



WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTE

279120
a
WHO/BS/03.1955

add. 1

EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION
Geneva, 17-21 February 2003

**INTERNATIONAL COLLABORATIVE STUDY TO REPLACE THE CURRENT
INTERNATIONAL (WHO) AND US STANDARDS FOR THROMBIN**

ADDENDUM: Stability study data.

Following the collaborative study to identify and calibrate a replacement for the existing International and US Standards for Thrombin a smaller study was organized to investigate the long term stability of the candidate preparations, C (01/578) and D (01/580). Preparation D is proposed as the new International and US Standard for Thrombin.

Three laboratories (identified as A, B and C) were recruited to this study from participants of the main study that had performed both clotting and chromogenic assays. Laboratories were requested to perform clotting and chromogenic assays on 3 sets of samples consisting of ampoules of candidate materials stored at 6 months at -20, 4, 20, 37, 45 and 56 °C. In addition, laboratory B performed 2 variations of a clotting assay (using an in-house protocol and the method originally supplied with the collaborative

© World Health Organization 2003

All rights reserved. Publications of the World Health Organization can be obtained from Marketing and Dissemination, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel: +41 22 791 2476; fax: +41 22 791 4857; email: bookorders@who.int). Requests for permission to reproduce or translate WHO publications – whether for sale or for noncommercial distribution – should be addressed to Publications, at the above address (fax: +41 22 791 4806; email: permissions@who.int).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

The World Health Organization does not warrant that the information contained in this publication is complete and correct and shall not be liable for any damages incurred as a result of its use.

study by NIBSC). Potencies were calculated at NIBSC relative to the potency in the -20 °C ampoules. Results for predicted loss of activity per year at various storage temperatures were determined by fitting data to the Arrhenius equation as previously described (1). Data for mean % activity remaining and a summary of results from the analysis are presented in Table 1 for Sample C (01/578) and Table 2 for Sample D (01/580). The result of 0.104% loss of activity per year at -20 °C in coagulation assays for sample D (01/580), the proposed replacement International and US Standard for Thrombin, indicates that this preparation is very stable.

References

1. Kirkwood TB. Predicting the stability of biological standards and products. *Biometrics* 1977; 33 (4):736-42

Table 1. Summary of mean % Activity remaining after 6 months' storage at elevated temperatures (relative to samples stored at -20°C) for sample C 01/578.

Method	Laboratory Code	Number of assays	Temperature °C				
			4	20	37	45	56
Clotting	A	4	101.0	101.6	96.0	94.3	86.9
	B(in-house)	3	99.9	97.2	92.4	93.5	85.8
	B(protocol)	2	100.7	95.4	93.3	90.1	86.6
	C	3	97.0	100.0	92.0	89.6	74.4
Summary		Loss of activity per year at -20°C = 0.126%					
Chromogenic	A	4	94.5	98.1	89.9	90.7	88.8
	B	3	100.7	100.4	99.8	97.4	93.2
	C	3	93.3	101.1	97.7	93.4	91.3
	Summary		Loss of activity per year at -20°C = 0.574%				

Table 2. Summary of mean % Activity remaining after 6 months' storage at elevated temperatures (relative to samples stored at -20°C) for sample D 01/580, the proposed new International and US Standard for Thrombin.

Method	Laboratory Code	Number of assays	Temperature °C				
			4	20	37	45	56
Clotting	A	4	101.7	102.2	96.1	93.3	84.2
	B(in-house)	3	104.3	105.5	96.4	92.8	90.1
	B(protocol)	2	98.8	99.5	92.0	97.0	96.7
	C	3	96.0	97.4	90.1	89.7	77.7
Summary		Loss of activity per year at -20°C = 0.104%					
Chromogenic	A	4	95.2	95.7	92.2	91.5	86.8
	B	3	100.6	100.5	95.5	95.6	90.7
	C	3	100.3	100.6	95.2	98.8	96.6
	Summary		Loss of activity per year at -20°C = 0.503%				

= = =