1. INTRODUCTION

The 1st International Standard for Protein C, Plasma, Human, consists of ampoules (code-labelled 86/622) containing approximately 1 ml aliquots of pooled, human plasma, freeze-dried. A potency of 0.82 International Units of Protein C has been assigned to each ampoule of the 1st International Standard.

2. CAUTION

THIS PREPARATION IS NOT FOR ADMINISTRATION TO HUMANS.

The preparation contains material of human origin, which has been tested and found negative for HBsAg, HIV antibody, HCV antibody and HCV RNA by PCR.

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 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.

3. DIRECTIONS FOR OPENING THE AMPOULE

a) Tap ampoule gently to collect material at the bottom (labelled) end.

b) Score the ampoule all the way round the circumference at the constriction of the ampoule using a sharp ampoule file. Heat a thin glass rod to white heat and apply firmly the hot end to the file score. If a crack does not appear, deepen the file score. Reheat the glass rod and re-apply. When a crack appears, hold the ampoule almost horizontally and gently remove the top (empty) portion.

c) Take care that no particles of glass fall into the ampoule and no material is lost from the ampoule.

4. USE OF AMPOULED MATERIAL

Reconstitute the total contents of each ampoule, at room temperature, with 1.0ml distilled water, using gentle shaking. Do not attempt to weigh out any portion of the freeze dried material. Transfer the solution to a plastic tube and keep on ice during the assays, which should be carried out as soon as possible after reconstitution. Unopened ampoules should be stored at -20°C or below.

5. PROTEIN C CONTENT OF THE STANDARD

The Protein C content of the 1st International Standard was measured by calibration against fresh pooled normal plasma in an international collaborative study involving 18 laboratories.
Assays were carried out using four different methods of measuring Protein C activity: thrombin activation/clotting assays (4 laboratories); thrombin activation/chromogenic assays (6 laboratories); snake venom activation/clotting assay (6 laboratories) and snake venom activation/chromogenic assays (8 laboratories). Measurement of Protein C antigen was carried out using the Laurell electro-immunoassay technique (10 laboratories) and ELISA methods (5 laboratories). The Protein C content of the preparation was estimated to be 0.82 International Units per ampoule with 95% confidence limits of 0.80 to 0.83 International Units per ampoule.

Uncertainty: the International unit of 86/622 is assigned without uncertainty. The uncertainty of the ampoule content of 86/622 may be considered to be the coefficient of variation, which was determined to be 0.0693%.

6. BULK MATERIAL

The 1st International Standard was prepared in August 1986, from a pool of 4.3 litres of fresh plasma collected from 15 donors. Blood was collected into CPD-adenine contained in plastic packs, at a ratio of 450 ml blood to 67.5 ml of the anticoagulant. After centrifugation, the individual plasma donations were buffered by addition of HEPES (hydroxyethylpiperazineethanesulphonic acid) to a final concentration of 0.05 M then centrifuged again and pooled.

7. DISTRIBUTION INTO AMPOULES

The pooled plasma was kept at 10°C throughout distribution into approximately 4,000 ampoules, then freeze dried under conditions used for International Standards (1). The mean liquid filling weight was 1.0049 gm (range 1.0022 to 1.0061 gm).

8. 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. 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.
9. CITATION

In all publications including data sheets in which this material is referenced, it is important that the WHO status of the preparation, specified by the title of the preparation, the name and address of the WHO International Laboratory for Biological Standards at NIBSC and the NIBSC code number are cited and cited correctly.

10. PRODUCT LIABILITY

Information emanating from NIBSC is given after the exercise of all reasonable care and skill in its compilation, preparation and issue, but is provided without liability in its application and use.

This product is intended for use as a standard or reference material in laboratory work in relation to biological research, manufacturing or quality control testing of biological products.

It is the responsibility of the user to ensure that he/she has the necessary technical skills to determine the appropriateness of this product for the proposed application. Results obtained from this product are likely to be dependent on conditions of use and the variability of materials beyond the control of NIBSC.

NIBSC accepts no liability whatsoever for any loss or damage arising from the use of this product, whether loss of profits, or indirect or consequential loss or otherwise, including, but not limited to, personal injury other than as caused by the negligence of NIBSC. In particular, NIBSC accepts no liability whatsoever for:-

(i) results obtained from this product; and/or
(ii) non-delivery of goods or for damages in transit.

In the event of any replacement of goods following loss or damage a customer accepts as a condition of receipt of a replacement product, acceptance of the fact that the replacement is not to be construed as an admission of liability on NIBSC's behalf.

11. ACKNOWLEDGEMENTS ARE MADE TO

Dr M. Contreras, North London Blood Transfusion Centre for arranging the supply of plasma, and to all the participants in the collaborative study.

12. REFERENCES

### 13. MATERIAL SAFETY SHEET

<table>
<thead>
<tr>
<th>Physical properties (at room temperature)</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Physical appearance</td>
<td>Freeze dried powder</td>
</tr>
<tr>
<td>Fire hazard</td>
<td>None</td>
</tr>
</tbody>
</table>

#### Chemical properties

| | |
| Stable | Yes |
| Hygroscopic | No |
| Flammable | No |
| Other (specify) | Contains material of human origin |

#### Handling

See caution

#### 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 a virucidal agent. Rinse area with a virucidal agent followed by water.

Absorbent materials used to treat spillage should be treated as biologically hazardous waste.