Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
First International Standard for Yellow Fever Vaccine
NIBSC code: 99/616
Instructions for use
(Version 5.0, Dated 14/10/2010)

1. INTENDED USE

The First International Standard for yellow fever vaccine was established by the Expert Committee for Biological Standardisation (ECBS) of the World Health Organisation in 2003. In october 2008, ECBS approved the amendment of the WHO requirements for potency of yellow fever vaccine to :

The dose recommended for use in humans shall not be less than 3.0 log10 IU at the end of shelf life. The release specification shall be approved by the National Regulatory Authority.

The following will apply should changes to the release specification or production be proposed:

- *Existing release specifications should not be changed unless justified by clinical data.*
- *Any changes to existing vaccines potentially impacting on safety or clinical efficacy e.g. during production or in formulation, should be justified by clinical data.*
- *Transfer of production from one manufacturer to another should include specifications in International Units and not mouse LD50.*
- *Specifications for release and at the end of shelf life new manufacturers (including manufacturers with production transfer) should be based on by clinical trial and expressed in International Units.*

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

This preparation is assigned a unitage of $10^{4.5}$ International Units (IU) per ampoule (recommended reconstitution volume 1.0ml, see section 6)

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each ampoule contains yellow fever vaccine from a typical vaccine bulk derived from 17D-204 strain

5. STORAGE

Ampoules should be stored at –20ºC on receipt.
Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.

6. DIRECTIONS FOR OPENING

DIN ampoules have an 'easy-open' coloured stress point, where the narrow ampoule stem joins the wider ampoule body. Various types of ampoule breaker are available commercially. To open the ampoule, tap the ampoule gently to collect material at the bottom (labelled) end and follow manufactures instructions provided with the ampoule breaker.

7. USE OF MATERIAL

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

This material is for use in the calibration of secondary reference materials for yellow fever vaccine

The contents of vials should be reconstituted with 1ml distilled water as described above. The resulting liquid vaccine will contain 4.5 log10 IU per ml or 4.2log10 IU per 0.5ml dose.
This material should be used following reconstitution and not stored for use at a later date.

Guidance on the calibration of a working standard
1 An adequate number of vials of vaccine from the same final container lot should be acquired.
2 This vaccine should be assayed along with the International Standard for Yellow Fever Vaccine (NIBSC code 99/616) on at least 20 occasions.
3 A fresh ampoule of the International Standard should be used in each assay.
4 The data should be analysed and the geometric mean potency of the in-house standard determined.
5 In thermostability assays of vaccines, the IS or reference vaccine should be taken directly from the recommended storage temperature of -20°.

8. STABILITY

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. Ampoules should be stored at -20°C or below on receipt.

The contents should be used following reconstitution and not frozen and re-used.

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

9. REFERENCES

Not applicable

10. ACKNOWLEDGEMENTS

Ferguson, M Heath A. (2004) Collaborative study to assess the suitability of a candidate International Standard for Yellow Fever Vaccine Biologicals 32 195-205

11. FURTHER INFORMATION

Further information can be obtained as follows;
This material: 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
Ordering standards from NIBSC:
http://www.nibsc.org/products/ordering.aspx
NIBSC Terms & Conditions:
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

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

National Institute for Biological Standards and Control,
Potters Bar, Hertfordshire, EN6 3QG. T +44 (0)1707 641000, nibsc.org
WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

World Health Organization

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: Yes	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	Does not contain material of human origin
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
Suggested First Aid	
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.
Action on Spillage and Method of Disposal	
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 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

Country of origin for customs purposes*: 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.
Net weight: 1.0g
Toxicity Statement: Non-toxic
Veterinary certificate or other statement if applicable**.** **Attached:** No

17. CERTIFICATE OF ANALYSIS

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 http://www.who.int/bloodproducts/publications/TRS932Annex2_Inter_biolefstandardsrev2004.pdf (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.