Factor VIII: Cの国際標準品（No. 4）の制定

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（平成2年1月4日受付）

ESTABLISHMENT OF INTERNATIONAL STANDARD FOR FACTOR VIII: C(4TH)

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Factor VIII: Cの国際標準品はFactor VIII:C測定の際の標準物質となっている。1983年に定められたFactor VIII: Cの国際標準品（No. 3）に代る国際標準品（No. 4）の力価を設定するための国際共同研究が1989年3月から5月にかけて行なわれた。この力価設定の研究に18カ国、30の研究機関が参加し、28の研究機関が成績を提出した。

intermediate製品（code number, 88/804）とmonoclonal抗体を用いて精製した製品（code number, 88/640）の2つを候補品とし、No. 3を対象に力価を測定した。No. 3は3.9iu/ampouleのintermediatepurityfreezedried concentrateである。力価は統計学的に処理された。88/804は同じ測定法ではLab.間でよく一致したが、3つの方法の間に若干の差があり、一段法とchromogenic法による差は統計学的大きかった（p<0.01）。88/640は3つの方法でよく一致していたが、同じ方法で測定した場合Lab.間で変動がみられた（表）。なお、前もって行なった安定性の試験では、いずれの候補品も十分な安定性を持っていたものであった。

これらの結果は8月19日、20日の両日、東京新宿・京王プラザホテルにて開催された第35回Scientific and Standardization Committee, SSC（従来のInternational Committee on Thrombosis and Haemostasis, ICTH）のsubcommitteeで議論された。intermediate製品はmonoclonal抗体を用いて精製した製品に比較してLab.間の変動が少なく、同Committeeとしてはintermediate製品の方を国際標準品（No. 4）に設定することに合意した。

これはGenevaで行なわれたWHOのExpert Committee on Biological Standardsで正式に制定された。

以下是Factor VIII: Cの国際標準品（No. 4）のmemorandumである。請求すれば入手出来ることになっている。

4th INTERNATIONAL STANDARD FOR BLOOD COAGULATION FACTOR VIII: C, CONCENTRATE 88/804 (established 1989)

1. THE STANDARD

The 4th International Standard for Blood Coagulation Factor VIII: C, Concentrate, consists of ampoules, coded 88/804, containing aliquots of a freeze-dried concentrate prepared from human plasma. This preparation was established as the 4th International Standard for Blood Coagulation Factor VIII: C, Concentrate, by the Expert Committee on Biological Standardization of the World Health Organization in 1989, and a potency of 6.3 International Units has been assigned to each ampoule.

2. BIOLOGICAL ACTIVITY

The 4th International Standard was calibrated in an international collaborative study involv-
ing 28 laboratories in 16 countries. A potency of 6.3 International Units has been agreed upon by the participants. This figure is based on comparison with the 3rd International Standard for Factor VIII: C, Concentrate, using 1-stage, 2-stage and chromogenic assays.

3. CAUTION
The preparation contains material of human origin which has been tested and found negative for HBsAg and anti-HIV. However, as with all preparations of human origin, this material cannot be assumed to be free from infectious agents. Suitable precautions should be taken in the use and disposal of the ampoule and its contents.

This material is not for administration for humans.

4. DIRECTIONS FOR OPENING AMPOULE
Tap the ampoule gently to collect the material at the bottom (labelled) end.
Score the ampoule on one side only using a sharp ampoule file. Surround the ampoule with a thick cloth or layers of tissue. Crack the ampoule open by applying pressure on the side opposite to the file score, taking care not to cut oneself. Take care that no material is lost from the ampoule and no glass falls into the ampoule.

Within the ampoule is dry nitrogen at slightly less than atmospheric pressure.

A new ampoule file is supplied with each package.

5. USE OF THE STANDARD
The total contents of the ampoule should be reconstituted with 1ml distilled water, dissolved by gentle swirling to avoid froth and transferred immediately to a suitable plastic tube. No attempt should be made to weigh out any portion of the freeze-dried material. The reconstituted Standard should be used as soon as possible, and the solution kept at room temperature during the assay. Unused material must be discarded, not frozen for later use.

Unopened ampoules should be stored at -20°C.

6. STABILITY
Accelerated degradation studies have shown that the 3rd International Standard is very stable in unopened ampoules stored at -20°C. The predicted loss of activity is 0.03% of the original potency per year when stored at that temperature.

7. BULK MATERIAL
The 4th International Standard for Blood Coagulation Factor VIII: C, Concentrate, consists of a freeze-dried concentrate prepared from human plasma. The manufacturing process included a specific viral inactivation step. The bulk material is an "intermediate purity" concentrate with a specific activity of 3.7iu/mg.

8. DISTRIBUTION INTO AMPOULES
In 1989 the bulk freeze-dried material was reconstituted in sterile distilled H2O and diluted to approximately 4.2 litres in 0.05M Tris, 0.15M NaCl, pH 7.0. 0.150μl of a 1% solution of protamine sulphate was added to neutralise the heparin in the product, and the solution was then filtered through a Gelman pre-filter, and distributed at room temperature into 4,000 ampoules, coded 88/804. The mean weight of liquid content of 69 check-weight ampoules taken at intervals during the fill was 1.0055 gm±0.20%. The contents of the ampoules were then freeze-dried under the conditions normally used for international biological standards. The bulk material and the final freeze-dried product were tested for hepatitis B surface antigen and HIV antibody and found to be negative.

9. ACKNOWLEDGEMENTS ARE MADE TO:
All participants in the international collaborative study. We are grateful to the following manufacturers who supplied materials for investigation, from which the international standard was selected: Alpha Therapeutics Ltd, Los Angeles; Baxter Hyland Division, Los Angeles; Rorer Pharmaceuticals, Kankakee, U.S. A. and Blood Products Laboratory, Elstree, UK.

10. REFERENCES