



**WHO International Standard  
The 1st International Standard for Smallpox Vaccine  
NIBSC code: SMV  
Instructions for use  
(Version 4.0, Dated 18/03/2008)**

**1. INTENDED USE**

This material has been prepared and characterised by the Statens Serum Institut (SSI), Copenhagen, Denmark. With effect from 1st July 1997, the National Institute for Biological Standards and Control (NIBSC), Potters Bar, UK is the custodian and distributor of this material.

**RELEVANT FACTORS**

For details of this International Standard, please refer to the enclosed package insert from the Statens Serum Institut.

The package insert from SSI is attached.

**2. CAUTION**

**This preparation is not for administration to humans or animals in the human food chain.**

The material is not of human or bovine origin. As with all materials of biological origin, this preparation should be regarded as potentially hazardous to health. It should be used and discarded according to your own laboratory's safety procedures. Such safety procedures should include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening ampoules or vials, to avoid cuts.

**3. UNITAGE**

See Attachment

**4. CONTENTS**

Country of origin of biological material: United Kingdom.

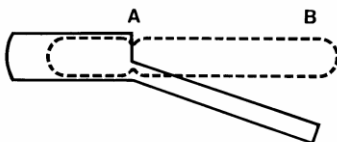
**5. STORAGE**

Store at -20 degrees centigrade or below.

**Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.**

**6. DIRECTIONS FOR OPENING**

Tap the ampoule gently to collect the material at the bottom (labelled) end. Ensure ampoule is scored all round at the narrow part of the neck, with a diamond or tungsten carbide tipped glass knife file or other suitable implement before attempting to open. Place the ampoule in the ampoule opener, positioning the score at position 'A'; shown in the diagram below. Surround the ampoule with cloth or layers of tissue paper. Grip the ampoule and holder in the hand and squeeze at point 'B'. The ampoule will snap open. Take care to avoid cuts and projectile glass fragments that enter eyes. Take care that no material is lost from the ampoule and that no glass falls into the ampoule.



Side view of ampoule opening device containing an ampoule positioned ready to open. 'A' is the score mark and 'B' the point of applied pressure.

**7. USE OF MATERIAL**

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution

**8. STABILITY**

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. Reference Materials should be stored on receipt as indicated on the label.

NIBSC follows the policy of WHO with respect to its reference materials.

**9. REFERENCES**

Krag, P. and Weis Bentzon, M. (1963) The international reference preparation for smallpox vaccine. *Bul Wld Hlth Org.* **29**, 299-309.

**10. ACKNOWLEDGEMENTS**

None

**11. FURTHER INFORMATION**

Further information can be obtained as follows:

This material: [enquiries@nibsc.org](mailto:enquiries@nibsc.org)

WHO Biological Standards:

<http://www.who.int/biologicals/en/>

JCTLM Higher order reference materials:

<http://www.bipm.org/en/committees/jc/jctlm/>

Derivation of International Units:

[http://www.nibsc.org/standardisation/international\\_standards.aspx](http://www.nibsc.org/standardisation/international_standards.aspx)

Ordering standards from NIBSC:

<http://www.nibsc.org/products/ordering.aspx>

NIBSC Terms & Conditions:

[http://www.nibsc.org/terms\\_and\\_conditions.aspx](http://www.nibsc.org/terms_and_conditions.aspx)

**12. CUSTOMER FEEDBACK**

Customers are encouraged to provide feedback on the suitability or use of the material provided or other aspects of our service. Please send any comments to [enquiries@nibsc.org](mailto:enquiries@nibsc.org)

**13. CITATION**

In all publications, including data sheets, in which this material is referenced, it is important that the preparation's title, its status, the NIBSC code number, and the name and address of NIBSC are cited and cited correctly.

**14. MATERIAL SAFETY SHEET**

Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not classified

Physical and Chemical properties	
Physical appearance: Freeze dried powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	Contains dried infectious virus of a vaccine strain
Toxicological properties	
Effects of inhalation:	Not established, avoid inhalation
Effects of ingestion:	Not established, avoid ingestion
Effects of skin absorption:	Not established, avoid contact with skin



<b>Suggested First Aid</b>	
Inhalation:	Seek medical advice
Ingestion:	Seek medical advice
Contact with eyes:	Wash with copious amounts of water. Seek medical advice
Contact with skin:	Wash thoroughly with water.
<b>Action on Spillage and Method of Disposal</b>	
Spillage of ampoule contents should be taken up with absorbent material wetted with an appropriate disinfectant. Rinse area with an appropriate disinfectant followed by water. Absorbent materials used to treat spillage should be treated as biological waste.	

