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The 1st International Standard for Rifamycin SV

NB: Since April 2006, the European Directorate for the Quality of Medicines & HealthCare (EDQM-Council of Europe) is in charge of the establishment and distribution of International Standards for Antibiotics instead of the National Institute for Biological Standards and Control (NIBSC-UK).

1. Introduction

A suitable sample (300 g) of the sodium salt of rifamycin SV was made available in 1966 by the generosity of Lepetit SpA, Milan, Italy and through the good offices of Professor P. Sensi, Director of the Research Laboratories of that company. The following data were supplied by the manufacturer.

Lot no.	R/140
Description	dark red crystals
Solubility	5 g dissolves in 5 mL of water at 25°C
Water (Karl Fischer method)	12.73%
pH (5% solution in water)	6.55
Sulphated ash	8.42%
Phosphorous (as sodium phosphate)	0.015%
Potency (as rifamycin SV free acid)	846 "micrograms"/mg

2. Caution

For laboratory use only. Handle in accordance with good occupational hygiene, safety and laboratory practices and take precautions to avoid exposure. This material is not for administration to humans or animals. The corresponding safety data sheet can be accessed via the EDQM website (Reference Standards Database) or is available upon request from the EDQM (Helpdesk-FAQ section).

3. Unitage

The material was established in 1967 as the International Standard of Rifamycin SV and, correcting for the change in water content, the International Unit was defined in 1967 as the activity contained in 0.001127 mg of the International Standard, corresponding to a potency of **887 IU/mg**.

4. The ampouled material

Since the manufacturer considered "the presence of water *necessary* for a good stability of the product" it was proposed in 1966 to the WHO Expert Committee on Biological Standardisation that this material should be distributed into ampoules at a relative humidity of approximately 30%, under which conditions no change in the content of water was expected to occur. The contents of the ampoules would then be allowed to equilibrate in an atmosphere of nitrogen, without drying, for several days before the ampoules were sealed. The committee considered that, since the preparation would have a high content of water, its stability under these conditions should be examined before its establishment and requested the NIMR, London to examine the material in this way. In March 1967 the contents of the bottle were mixed by rotation for 2 days at room temperature (20°C). The powder was then distributed into approximately 2500 ampoules (non-actinic glass) in a controlled atmosphere of 29% +/- 2% relative humidity so that each ampoule contained approximately 100 mg of material. The unplugged ampoules were allowed to remain open at room temperature at this constant humidity for 2 days for equilibration to occur, and were then fitted with capillary plugs filled with dry nitrogen, and equilibrated in an atmosphere of nitrogen at a pressure of 680 mm Hg for 3 days, after which they were refilled with dry nitrogen and sealed by fusion of the glass. The moisture content of the material in the ampoules, determined as loss in weight after 5h over phosphorous (V) oxide at 56°C and a pressure of less than 0.05mm Hg, was found to be 8.55% w/w (mean of 19 ampoules). When the material

in the ampoules was exposed to an atmosphere at a relative humidity of 57% it increased in weight by approximately 1% in 2 minutes and approximately 1.5% in 15 minutes.

5. Stability

It is the policy of WHO not to assign an expiry date to their International Standard. They remain valid with the assigned potency and status until withdrawn or amended. Samples of the ampoules were stored at +56°C in order to assess stability. Assays of these samples gave the following results, indicating that the material had satisfactory stability.

Days at 56°C	Percentage change of potency (mean of 2 ampoules)
21	-0.6%
104	-4.3%
183	-7.25%

6. Citation

In all publications (or data sheets for kits) in which this Standard is used as an assay calibrant, it is more important that the title of the Standard, code and the name and addresses of EDQM are cited correctly.

7. Product Liability

The Council of Europe accordingly makes no representation, contractual statement, or expression of opinion concerning the quality or safety of any item supplied, the presence of any defect in it, or its fitness for any particular purpose. The product must be handled by professional persons having technical skill and at their own discretion and risk. It is for the purchasers of any such item who are responsible for persons in a workplace to determine independently the risks associated with the item according to the conditions of use and to take appropriate safety measures, including provision of appropriate information to persons working with the substance. Any liability of the Council of Europe for injury, loss or damage arising from the supply or use of any such item is in any event hereby excluded to the fullest extent permitted by law; in particular, no liability is accepted for loss of profits or indirect or consequential loss.

8. Disputes

In accordance with the provisions of article 21 of the General Agreement on the Privileges and Immunities of the Council of Europe, all disputes between the Council of Europe (EDQM) and the customer as regards the application of this contract shall be submitted, if a mutual agreement cannot be reached between the parties, to arbitration as laid down in Order No. 481 of the Secretary General, approved by the Committee of Ministers.

9. References

1) (1966) WHO Technical Report Series, No. 329.

2) (1967) WHO Technical Report Series, No. 361.

3) (1968) WHO Technical Report Series, No. 384.

Abstracted from Bull. WHO 1972, 47, 343-356. For outline of the procedure for preparing ampoules of material, see this paper.

10. Signature

This document is electronically signed by:

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