WHO International Standard
2nd International Standard for Granulocyte Colony Stimulating Factor (Human rDNA derived)
NIBSC code: 09/136
Instructions for use
(Version 2.0, Dated 12/04/2013)

1. INTENDED USE
The preparation coded 09/136 was established as the 2nd International
Standard for Granulocyte Colony Stimulating Factor (G-CSF) following
evaluation in an international collaborative study. This 2nd International
Standard is the primary biological standard for Granulocyte Colony
Stimulating Factor and replaces the 1st International Standard for
Granulocyte Colony Stimulating Factor coded 88/502.

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
The assigned potency agreed on the basis of an International
Collaborative Study is 95,000 International Units of biological activity per
ampoule. The biological potency of 09/136 was derived relative to the 1st
International Standard for Granulocyte Colony Stimulating Factor coded
88/502.

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:

G-CSF, approximately 1000 ng
10 mg L-Arginine
10 mg L-Phenylalanine
5 mg Trehalose
2 mg Human Serum Albumin
0.01 % Tween 20

The G-CSF 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. 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 manufacturers 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
Dissolve the total contents of the ampoule in 1.0ml of sterile distilled water.
This solution will contain G-CSF at a concentration of 95,000 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 aliquotted, 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
This standard was produced under WHO guidelines cited in the WHO
Report on a Collaborative study for proposed 2nd International standard for
Granulocyte colony stimulating factor (G-CSF) WHO/BS/10.2133
http://www.who.int/biologicals/expert_committee/BS_2133_2ndSGCSF1907
10-Final.pdf

10. ACKNOWLEDGEMENTS
We are thankful to several manufacturers for their generous donations of
G-CSF preparations used in the collaborative study, and to the study
participants for their contributions in evaluating the preparations.

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/jcjctlm/
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
### Physical and Chemical Properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008:</td>
<td>Not applicable or not classified</td>
</tr>
<tr>
<td>Physical appearance:</td>
<td>Freeze dried powder</td>
</tr>
<tr>
<td>Corrosive:</td>
<td>No</td>
</tr>
<tr>
<td>Stable:</td>
<td>Yes</td>
</tr>
<tr>
<td>Oxidising:</td>
<td>No</td>
</tr>
<tr>
<td>Flammable:</td>
<td>No</td>
</tr>
<tr>
<td>Hygroscopic:</td>
<td>No</td>
</tr>
<tr>
<td>Irritant:</td>
<td>No</td>
</tr>
<tr>
<td>Handling:</td>
<td>See caution, Section 2</td>
</tr>
<tr>
<td>Other (specify):</td>
<td>Contains material of human origin</td>
</tr>
</tbody>
</table>

### Toxicological Properties

<table>
<thead>
<tr>
<th>Aspect</th>
<th>Description</th>
</tr>
</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>

#### 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**: 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 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.