COMMITTEE REPORTS

REPORT OF THE VITAMIN ASSAY COMMITTEE OF THE AMERICAN DRUG MANUFACTURERS' ASSOCIATION—TWENTIETH ANNUAL MEETING—MAY 1931.

BY ARTHUR D. HOLMES, CHAIRMAN.

Historical.—In April 1927 the American Drug Manufacturers' Association created a Vitamin Assay Committee to make a careful study of the U. S. P. X method for "Vitamin A Assay for Cod Liver Oil." Subsequently the Vitamin Assay Committee was directed to extend its activities to include a study of methods for the determination of the vitamin A and vitamin D content of cod liver oil and related products. Before procceding to a discussion of the activities and the results obtained by the Vitamin Assay Committee it may not be out of place to briefly review the events which lead up to the development of the U. S. P. X Method for "Vitamin A Assay for Cod Liver Oil." At the September 1921 meeting of the American Chemical Society, Emmett presented a paper (*Jour. Ind. and Eng. Chem.*, 13, No. 12 (Dec. 1921), 1104) on the urgent need of "Standardized Methods for the Study of Vitamines"—emphasizing the value of coöperative test assays between several laboratories. As a result a Committee of Vitamin Research was appointed by that Society. Since that time this committee has functioned as a clearing house for information obtained from vitamin researches rather than as an active agent for directing laboratory investigation of methods for vitamin assay. During the summer of 1924 certain individuals, who foresaw the important economic rôle that vitamins were to play in medicine, pharmacy, and in animal and human nutrition, felt that steps should be taken to develop methods for the accurate determination of the vitamin content of cod liver oil and other materials intended as supplementary sources of vitamins.

Believing that such methods should be developed with painstaking care by some organization whose professional standing was beyond question, it was proposed to the Division of Biological Chemistry of the American Chemical Society, during its sessions at Ithaca, New York, September 1924, that it should sponsor the preparation of methods for the quantitative determination of vitamins. This proposal was rejected by the Division of Biological Chemistry.

Subsequently it was suggested to the Revision Committee of the United States Pharmacopœia that the preparation of vitamin assay methods could be very properly considered by that Committee during its deliberations in connection with the Tenth Decennial Revision of the United States Pharmacopœia. The Revision Committee, fully realizing the urgent need for vitamin methods, acted upon this suggestion. Invitations were extended to the prominent vitamin investigators to attend a conference which would consider the preparation of vitamin assay methods. The conference was attended by representatives of the medical profession, pharmaceutical manufacturing concerns and Academic Laboratories. During the conference it was agreed that the need for official vitamin assay methods was imperative. Accordingly, the conference developed the method for vitamin A which is described in detail in the U. S. P. X.

To fully appreciate the true significance and the important function performed by this optional U. S. P. X vitamin method one should not attempt to evaluate this method in the light of present-day knowledge concerning vitamins and their reactions. Instead one must attempt to visualize the situation as it existed in 1925. The U. S. P. X Vitamin A Method was a pioneer method and it therefore represented the first concerted attempt anywhere to place vitamin assay on a quantitative basis.

A careful review of the U. S. P. X Vitamin Method will reveal that a large portion of the details now believed essential for vitamin determinations are discussed in that method. The method provided for vitamin B requirements and called attention to the need for considering antirachitic requirements at a time when some of those now prone to criticize the method were denying the existence of the antirachitic vitamin. In the hands of an experienced person the method is entirely workable as is attested by the fact that comparable results have been obtained by laboratories employing this method. In recognition of the important service rendered by this method, it may be stated that the quality of the cod liver oil sold in this country has been maintained at a much higher level than would have otherwise been the case if no standard procedure had been developed. To this end it has served its purpose and served it well.

Discussion.—However, it is frankly recognized that the use of the U. S. P. X Method presents some difficulties, particularly in the hands of inexperienced workers and furthermore the U. S. P. X does not require the determination of vitamin D. It is our opinion that the forthcoming U. S. P. XI should require assay methods for both vitamin A and vitamin D in cod liver oil and related products. Accordingly, your Vitamin Assay Committee has for more than four years been giving careful attention to the development of vitamin A and vitamin D assay methods which combine the advantages of accuracy, convenience, the least possible demand of time and expense, and workability in the hands of those possessing only a moderate amount of experience in vitamin research.

