COMMITTEE REPORTS

REPORT OF COMMITTEE ON PHYSIOLOGIC ASSAYING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

Owing to several unavoidable delays, the Committee was not completely organized until February of this year, and after organization the exigencies of abnormal conditions due to the war resulted in such an enormous increase in regular routine work that it was impossible for the members of the Committee to attempt any researches which were not absolutely essential.

We beg, however, to submit the following report of our work to date:

The incorporation of the chapter on "Biologic Assays" in the U. S. P. IX is epochal in the history of standardization and it is to be hoped that with this start a much wider publicity and experience will be gained so that the next Committee of Revision will readily be able to select from the proposed methods and make official the methods and technique which prove to be the most satisfactory and convenient for each drug.

The Committee is unanimous, however, in its opinion that the biologic assay methods of the U. S. P. IX are unsatisfactory, due to the fact that in many cases *they lack the details* which workers in the practical laboratory have found essential in order to obtain accurate results.

In other words, the methods are in many instances *not as accurate and up-to-date* as the methods in common use at the present time in the commercial laboratories.

Specific criticisms of the U. S. P. methods are given in the following four papers by members of this Committee:

"Biologic Standardization, by H. C. Hamilton. *Amer. Jour. of Pharm.*, Feb. 1917.

"The Physiologic Standardization of Cannabis," by W. A. Pearson, J. A. PH. A., Nov. 1916, p. 1194, and Oct., 1917, p. 876.

"Biologic Standardization of the Heart Tonic Preparations." By H. C. Colson, Jr. J. A. PH. A., 1918, Vol. 7, No. 1.

"Biologic Assay Methods of the U. S. P. IX." By Paul S. Pittenger, J. A. PH. A., Oct. 1917, p. 865.

The above papers show very conclusively that many of the shortcomings of the U. S. P. Biologic Methods are due to the fact that the Revision Committee failed to give due consideration to the viewpoint of the manufacturer.

"The importance of this feature is in the fact that the manufacturers were in many instances the originators of the tests in use, and had of necessity developed them from scientifically interesting facts to a practical working basis. These manufacturers through years of experience were in a position to eliminate the non-essentials and to arrive at some common ground by compromise. A method which under certain conditions can be made fairly satisfactory may fail entirely when attempts are made to apply it under practical working conditions." (Hamilton).

Owing to the facts stated, very little attention has been paid to the methods of the U. S. P. IX as all evidence tends to prove that they are less accurate and reliable than the methods in common use.

It is only natural that pharmacologists should differ in their opinions as to which reaction more nearly represents the activity of a drug, when it has more than one therapeutic use, and that each worker should be partial to the method with which he has had the most experience.

Your Committee feels, therefore, that it bears the responsibility of a very important part of the work of this Association and that *it is the duty of its members to coöperate in a thorough, impartial investigation as to the relative applicability, degree of accuracy and ways of improving the various biologic assay methods.*

It was decided that we first adopt a definite plan of work for the Digitalis series and after this was well under way that we decide upon definite plans of work for Epinephrin and products of the Suprarenal gland, Liquor Hypophysis, Cannabis, Ergot, etc.

The Chairman compiled a tentative plan of work and submitted the same to the Committee for further criticisms and suggestions.

The tentative plan was changed accordingly, and we are now in position to submit the following plan of work for this Committee:

SUGGESTED PLAN OF WORK ON DIGITALIS.

1. Compare the accuracy and practicability of M. L. D. Frog Heart Method, One Hour Frog Heart Method, Cat Method and Guinea Pig Method for the heart tonics and depressants.

(*a*) A Tincture of Digitalis will be prepared by the Chairman, and samples of this tincture sent to the other members of the committee. The samples will be sufficiently large for further investigations as to deterioration, etc.

(*b*) The M. L. D. of this sample should be estimated by the different members, using Ouabain as a standard which will also be supplied by the Chairman, in order to find out if concordant results can be obtained by the One Hour Method. If the results are satisfactory, the tincture should be diluted according to the results obtained, and

(*c*) To this diluted tincture, the other methods should be applied together with the M. S. S. method.

These experiments will test the accuracy of the method and at the same time convert the standards of the Pharmacopoeia into terms of the M. L. D. Frog Heart and Guinea Pig Method, and thus enable each member to compare the U. S. P. standard with the standards adopted by his laboratory and to state whether in his opinion the U. S. P. standards are O. K. or whether they should be raised or lowered.

2. As a difference of opinion exists as to the proper substance for standardizing animals which are subject to seasonable variation, chemical and pharmacological tests for the identity and purity of both Ouabain and Kombe Strophanthin should be studied with the object of deciding which is the better standard.

3. In order that the methods of standardization and rate of deterioration may be considered at one and the same time, and with minimum labor, a sufficient quantity of Tinctures of Digitalis and Ouabain will be submitted for No. 2 that the tests may be repeated at intervals of 4 months for a period of two years.

(*a*) A summary of the results obtained will be valuable in determining the rate of deterioration of Digitalis preparations and in enabling us to come to a conclusion as to the choice of methods.

Accordingly, the Chairman prepared a lot of Tincture of Digitalis and distributed it together with a sample of Ouabain to each member of the Committee with a request that laboratory work be conducted according to the above outline.

To date, three members of the Committee have assayed the Tincture by the "One Hour Frog Method" and reported as follows:

H. C. Hamilton	102.8%
H. C. Colson	101.5%
P. S. Pittenger	108.3%

You will note, therefore, that there is a variation of only 6.8 percent in the results obtained with the "One Hour Frog Method" by the three different workers.

These results are indeed very satisfactory and encouraging, especially when we consider the fact that non-standardized tinctures of Digitalis vary hundreds of percent in activity.

I would call your particular attention to the above results as only too frequently we hear rather caustic criticisms of the value of biologic assaying, which leave the impression that biologic assay methods are practically valueless because the results obtained by different workers vary from 50 to 100 percent, whereas this report shows a variation of only 6.8 percent in the results obtained by workers in three different laboratories.

These results would indicate, therefore, that if the experiment is properly conducted, very reliable results can be obtained by the "One Hour Frog Method."

The Committee will continue its work according to the above plan during the next year, and hope to be in a position to make some definite recommendations to the Association at its next annual meeting.

Respectfully submitted,

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H. C. COLSON, JR.
W. A. PEARSON,
PAUL S. PITTENGER,
Chairman.