1. INTENDED USE
The 1st WHO Reference Preparation of Human Serum Immunoglobulin E (IgE) was established in 1973. (BWHO 1970; WHO ECBS 1971; WHO ECBS 1973; BWHO 1973). It was subsequently found to contain hepatitis B antigen (HBsAg) (WHO/BS/1979) and in response to the request of the WHO Expert Committee on Biological Standardisation, a suitable HBsAg negative preparation was sought. In 1977 the National Institute for Biological Standards and Control established the 1st British Standard for Human Serum Immunoglobulin E, (ampoules coded 75/502). The pooled bulk filling material was tested for hepatitis B antigen and was found to be negative. A portion of the batch of the 1st British Standard for Human Serum Immunoglobulin E (IgE), was offered to the WHO Expert Committee on Biological Standardisation and upon its acceptance, it was established in 1981 as the 2nd WHO International Reference Preparation of Human Serum Immunoglobulin E (IgE) and the potency of the preparation was defined as 5,000 International Units per ampoule. (WHO ECBS 1981).

2. CAUTION
This preparation is not for administration to humans.

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, 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
The 2nd WHO International Reference Preparation (IRP) of Human Serum Immunoglobulin E (IgE) consists of part of a batch of ampoules coded 75/502 containing approximately 0.5 ml aliquots of pooled fresh human serum freeze-dried.

5,000 International Units per ampoule.

Uncertainty: the assigned unitage does not carry an uncertainty associated with its calibration. The uncertainty may therefore be considered to be the variance of the ampoule content and was determined to be +/- 0.31%.

4. CONTENTS
Country of origin of biological material: United Kingdom.

The 2nd WHO International Reference Preparation (IRP) of Human Serum Immunoglobulin E (IgE) consists of part of a batch of ampoules coded 75/502 containing approximately 0.5 ml aliquots of pooled fresh human serum freeze-dried.

4.1. Bulk material
Sera from 9 donors were collected by Professor J. Pepys, Brompton Hospital, London, from patients suffering with allergic disorders. The sera were tested for the presence of hepatitis B antigen and those that were negative by radio-immunoassay were combined to form a bulk. Individual samples were stored at -20°C until the bulk was prepared.

4.2. Distribution into ampoules
Each individual container of frozen serum was thawed at 37°C and pooled to give a volume of approximately 2 litres. This was sterilised by filtration through a millipore membrane a.p.d. 0.45µ. This homogeneous bulk was distributed into ampoules in 0.5 ml aliquots and freeze dried as described by Campbell (1974).

4.3. Ampoule Contents
Each ampoule of the Reference Preparation contains the residue after freeze drying, of approximately 0.5 ml of the sterile homogeneous bulk. A total of 70 check-weight ampoules were taken at intervals throughout the fill and the mean weight of liquid contents was 0.478gm +/- 0.31% (range 0.477-0.480gm). The mean weight of the freeze-dried contents of 6 ampoules was 41.82mg (range 41.49-42.18mg) and the mean oxygen content of the atmosphere within the sealed ampoules was 0.10% (3 samples, range 0.04-0.16%).

4.4. Biological Activity
Each ampoule of the 2nd International Reference Preparation of Human Serum Immunoglobulin E (IgE) contains 5,000 International Units in terms of the 1st International Reference Preparation of Human Serum Immunoglobulin E (IgE). This figure was obtained by an international collaborative study.

5. STORAGE
Store unopened ampoules at -20°C 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.

[Diagram showing the ampoule opening device]

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.

Reconstitute the total contents of the ampoule with 0.5 ml of distilled water. No attempt should be made to weigh out any portion of the freeze dried material. A suitable buffer solution should be used for further dilution of the reconstituted preparation.

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.

Ampoules of the International Reference Preparation held at +20°C for 12 months showed no detectable loss of potency. The recommended storage temperature for un-opened ampoules of the International Reference Preparation is -20°C.
Once reconstituted, diluted or aliquotted, users should determine the stability of the material according to their own method of preparation, storage and use.

9. REFERENCES
WHO/BS/79, 1240.

10. ACKNOWLEDGEMENTS
Professor Pepys collected the sera. We thank the participants of the collaborative study.

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.bpim.org/en/committees/jc/jctlm/
Derivation of International Units:
http://www.nibsc.org/products/biological_reference_materials/frequently_asked_questions/how_are_international_units.aspx
Ordering standards from NIBSC:
http://www.nibsc.org/products/ordering_information/frequently_asked_questions.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

<table>
<thead>
<tr>
<th>Physical and Chemical properties</th>
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<tbody>
<tr>
<td>Physical appearance:</td>
<td>Lyophilisate</td>
</tr>
<tr>
<td>Stable:</td>
<td>Yes</td>
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<tr>
<td>Hygroscopic:</td>
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<tr>
<td>Flammable:</td>
<td>No</td>
</tr>
<tr>
<td>Other (specify):</td>
<td>See caution, section 2</td>
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</table>

<table>
<thead>
<tr>
<th>Toxicological properties</th>
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</thead>
<tbody>
<tr>
<td>Effects of inhalation:</td>
<td>Not established, avoid inhalation</td>
</tr>
<tr>
<td>Effects of ingestion:</td>
<td>Not established, avoid ingestion</td>
</tr>
<tr>
<td>Effects of skin absorption:</td>
<td>Not established, avoid contact with skin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Suggested First Aid</th>
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</thead>
<tbody>
<tr>
<td>Inhalation:</td>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Ingestion:</td>
<td>Seek medical advice</td>
</tr>
<tr>
<td>Contact with eyes:</td>
<td>Wash with copious amounts of water. Seek medical advice</td>
</tr>
</tbody>
</table>

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**: 0.04g

**Toxicity Statement**: Toxicity not assessed

**Veterinary certificate or other statement** If applicable.

**Attached**: No

17. CERTIFICATE OF ANALYSIS
NIBSC does 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_International_biological_reference_standardsrev2004.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.