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WHO Expert Committee on Biological Standardization

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WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Geneva, 6–12 December 1977

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WHO EXPERT COMMITTEE ON BIOLOGICAL STANDARDIZATION

Twenty-ninth Report

GENERAL

The WHO Expert Committee on Biological Standardization met in Geneva from 6 to 12 December 1977. The meeting was opened on behalf of the Director-General by Dr Ch'en Wen-chieh, Assistant Director-General.

The Committee considered that one of the most useful documents made available at the meeting was Guidelines for the Preparation and Establishment of Reference Materials and Reference Reagents for Biological Substances. It was formulated for the guidance of international associations that were helping in setting up international standards as well as for the guidance of national authorities that were faced with the task of establishing national standards. The guidelines had been amended in the light of comments received from a number of scientists, and further amendments were made by the Expert Committee. The final version was annexed to the report (see Annex 4).

Another important matter was the Requirements for the Collection, Processing and Quality Control of Human Blood and Blood Products (see Annex 1). It was agreed that it would be most useful to have a single set of requirements applicable to all organizations and laboratories involved in the collection or fractionation of blood and blood products.

There is a need for better understanding of the distinction between estimates of hormone concentration using bioassays, which are based on the biological activity or function of a hormone, and estimates using binding assays (particularly radioimmunoassays), which are based on aspects of hormone structure that may not be related to biological activity or function. Failure to understand this distinction had led to considerable confusion in the literature and in clinical practice, and the confusion is even worse when the results of structure-based assays are misinterpreted as measures of biological activity. Measures recommended by the Expert Committee in its twentieth, twenty-first, and twenty-sixth reports had proved insufficient to maintain a clear distinction between the results of these two types of assay.

Experience gained in various assay performance studies, including the WHO human reproduction matched reagent programme, shows that the results of radioimmunoassay determinations cannot always be reproduced reliably with different sets of reagents. In addition, preparations containing heterogeneous forms of a hormone can yield markedly different potency ratios when tested in different *in vivo* and *in vitro* comparative bioassay systems.

It is recommended, therefore, that a report of an assay shall always be accompanied by a statement of the assay method employed, the standard used and its stated unitage, and the calibration method used (bioassay or binding assay). Unless this is done, confusing and possibly dangerous misinterpretations of potency estimates may be made. The Committee requested WHO to investigate this further in order to formulate guidance on the use of hormone preparations.

The Committee observed that until now the international unit of activity of all international reference materials has been expressed as that contained in a given weight or volume of the preparation contained in a sealed ampoule. The Committee has been aware for some time that the activity of some reference materials may not be distributed evenly throughout the freeze-dried preparation and that it may therefore be misleading to give the impression that the unit of activity is contained in a given weight of the preparation. In practice, irrespective of the definition of the unit by weight or by volume, for those preparations that have been filled as accurately reproduced volumes, instructions are given to the user to treat the contents of an ampoule as containing a defined number of units. The Committee was informed that there appears to be no legal objection to assigning a finite number of international units to the contents of an ampoule of material. Such a policy, however, calls for great accuracy in filling and care in freeze-drying in order to ensure that the variation of fill is not greater than 1%.

The Committee was informed of the increased use of certain antitumour antibiotics for the treatment of human tumours and leukaemias in a number of countries, some of which have national reference materials for control purposes. The measurement of activity, however, causes problems, and although an antitumour activity test in animals can be included in the original characterization of the preparation such tests cannot be used for the quantitative assessment of individual batches. For routine batch control, reliance must be placed partly on quantitative antimicrobial activity tests. The Committee noted that some of these antibiotics are pure crystalline materials, for which a chemical reference preparation would be suitable, while others consist of a mixture of several closely