Certification of Standard Reference Materials

To the Editor:

We have not been able to locate any published study on the structure and validity of the Certificate of Analysis provided with a Standard Reference Material (SRM), and our present aim in this Letter is to summarize some of our recent studies on this matter.

The Certificate that we first assessed was that provided by the U.S. National Bureau of Standards since 1974 to purchasers of high-purity cholesterol (SRM 911a), and this was chosen because of our long interest in the assay of cholesterol (1). We find that:

(1) The following key items are not defined on the Certificate:
(a) the term "purity";
(b) the variation in the purity figure;
(c) the term "very little absorption" in the description concerning the ultraviolet absorption spectrum of SRM 911a in the 40 g/L solution in methylene chloride.

(2) The statement concerning the stability of the solution of the SRM cholesterol in glacial acetic acid is incorrect, because we (2) and others (3,4) have shown that when cholesterol is stored in this solvent at room temperature, cholesterol acetate is formed.

With regard to these two findings, we would like to suggest that when new certificates are published, the missing definitions listed in (1) above should be provided and that attention should be drawn to the possibility of the formation of cholesterol acetate in stored solutions of the SRM in glacial acetic acid.

In addition, in view of the use of Standard Reference Materials as primary standards in clinical chemistry, we believe that the utility of these materials would be much improved if (a) batch/lot numbers of the samples purchased were recorded on the certificate and (b) if the date of analysis of the batch was recorded on the sample container itself.

Finally, we feel sure that it would be much appreciated by all SRM users who wish to check the purity of their samples before use if complete details of the assay procedures adopted by the certifying agency were provided or were fully documented and made readily available on request.

References

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A representative of the U.S. NBS comments:

The batch/lot is in fact already uniquely identified on the Cholesterol SRM certificate. The letter "a" in the SRM designation 911a denotes that this lot of material is the second batch produced by NBS. The original batch was designated as SRM 911. The next batch of cholesterol certified by NBS would be labeled SRM 911b. An insert accompanying each package explains the NBS batch-designation system and is in conformance with FDA labeling requirements. Because the complete batch of material is certified, rather than individual bottles, the important date on the certificate is the date of certification rather than the date of analysis. In fact there is no unique date of analysis in this case, because many analyses were done over a period spanning nearly six months.

Although an NBS study of the stability of a cholesterol solution in glacial acetic acid has not been completed, we agree that cholesterol acetate will probably form, and if so, the certificate for SRM 911a will be reprinted. This reprint will also indicate that some of the data are provided for information only and, as such, may very well be qualitative. The ultraviolet absorption spectrum is a case in point.

Ideally, it would be desirable to publish a complete detailed description of the assay procedures or methods used in certifying every NBS SRM (clinical or otherwise). However, in practice, we do not find it feasible to formally publish detailed method descriptions and certification data for all SRM's, but NBS policy is to supply such information and data to individuals upon request. The main purpose of an SRM certificate is to indicate that the particular property being certified falls within the claims made on the certificate. The certificate also provides sufficient information to ensure the proper use of the SRM for standardization purposes. The certificate is not intended to provide sufficient details of analyses or experiments for the user to duplicate NBS certified procedures, nor is this an intended use of an SRM.

I should also point out that many issues related to the format and contents of reference material certificates are being discussed by the Council Committee on Reference Materials (REMCO) of the International Standards Organization, Geneva, Switzerland. Dr. T. W. Steele (representing the South African Bureau of Standards) has completed a draft report entitled "The Feasibility of a Standard Certificate for Reference Materials," which is being circulated throughout the world for comments.

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Pseudoproteinuria Due to Penicillins, in the Turbidometric Measurement of Proteins with Trichloroacetic Acid

To the Editor:

Among the many substances reportedly causing falsely positive reactions for urinary proteins as measured by the trichloroacetic acid method are the penicillins and salicylates (1, 2). Recently, interference by penicillins in the biuret reaction has also been reported (3).

In our laboratory, using an automated trichloroacetic method to estimate urinary protein (4), we encountered two cases of pseudoproteinuria; both patients were being treated with methicillin and cephalothin. That protein was not the cause of turbidity was evidenced by the different precipitation kinetics from those observed with protein. We have investigated the effect of ampicillin, carbenicillin, amoxycillin, procaine penicillin, cloxacinill, benzylpenicillin, methicillin, cephalothin, salicylic acid, acetylsalicylic acid, and dexamethasone on the method. We weighed the drugs into protein-free urine to give concentrations corresponding to the maximum prescribed dosage for each drug, assuming that the drugs would be excreted unchanged in the urine. The kinetic