#### 15. LIABILITY AND LOSS

In the event that this document is translated into another language, the English language version shall prevail in the event of any inconsistencies between the documents.

Unless expressly stated otherwise by NIBSC, NIBSC's Standard Terms and Conditions for the Supply of Materials (available at [http://www.nibsc.org/About\\_Us/Terms\\_and\\_Conditions.aspx](http://www.nibsc.org/About_Us/Terms_and_Conditions.aspx) or upon request by the Recipient) ("Conditions") apply to the exclusion of all other terms and are hereby incorporated into this document by reference. The Recipient's attention is drawn in particular to the provisions of clause 11 of the Conditions.

#### 16. INFORMATION FOR CUSTOMS USE ONLY

<b>Country of origin for customs purposes*:</b> United Kingdom * Defined as the country where the goods have been produced and/or sufficiently processed to be classed as originating from the country of supply, for example a change of state such as freeze-drying.
<b>Net weight:</b> 0.1g
<b>Toxicity Statement:</b> Non-toxic
<b>Veterinary certificate or other statement</b> if applicable. <b>Attached:</b> No
<b>17. CERTIFICATE OF ANALYSIS</b> NIBSC does not provide a Certificate of Analysis for WHO Biological Reference Materials because they are internationally recognised primary reference materials fully described in the instructions for use. The reference materials are established according to the WHO Recommendations for the preparation, characterization and establishment of international and other biological reference standards <a href="http://www.who.int/bloodproducts/publications/TRS932Annex2_Inter_biolefststandardsrev2004.pdf">http://www.who.int/bloodproducts/publications/TRS932Annex2_Inter_biolefststandardsrev2004.pdf</a> (revised 2004). They are officially endorsed by the WHO Expert Committee on Biological Standardization (ECBS) based on the report of the international collaborative study which established their suitability for the intended use.



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STATENS  
SERUM  
INSTITUT  
*prevention and control  
of infectious diseases  
and congenital disorders*

**THE INTERNATIONAL REFERENCE PREPARATION  
for  
SMALLPOX VACCINE  
(1st international reference preparation)**

**1. THE REFERENCE PREPARATION**

The reference preparation which was established in 1962<sup>1</sup> is a purified, concentrated sheep vaccine prepared from a vaccinia strain used in the United Kingdom for vaccine production for more than 60 years<sup>2</sup>.

**2. AMPOULE CONTENTS**

Each ampoule contains about 14 mg of freeze-dried smallpox vaccine.

**3. USE OF THE REFERENCE**

For use the total contents of an ampoule is dissolved in 2.5 ml of McIlvaine buffer gives a vaccine dilution of 1:10. The average strength of the vaccine. This has been found to be:

Pock count on chorio-allantoic membrane about . . . . .	10	<sup>8.4</sup>	per ml
Scarification, lesion value . . . . .	10	<sup>4.9</sup>	- -
Intracutaneous test . . . . .	10	<sup>5.2</sup>	- -
LD <sub>50</sub> in eggs . . . . .	10	<sup>7.9</sup>	- -
LD <sub>50</sub> in tissue culture . . . . .	10	<sup>5.8</sup>	- -
LD <sub>50</sub> in newborn mice . . . . .	10	<sup>6.0</sup>	- -

**4. GENERAL REMARKS ABOUT INTERNATIONAL REFERENCE MATERIALS**

International biological standards and international biological reference reagents provide a means of ensuring uniformity throughout the world in the designation of the potency or activity of preparations used in the prophylaxis, therapy, or diagnosis of disease, where this cannot be expressed in terms of physical or chemical quantities. The International Units are units of quantities of "effective constituent"<sup>3</sup>.

The standard is the material as it exists in the ampoules; the "material" thus includes the effective constituents together with all the other constituents that may be present (moisture, carrier, buffer, salt etc., according to the form in which the standard is available).

International biological reference materials are intended for use in the calibration of the contents of "effective constituent" in national or working standard preparations and for the expression of these contents in the respective International Units. For the routine use in the laboratory the national or working standards should be used in order to save as much as possible the international reference materials. These are only sent to individual laboratories in very limited amounts. The preparations are sent free of charges but sometimes a small charge might be claimed for the air-freighting.

January 1997

**5. REFERENCES**

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- 585-175, 201 control  
PP11 58 control 201 T
1. WHO Technical Report Series No. 259, 1963, 17.
  2. Krag, P., Weis Bentzon, M., The International Reference Preparation of Smallpox Vaccine. Bull. Wld. Hlth. Org. 1963, 29, 299-309.
  3. Jerne & Wood, The Validity and Meaning of the Results of Biological Assays, Biometrics vol. 5, December 1949.

SMV