SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY

SAHPRA
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CEPHALOSPORIN MANUFACTURING

This document has been prepared to serve as a recommendation to manufacture Cephalosporins. It represents the South African Health Products Regulatory Authority's current thinking on the safety, quality and efficacy of medicines. The guideline should be read in conjunction with the SA Guidelines to Good Manufacturing Practices published December 2017

CHIEF EXECUTIVE OFFICER (CEO)

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1 INTRODUCTION

These standards do not have direct statutory force, but will be used by the inspectors of South African Health Products Regulatory Authority, in order to evaluate the suitability of a pharmaceutical plant to manufacture cephalosporin products and to evaluate whether non-cephalosporin products are free and likely to remain free from cephalosporin contamination.

These standards will therefore be one of the criteria used by SAHPRA, to decide on the registration and the continued registration of pharmaceutical products.

These standards do not replace any of the generally accepted GMP standards, but must be seen as an addition to them, the main focus being on the specific problem of cross-contamination.

2 GLOSSARY

For the purpose of these standards, cephalosporins include cephalosporin P, cephalosporin N, cephalosporin C, semisynthetic compounds derived from 7 aminocephalosporanic acid as well as the cephamycins. This definition includes both Category A and B substances of Act 101 of 1965.

3 PREMISES

3.1 Cephalosporin products should only be manufactured in separate, dedicated self-contained areas with separate air handling facilities dedicated to these products and on a different site to that of the manufacture of non-cephalosporin products.

This means complete separation of:

3.1.1 Active raw material storage

3.1.2 weighing

3.1.3 mixing

3.1.4 processing

3.1.5 filling

3.1.6 packaging

3.1.7 any other associated processes

3.2 Entry into and exit from the cephalosporin area should only be through a properly constructed air-lock.

3.3 Change rooms should be provided for the personnel to shed their street clothes and put on their protective clothing for the cephalosporin area.

3.4 Adequate shower facilities should be available for the personnel to shower when they leave the cephalosporin area.

4 SECONDARY PACKAGING

Secondary packaging i.e. labelling and cartooning of the finished cephalosporin products may be done in a general packaging area, provided that the operation is separated from the general area in such a way as to contain any spillage of cephalosporin.

5 AIR HANDLING SYSTEMS

5.1 Separation

Completely separate air supply systems must be provided for cephalosporin and non-cephalosporin products

5.2 Air pressure Differentials

5.2.1 Air pressure differentials must be adjusted to provide a NEGATIVE PRESSURE in relation to the outside air in the cephalosporin area. The air must enter the area and be vented from the area in such a way as to ensure that no cephalosporin contaminated air enters the atmosphere.

5.2.2 Air pressure differentials should be adjusted to be the greatest in the areas where the most dust is generated and cascade down to those areas where the least dust is generated.

5.2.3 For sterile products positive air pressure differentials are required initially: however, the air pressure differentials in the area immediately adjacent to the non-cephalosporin area must be negative The same precautions for the contamination of the atmosphere areapplicable.

5.2.4 The air handling system must be validated at regular intervals.

6. EQUIPMENT

6.1 Equipment should be dedicated to the cephalosporin manufacturing area only.

6.2 Any maintenance of the equipment should be done in the cephalosporin area. If the equipment needs removal from the cephalosporin area proper validated decontamination procedures should be available and should be followed.

7 PERSONNEL

7.1 Clothing

7.1.1 Overalls, shoe covers, head gear, mask and gloves to be used for cephalosporin manufacture only, must be provided.

7.1.2 All clothing used in the cephalosporin manufacturing area must be properly decontaminated according to a validated procedure before being removed from the area for laundering.

7.2 Procedures

Written procedures with respect to dress, movement into and out of the area and all other special precautions must be compiled and available at the point of implementation.

7.3 Training

Training with respect to the special problems of cephalosporin manufacture must be provided in addition to normal GMP training.

7.4 Health Checks

Health checks must be done on a regular basis.

8 MONITORING

Air quality outside the cephalosporin area must be monitored on a regular basis to detect any cephalosporin contamination.

9 DECONTAMINATION

Validated decontamination procedures must be compile and implemented where necessary.

10 CONTAMINATION LIMITS

Contamination limits of non-cephalosporin products have to be determined on the basis of accumulated validation data and the sensitivity of the analytical methods.

11 VALIDATION

All methods and processes should be validated and re-validated at regular intervals Equipment should be qualified at regular intervals.

12 CONTACT DETAILS

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13 UPDATE HISTORY

Date	Reason for update	Version & publication
Nov 2019	Authority: “MCC” to “SAHPRA” Authority Logo: “MCC Logo” to “SAHPRA Logo” Registrar of Medicines to Chief Executive Officer (CEO) Council to SAHPRA Contact Details: Address changes/ amendments Included: Table of contents and Update History	v1.1 November 2019