Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

WHO International Standard
Prostate-Specific Antigen Free
NIBSC code: 96/668
Instructions for use
(Version 6.0, Dated 30/11/2011)

1. INTENDED USE

This consists of a batch of vials (coded 96/668) containing seminal plasma-derived prostate-specific antigen (PSA) (1) analysed by international collaborative study and established as the First International Standard for Prostate-Specific Antigen (Free) by the Expert Committee on Biological Standardization of the World Health Organisation (2,3).

2. CAUTION

This preparation is not for administration to humans or animals in the human food chain.
The preparation contains material of human origin, and either the final product or the source materials, from which it is derived, have been tested and found negative for HBsAg, anti-HIV and HCV RNA. As with all materials of biological origin it should be regarded as potentially hazardous. It should be used and discarded according to your own laboratory's safety procedures. Such safety procedures probably will include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening ampoules or vials, to avoid cuts by glass and metal edges.

3. UNITAGE

The assigned content is 1µg total PSA per vial.

Uncertainty: the International Unit of 96/668 is assigned without uncertainty. Where required, the uncertainty of the ampoule content of 96/668 may be considered to be the co-efficient of variation of the fill volume, which was determined to be 0.46%.

4. CONTENTS

Country of origin of biological material: USA.
Each vial contains the residue after freeze-drying of 2ml 20mM PBS, pH 7.4 solution that contained:

Bovine serum albumin	10g/L
Prostate-specific antigen (free)	500µg/L

5. STORAGE

Unopened ampoules should be stored at –20ºC
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

For practical purposes each vial contains the same quantity of PSA. The entire content of each vial should be completely dissolved in an accurately measured amount of distilled water. No attempt should be made to weigh out portions of the freeze dried powder. On reconstitution with 2ml distilled water, each vial will contain 500ng/ml free PSA. Subsequent dilutions should be carried out with an appropriate diluent. Free PSA retains some enzymatic activity and can react with protease inhibitors so serum-based matrices should not be used. The material has not been sterilized and the vials contain no bacteriostat. Unopened vials of the IS should be stored below -20°C in the dark

8. PREPARATION AND TRANSFER OF VIALS

The batch consists of 2000 glass vials containing 1µg of free PSA prepared from seminal plasma (4). The material was filled at the Ciba-Corning facility in Irvine, CA, USA and lyophilized under the same controlled conditions as used for preparation of the College of American Pathologist's Survey Panels. Fill precision as measured by weight checks during filling was 0.46% and residual moisture content of the preparation was 2.23% (CV 6.3%). The vials were donated to WHO by Prof T Stamey, Stanford University, CA, USA and, after transfer to NIBSC, were coded 96/668 and stored at -20°C.

9. COLLABORATIVE STUDY

9.1 Aims of the study

The preparation in vials coded 96/668, together with a preparation of PSA 90:10 (96/670), was evaluated by international collaborative study in which ten laboratories in six countries took part. The study was designed:

1) To compare the immunoreactivity of the preparations in immunoassay systems representative of those commonly used in clinical practice or research and assess their suitability to serve as WHO International Standards.

2) To assess the stability of the PSA in the lyophilised preparations by assay of the contents of vials which had undergone accelerated thermal degradation.

3) To compare the PSA immunoreactivity of different serum samples in the immunoassay systems included in the study in terms of both local standards and the candidate preparations.

9.2 Activity of vial contents and stability

Estimates of the contents of 96/668 by immunoassay were similar and consistent with local standards, giving a geometric mean estimate of 1.10 µg/vial (95% confidence limits: 0.99 – 1.21). Therefore the preparation coded 96/668 was established as the First International Standard for PSA (free) with a defined content of 1 microgram per vial (2,3). A predicted degradation rate (5) of 0.042% per year is estimated for samples stored at -20°C.

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.

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WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

World Health Organization

10. STABILITY

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.

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. Reference Materials should be stored on receipt as indicated on the label. For information specific to a particular biological standard, contact standards@nibsc.ac.uk.

In addition, once reconstituted, diluted or aliquoted, users should determine the stability of the material according to their own method of preparation, storage and use.

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

Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.
Although the predicted degradation rates for the two PSA International Standards [PSA (free) coded 96/668 and PSA (90:10) coded 96/670] indicated that the long term stability of these preparations was acceptable for their use as International Standards, ECBS recommended at the time of their establishment, that the PSA standards should be the subject of an ongoing stability monitoring programme, as they are filled in vials. In light of this, a recently completed study (2011) has supported the initial stability assessment and confirms the long term stability of these International Standards.

11. REFERENCES

1. Stamey T.A., Chen Z. & Prestigiacomo A.F. Reference material for PSA: the IFCC standardization study. Clin Biochem 1998 31: 475-481
.
2. WHO TRS 50th Report No. 904

3. Rafferty B, Rigsby P, Rose M, Stamey T & Gaines Das R (2000). Reference reagents for prostate-specific antigen (PSA): establishment of the First International Standards for free PSA and PSA (90:10). Clin Chem 46(9): 1310-1317.

4. Sensabaugh G.F. & Blake E.T. Seminal plasma protein p30: simplified purification and evidence for identity with prostate-specific antigen. J Urol 1990 144: 1523-6

5. Kirkwood T.B.L. Predicting the stability of biological standards and products. Biometrics 1977 33: 736-742.

10. ACKNOWLEDGEMENTS

We gratefully acknowledge the important contributions of all the participants, and particularly Dr T. Stamey, Stanford University School of Medicine, who kindly donated the PSA material. We would also like to acknowledge the collaboration and support of the IFCC Scientific Division Working Group on Standardisation of PSA.

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: White lyophilised powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: Yes	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	Contains 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*: USA * 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: 20mg
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.