1. INTENDED USE
This standard is the primary biological standard for Interleukin-18 (IL-18).

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, 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
In a limited collaborative study, the preparation coded 03/200 was found to possess IL-18 activity comparable to in-house standards, based on its ability to stimulate release of IFN-gamma from a human myelomonocytic cell line. The preparation is therefore established as the WHO Reference Reagent for IL-18 for bioassay, with an assigned potency of 10,000 Units per ampoule. It should be noted that this assigned potency is arbitrary, and does not reflect any pre-existing units for IL-18 activity, and it does not establish continuity with any pre-existing in-house standards. Users of the material should also note that the preparation 03/200 may be suitable to serve as a standard for the bioassay of IL-18 using assay methods based on other biological activities of IL-18, but such applications have not been demonstrated for 03/200, and would require appropriate validation. Users who have data supporting the use of this preparation in another biological assay are encouraged to contact NIBSC.

The preparation 03/200 was also shown to possess immunoreactivity comparable to in-house IL-18 standards, in a limited number of in-house immunoassay systems. Whilst 03/200 is not formally established as an immunoassay standard, it may be suitable as an immunoassay standard, subject to appropriate validation. Users should note particularly that the immunological stability of this preparation, stability after freezing and thawing of the reconstituted ampoule contents has not been demonstrated for all immunoassay systems, and such studies should be undertaken by the user as part of such immunoassay application validation.

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

Each ampoule contains the residue after freeze-drying of 1.0 ml of a solution comprising:
- IL-18 approximately 1 microgram
- 9.0 mg sodium chloride
- 1.0 mg trehalose
- 2.0 mg human serum albumin
- 0.1 micrometre Tween 20

The IL-18 protein was expressed in E.coli

5. STORAGE
For economy of use, it is recommended that the solution be sub divided into several small aliquots and stored at -40°C or below. Avoid repeated thawing/freezing. 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. Tap the ampoule gently to collect the material at the bottom (labeled) end. Ensure that the disposable ampoule safety breaker provided is pushed down on the stem of the ampoule and against the shoulder of the ampoule body. Hold the body of the ampoule in one hand and the disposable ampoule breaker covering the ampoule stem between the thumb and first finger of the other hand. Apply a bending force to open the ampoule at the coloured stress point, primarily using the hand holding the plastic collar.

Care should be taken to avoid cuts and projectile glass fragments that might enter the eyes, for example, by the use of suitable gloves and an eye shield. Take care that no material is lost from the ampoule and no glass falls into the ampoule. Within the ampoule is dry nitrogen gas at slightly less than atmospheric pressure. A new disposable ampoule breaker is provided with each DIN ampoule.

7. USE OF MATERIAL
No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution.

Dissolve the total contents of the ampoule in 1.0 ml of sterile distilled water. This solution will contain IL-18 at a concentration of 10,000 International Units/ml. Use carrier protein where extensive dilution is required.

8. STABILITY
Reference materials are held at NIBSC within assured, temperature-controlled storage facilities and they should be stored on receipt as indicated on the label. It is the policy of WHO not to assign an expiry date to their international reference materials. Accelerated degradation studies have indicated that this material is suitably stable, when stored at -20°C or below, for the assigned values to remain valid until the material is withdrawn or replaced. These studies have also shown that the material is suitably stable for shipment at ambient temperature without any effect on the assigned values. Once reconstituted, diluted or aliquoted, users should determine the stability of the material according to their own method of preparation, storage and use. Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

9. REFERENCES
The standard was produced under WHO guidelines cited in the WHO Technical Reports Series, No. 927, 2005.

For details of the collaborative study report please refer to WHO document reference WHO/BS/06/2040.

10. ACKNOWLEDGEMENTS
N/A

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:
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 human origin

**Toxicological properties**

- **Other (specify):** Contains material of human origin
- **Flammable:** No
- **Hazardous to the Environment:** No
- **Toxic to the Environment:** No
- **Appearance:** Free
- **Odour:** None

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 conditions of any offer to the Recipient. By completing the order form, the Recipient acknowledges and agrees to the terms and conditions of the Sale of Biologicals (including this material) supplied by NIBSC. Any applicable terms and conditions of the Recipient are hereby excluded.

16. INFORMATION FOR CUSTOMS USE ONLY

- **Country of origin for customs purposes:** United Kingdom
- **Net weight:** 4.6g
- **Toxicity Statement:** Toxicity not assessed
- **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 (revised 2004). They are officially endorsed by the World Health Organization, which verifies their accuracy and purity.

Attached: No