



**WHO International Standard
Bordetella pertussis Vaccine (Whole Cell) 41S
NIBSC code: 94/532
Instructions for use
(Version 3.0, Dated 09/04/2013)**

1. INTENDED USE

A candidate replacement standard (ampoule code 94/532) was prepared in 1994 from a bulk material kindly donated by CSL, Australia, in early 1994. A first collaborative study to compare this candidate with the Second International Standard (ampoule code 66/302) was organized by Dr Gert Albert Hansen, Statens Seruminstitut (SSI), Copenhagen. This study was carried out by 15 laboratories in 1995-1996. In 1997, the remaining ampoules of this material were transferred to National Institute for Biological Standards and Control (NIBSC), UK. The second collaborative study launched in 2005 in which the candidate standard has been compared with the current Third International Standard for Pertussis Vaccine (IS3) by 16 laboratories in 14 countries. Analysis of data from these two studies gives a consistent calibration of 40 IU (95% limits 37 to 43 IU) per ampoule for 94/532 in terms of IS2 and IS3. On the basis of the results of the studies, it is recommended that the candidate standard be established as the Fourth International Standard for Whole Cell Pertussis Vaccine and that it be assigned an activity of 40 IU per ampoule on the basis of its calibration in terms of the Second and Third International Standards for Pertussis Vaccine (Whole Cell).

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

40 International Units per ampoule.

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each ampoule contains the freeze-dried residue of 1.0 ml aliquots of an aqueous solution which contained: six litres of bacterial suspension in phosphate buffered saline (pH 6.8- 7.4) with 8% dextran and 5% glucose. (equivalent to 150 International Opacity Units in terms of the International Opacity Standard)

5. STORAGE

Unopened ampoules should be stored at -20°C.

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

Six litres of killed *B.pertussis* suspension was generously supplied by CSL Australia in 1994 (lot 0588196)

and was stated by the manufacturer to have a density of 150 International Opacity Units in terms of the International Opacity Standard.

One ml aliquots of the material (in phosphate buffered saline (pH 6.8- 7.4) with 8% dextran and 5% glucose) were filled into glass ampoules and then freeze dried on a five day cycle (starting shelf temperature of -40°C) followed by secondary desiccation for a further six days over phosphorus pentoxide under vacuum and the ampoules finally back filled with high purity nitrogen before sealing. The precision of fill was determined by weighing 75 ampoules taken at 2-3 minute time intervals and the results showed a mean of 1.018gs with a CV of 0.26%.

For practical purposes each ampoule contains the same quantity of *B. pertussis* organisms. The entire contents of each ampoule should be completely resuspended in an accurately measured amount of water or buffer solution. No attempt should be made to weigh out any proportion of the freeze dried powder. It is recommended that the suspension, not for immediate use, is stored at +4°C. The suspension should not be frozen. The ampoules contain no bacteriostat and the preparations should not be assumed to be sterile

COLLABORATIVE STUDIES

The first collaborative study launched in 1995 with the aim of assessing the suitability of the candidate standard 94/532 by comparing it with the Second International Standard for Pertussis Vaccine. The second collaborative study launched in 2005. In this study the preparation 94/532 has been compared with the current Third International Standard for Pertussis Vaccine.

The primary aim of these studies is to assess the suitability of the candidate standard 94/532 to serve as an International Standard for whole cell Pertussis Vaccine and, subject to its suitability and stability, to assign to it a unitage which as far as possible maintains continuity of the international unit assigned to pertussis vaccine. A total of 13 laboratories from 11 countries participated in the first collaborative study and 16 laboratories from 14 countries participated in the second collaborative study.

On the basis of the results of these studies indicating stability and continuity of unitage among International Standards for Pertussis Vaccine, it is recommended that preparation 94/532 be established as the Fourth International Standard for Whole Cell Pertussis Vaccine and that it be assigned an activity of 40 IU per ampoule on the basis of its calibration in terms of the Second and Third International Standards for Pertussis Vaccine (Whole Cell).

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. It is the policy of WHO not to assign an expiry date to their International Reference Materials. They remain valid with the assigned potency and status until withdrawn or amended.

Users who have any data supporting any change in the characteristics of this material are encouraged to contact NIBSC.

9. REFERENCES

1) International collaborative study to evaluate a candidate replacement International Standard for Whole Cell Pertussis Vaccine, Code 94/532 WHO/BS/06.2036

10. ACKNOWLEDGEMENTS

Grateful acknowledgement is made to CSL for the bacterial suspension, to the collaborative study participants and Standard Processing Division for the filing



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

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 material of biological 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 - 2g
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_biol_efstandardsrev2004.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.