WHO Reference Reagent
First WHO Reference Reagent for Anti-malaria (Plasmodium falciparum) human serum

NIBSC code: 10/198

Instructions for use
(Version 2.0, Dated 04/05/2016)

1. INTENDED USE
This preparation is derived from individuals based in Kimusu Kenya with a history of malaria. Single plasma donations were collected by the Kisumu Blood Bank, Kenya. Samples were screened for antibodies against 5 Plasmodium falciparum antigens, MSP-1-19 (K1), MSP-1-42 (3D7), MSP-2 (3D7), MSP-3 (K1), AMA-1 (3D7, FC27, FP3), 77% positive for at least one antigen. Each ampoule contains a freeze-dried residue comprising, under an atmosphere of nitrogen, of diluted human plasma containing antibodies to P. falciparum. The intended uses of this Reference reagent, a single multivalent preparation, are (1) to allow cross-comparisons of results of vaccine trials performed in different centers / with different products; (2) to facilitate standardization and harmonization of immunological assays used in epidemiology research; and (3) to allow optimization and validation of immunological assays used in malaria vaccine development. This material is not intended for in vitro diagnostic use.

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 glasses and avoiding the generation of aerosols. Care should be exercised in opening ampoules or vials, to avoid cuts.

3. UNITAGE
The content of this preparation has been assessed by a collaborative study to have an immunological reactivity of 100 units to malaria P. falciparum antigens.

4. CONTENTS
Country of origin of biological material: Kenya
Pooled plasma collected from a malaria endemic area was defibrinated and diluted (1: 5) with sterile water and filled at 1 ml/ ampoule. This gives a content equivalent to 0.2 ml serum/ampoule.

5. STORAGE
This preparation should be stored at -20°C in the dark for long-term storage to preserve activity.
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 ampoules with 1 ml of deionised water. Ensure that the entire freeze dried residue is dissolved in this solution.

Reconstituted ampoules should be used immediately or can be stored between 2°-8°C for 3 months without loss of activity.

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.

9. REFERENCES

10. ACKNOWLEDGEMENTS
Special thanks are due to the National Blood Bank in Kisumu and to CDC/ KEMRI malaria laboratory for sourcing and donating the material used in this preparation. Thanks also go to NIAID/ NIH for donating purified malaria antigen preparations used in this study. Speical thanks also due to all the participating laboratories and scientists involved in 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.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

<table>
<thead>
<tr>
<th>Physical and Chemical properties</th>
<th></th>
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<tbody>
<tr>
<td>Physical appearance: White freeze dried powder</td>
<td>Corrosive: No</td>
</tr>
<tr>
<td>Stable: Yes</td>
<td>Oxidising: No</td>
</tr>
<tr>
<td>Hygroscopic: Yes</td>
<td>Irritant: No</td>
</tr>
<tr>
<td>Flammable: No</td>
<td>Handling: See caution, Section 2</td>
</tr>
<tr>
<td>Other (specify): Contains material of human origin</td>
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</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Country of origin for customs purposes*: United Kingdom</th>
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<tbody>
<tr>
<td>* 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.</td>
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<tr>
<td>Net weight: 0.0185g</td>
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<tr>
<td>Toxicity Statement: Non-toxic</td>
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<tr>
<td>Veterinary certificate or other statement if applicable.</td>
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<tr>
<td>Attached: No</td>
</tr>
</tbody>
</table>

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_bioolefstandardsrev2004.pdf (revised 2004). They are officially endorsed by the WHO Expert Committee on Biological Standardization (ECBS)