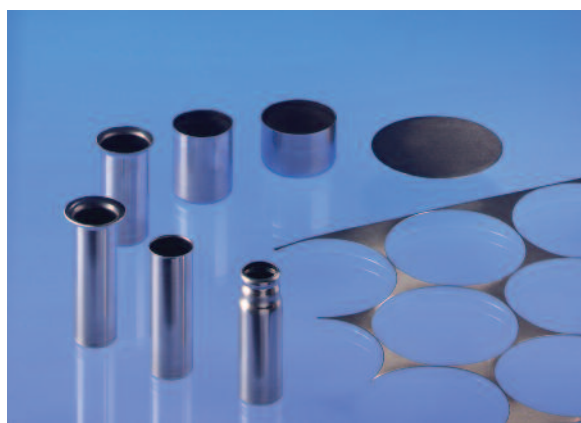
Table 1**Aerosol pressure requirements for MDI propellants**

Propellant	Temperature (°C)						
	20	30	40	50	55	60	65
CFC 11/12	1.0 bar	1.5 bar	3.0 bar	4.0 bar	5.0 bar	5.5 bar	7.0 bar
HFA 227	3.0 bar	4.5 bar	6.0 bar	8.0 bar	9.5 bar	11.0 bar	12.2 bar
HFA 134A	5.0 bar	7.0 bar	9.0 bar	12.0 bar	14.0 bar	16.0 bar	18.0 bar

Although the vast majority of MDI cans are made from aluminum alloys, a few other materials are available. Stainless steel canisters can provide extra strength for the higher pressure propellants, as well as a non-reactive surface for sensitive formulations. Some MDI products have used glass canisters, and glass can also be useful for visualizing the product during development.

Manufacturing method

Manufacturers most commonly use one of two methods to manufacture metal canisters for MDIs: deep drawing or impact extrusion. Impact extrusion forms a hollow shell from cold metal billets using a single stage, high impact punch, whereas deep drawing forms a properly contoured can over multiple stages from a rolled metal sheet (Fig. 1). The deep drawing method has several advantages over impact extrusion, particularly for meeting the stringent requirements of the pharmaceutical industry.

Figure 1**Stages in the deep-drawn manufacturing process**

First, deep drawing offers multiple control opportunities within the high precision process. The formation of the finished canister through several pressing stages, as opposed to a single punch, reduces variation, resulting in tighter tolerances in the weight and dimensions of the finished products when compared

with impact extruded cans. For example, the weight of impact extruded canisters can be controlled to within ± 0.1 g at best, compared to ± 0.05 g for deep-drawn canister tolerances (Table 2). Tight tolerances control leakage and ensure accurate filling weights.

Table 2**Comparison of tolerances for canisters produced by deep drawing or impact extrusion**

Tolerances	Deep-drawn	Impact extruded
Height (mm)	0.5	0.8
Diameter (mm)	0.1	0.4
Neck height (mm)	0.2	0.6
Neck inner diameter (mm)	0.3	0.9
Weight (g)	0.05	0.1

In addition, deep drawing works with a variety of aluminum and stainless steel substrates, while impact extrusion techniques work with only one metal substrate, aluminum 1050. For new MDIs that contain non-CFC propellants, having material options is vital because many aluminum alloys are more robust than aluminum 1050 and are therefore safer at pressures greater than 10 bar that are typical of HFA formulations at elevated temperatures.

Impact extrusion of canisters also requires a secondary process after the initial shell formation to form the neck of the can. The rolled edge design produced by this process can entrap contaminants and affect tolerances. At the higher temperatures and pressures used during later MDI manufacturing steps, the neck may unroll. By contrast, the deep drawing process uses a cut edge design that eliminates the rolled neck with its associated risks and forms a more effective seal with the inhaler's valve gasket.

Coatings

With HFA suspension drug formulations, interaction between the formulation and the canister material



Canister manufacturing

can result in drug deposition on the canister wall or exposed surfaces of the valve components. Solution formulations more commonly cause degradation, resulting in increased impurity levels. In both cases, the interaction between the formulation and the canister leads to a reduction in the drug content in the formulation, resulting in the patient receiving less than the prescribed dose. Applying a coating to the inside of the canister in those cases can protect the contents from deposition and degradation, improving product performance and the stability of the formulation, as well as helping to extend the product's shelf life.

For solution formulations, internal coating with a polymer or anodization of the canister can change the surface characteristics of the canister and ultimately act as a protective barrier. Low surface energy coatings can be used with suspension formulations to reduce drug deposition.

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