SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY

SAHPRA
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PENICILLIN MANUFACTURING

This document has been prepared to serve as a recommendation for penicillin manufacturing. It represents the South African Health Products Regulatory Authority's current thinking on this subject.
This guideline should be read in conjunction with the SA Guidelines for Good Manufacturing Practices.

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 penicillin products and to evaluate whether non-penicillin products are free and likely to remain free from penicillin contamination.

These standards will therefore 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, penicillin includes all forms of penicillin i.e. all naturally produced penicillin, all synthetic and semi-synthetic preparations as compounds derived from 6-amino-penicillanic acid. This definition includes both Category A and B substances in terms of Act 101 of 1965

3 PREMISES

3.1 Penicillin 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-penicillin 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 penicillin 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 penicillin area.

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

4 SECONDARY PACKAGING

Secondary packaging i.e. labelling and cartooning of the finished penicillin 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 penicillin.

5 AIR HANDLING SYSTEMS

5.1 Separation

Completely separate air supply systems must be provided for penicillin and non-penicillin 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 penicillin area. The air must enter the area and be vented from the area in such a way as to ensure that no penicillin 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 from this area to those areas where the least dust is generated.

5.3 For sterile products positive air pressure differentials are required initially: however, the area immediately adjacent to the non-penicillin area must benegative.
The same precautions for the contamination of the atmosphere is applicable

5.4 The air handling system must be validated and re-validated at suitable intervals.

6 EQUIPMENT

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

6.2 Any maintenance of the equipment should be done in the penicillin area. If the equipment needs removal from the penicillin 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 penicillin manufacture only, must be provided.

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

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 penicillin manufacture must be provided in addition to normal GMP training.

7.4 Health checks

Health checks with respect to penicillin sensitivity must be done on a regular basis.

8 MONITORING

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

9 DECONTAMINATION

Validated decontamination procedures must be compiled and implemented where necessary

10 TESTING OF NON-PENICILLIN PRODUCTS

No detectable levels of contamination should be allowed, employing a test method acceptable to SAHPRA. The accuracy of the method should be such as to detect quantities of not less than 0,05 units of penicillin.

11 VALIDATION

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

12 CONTACT DETAILS

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13 UPDATE HISTORY

Date	Reason for update	Version & publication
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