MEDICINES CONTROL COUNCIL

AEROSOL MANUFACTURING

This document has been prepared to serve as a recommendation to manufacture aerosol-based medicines. It represents the Medicines Control Council's current thinking on the manufacture of aerosol-based medicines.

These guidelines should be read in conjunction with the SA Guidelines for Good Manufacturing Practices.

REGISTRAR OF MEDICINES
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1. INTRODUCTION

The manufacture of pressurized aerosol products for inhalation with metering valves requires special consideration because of the particular nature of this form of product. It should be done under conditions which minimise microbial and particulate contamination. Assurance of the quality of the valve components and, in the case of suspensions, of uniformity is also of particular importance.

2. GENERAL

2.1 There are presently two common manufacturing and filling methods as follows:

2.1.1 Two-shot system (pressure filling). The active ingredient is suspended in a high boiling point propellant, the dose is put into the container, the valve crimped on and the lower boiling point propellant is injected through the valve stem to make up the finished product. The suspension of active ingredient in propellant is kept cool to reduce evaporation loss.

2.1.2 One-shot process (cold filling). The active ingredient is suspended in a mixture of propellants and held either under high pressure or at a low temperature, or both. The suspension is then filled directly into the container in one shot.

3. PREMISES AND EQUIPMENT

3.1 Manufacture and filling should be carried out as far as possible in a closed system.

3.2 Where products or clean components are exposed, the area should be fed with treated filtered air, and should be entered through airlocks.

3.3 Suitable systems should exist to determine required environment conditions and to monitor and control these conditions, e.g. temperature controls and propellant loss.

4. PRODUCTION AND QUALITY CONTROL

4.1 Metering valves for aerosols are more complex pieces of engineering than most items used in pharmaceutical production. Their specifications, sampling and testing should recognise this. Auditing the Quality Assurance system of the valve manufacturer is of particular importance.

4.2 All fluids (e.g. liquid or gaseous propellants) should be filtered to remove particles greater than 0,2 micrometer. An additional filtration where possible immediately before filling is desirable.

4.3 Containers and valves should be cleaned using a validated procedure appropriate to the use of the product to ensure the absence of any contaminants such as fabrication aids (e.g. lubricants) or undue microbiological contaminants. Containers should be fed to the filling line in a clean condition or cleaned on line immediately before filling.

4.4 Precautions should be taken to ensure uniformity of suspensions at the point of fill throughout the filling process.

4.5 When a two-shot filling process is used, it is necessary to ensure that both shots are of the correct weight in order to achieve the correct composition.

4.6 Controls after filling should ensure the absence of undue leakage. Any leakage test should be performed in a way which avoids microbial contamination or residual moisture.

5. CONTACT DETAILS

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