At the Nineteenth Annual Convention, this Committee presented a report of the results of its study during the year preceding April 1930. During the past year the Committee has given attention to improving the methods for vitamin A and vitamin D assays which it tentatively suggested at the annual meeting.

As the studies of the Vitamin Assay Committee have become more detailed and more extended it has become increasingly evident that it was imperative to develop specifications for the various ingredients of the experimental rations which would insure uniformity of ingredients purchased by the several coöperating laboratories. For instance, it was found that dextrinized corn starch, when purchased by name only, might contain from 5% to 95% of dextrin. A similar condition existed regarding other ingredients. Hence it was evident that attention should be given to the preparation of definite specifications for all ingredients to be included in the experimental rations. As a result of extensive correspondence such specifications have been prepared and are appended to this report. It will be noted that the nature or quality of a number of the ingredients are specified by brand name, or through the courtesy of various individuals associated with the concern providing the material in question. While this arrangement has provided for the present needs of the Committee members, it is obvious that all the specifications should be so carefully developed that uniform materials are assured regardless of the source of supply.

The April 1930 Report contained a suggestion by your committee that "Cod liver oil may be assayed for its vitamin A content by the following process or method. When so assayed the oil shall contain at least 250 vitamin A units per Gm." In the light of recent developments and additional information the committee now recommends that "Cod liver oil shall be assayed for its vitamin A content by the following process or method. When so assayed the oil shall contain at least 400 vitamin A units per Gm."

During the past year a comparison has been made of the effectiveness of the methods as outlined in the 1930 report when the Vitamin Restricted Diet was included and when it was omitted. The object of this test was to determine whether the method could be simplified by omitting this Restricted Diet and continuing the young animals on the Breeders' Diet until they were put on the Vitamin A Free Diet. It was found when the Vitamin Restricted Diet was included that (*a*) xerophthalmia developed about five days earlier and (*b*) xerophthalmia and declining weight occurred simultaneously more frequently than when the Vitamin Restricted Diet was omitted. Hence the Committee recommends that the Vitamin Restricted Diet be included.

Evidence has been collected that cod liver oil, highly diluted with peanut or corn oil and frequently exposed to the air, loses vitamin A value. Accordingly, instead of making a single dilution of cod liver oil to be used for the entire 35-day test period, the Committee recommends that dilutions of cod liver oil in peanut or corn oil be prepared at weekly intervals.

From time to time reports have appeared in the literature of studies of the value of the so-called colorimetric methods for determining the vitamin A content of cod liver oil. By some it is stated that the antimony trichloride colorimetric method can be relied on for assaying cod liver oil for its vitamin A content. Others are equally certain that the method is untrustworthy. This question is of major importance to those interested in the vitamin assay of cod liver oil for if a reliable rapid method were available the time and expense of the present biological method would be materially reduced. Your Committee recommends that this subject be given further study.

Your Committee's 1930[1] report also recommended that the vitamin D method should provide that "when so assayed the oil shall contain at least 60 vitamin D units per Gm." Results obtained during the past year indicate that this requirement is too low and your Committee there-

[1] JOUR. A. PH. A., 19 (1930), 616.

fore suggests that this provision be modified to read: "When so assayed the oil shall contain at least 100 vitamin D units per Gm."

It has been observed that the results attained in testing for vitamin D are influenced to some extent by the degree of rickets produced in the experimental animals previous to the administration of the vitamin containing substance. Hence it appeared desirable to provide means for describing the degree of rickets which could best serve as a criterion for commencing administration of the vitamin containing substance to be tested. Accordingly, a series of measurements were made of the width of the cartilage in the tibiæ of animals which were considered as having developed a satisfactory degree of rickets. While the width was found to be quite uniform it depended upon the section at which the measurement was taken. Since no section can be satisfactorily designated at which this measurement should be taken it appeared impractical to carry out this procedure and the Committee does not recommend it.

Further experience in the use of the vitamin D test as outlined in the 1930 report which recommended that the test animals be fed cod liver oil for eight consecutive days and killed at the end of the tenth day shows that this procedure yields reliable results. The Committee, therefore, strongly recommends the general adoption of this procedure.

Recently the Revision Committee of the United States Pharmacopœia has been formulating plans for a sub-committee which shall develop vitamin A and vitamin D methods to be included in the forthcoming U. S. P. XI. After careful consideration your Committee has unanimously agreed that the methods which will be developed by the U. S. P. Vitamin Sub-Committee should be put to actual test before becoming official. In view of this decision the chairman of your Vitamin Assay Committee inquired of the Revision Committee of the U. S. P. whether it desired to have the forthcoming vitamin methods tested. The chairman replied that the Revision Committee was very much interested in having the forthcoming U. S. P. methods given an actual test under typical laboratory conditions. Your Vitamin Committee now awaits the direction of the American Drug Manufacturers' Association as to your pleasure in the matter.

The various modifications that have been made in the vitamin A and vitamin D methods since the 1930 report appeared are included in the detailed outline that follows. Your Committee recommends the adoption of these improved methods fully appreciating that as additional data accumulate modifications may become necessary.

VITAMIN A AND D ASSAY FOR COD LIVER OIL AND RELATED PRODUCTS—MAY 1931.

I. Vitamin A.—Cod liver oil shall be assayed for its vitamin A content by the following process or method. When so assayed the oil shall contain at least 400 vitamin A units per Gm.

This assay is based upon the estimation of the minimum amount of cod liver oil necessary to meet specific growth-promoting as well as relative antiophthalmic requirements in a standard test animal kept under definite control as regards source, age and food supply. The test animal shall be albino rats from known source and bred preferably under the direction of the experimenter.

BREEDERS' DIET.

Wheat meal (entire kernel)	33.0%
Yellow corn meal (entire kernel)	34.0%
Whole milk powder	21.0%
Old process linseed oil meal	7.0%
Alfalfa leaf flour (green color)	2.0%
Liver (vacuum dried)	2.0%
Calcium carbonate ($CaCO_3$)	0.5%
Sodium chloride (NaCl)	0.5%

The vitamin A potency of cod liver oil shall be expressed in units per Gm. of oil, the unit to be the minimum daily amount (in mg.) of cod liver oil required to cause, in sixty per cent of the animals in any one group, a gain in weight of at least 15 Gm. within a period of thirty-five days under the conditions of growth and diet specified in this assay. The maximum weight must be attained at the end of the test and the eye condition must be corrected by an amount of cod liver oil not to exceed three times the minimum growth factor.

The vitamin A content per Gm. of cod liver oil is computed by dividing 1000 mg. (1 Gm.) by the determined minimum daily amount of oil, in mg., required to induce the requisited growth recovery.

Method.—It is desirable that each laboratory should establish its own breeding colony or else secure rats under known conditions as to age and dietary history.[1]

To obtain suitable test rats for vitamin A and D assay, females from the colony should be used to rear the actual test animals. These females should be taken off the Colony Diet as soon as weaned and fed the Breeders' Diet below. Later they are placed on a Restricted Diet as stated elsewhere.

This diet must be supplemented daily by the addition of fresh green leafy material preferably lettuce or spinach, about 5 Gm. being sufficient per rat per day.

When about 100 days old, the females are mated with males which are continuously maintained on the Breeders' Diet. When the young are five to seven days old, the litters should be adjusted to seven animals for each female. On the tenth to twelfth day the mothers are given the Vitamin Restricted Diet.

VITAMIN RESTRICTED DIET.

Wheat meal (entire kernel)	33.0%
Yellow corn meal (entire kernel)	34.0%
Skimmed milk powder	21.0%
Old process linseed oil meal	7.0%
Yeast (dried) (1)	4.0%
Calcium carbonate ($CaCO_3$)	0.5%
Sodium chloride (NaCl)	0.5%

Later when these rats are weaned (21–23 days old) the mothers are then returned to the Breeders' Diet (not the Colony Diet). The young are continued on the Vitamin Restricted Diet until they are twenty-five to twenty-nine days old at which time they should weigh thirty-eight to forty-five Gm. They are then fed the Vitamin A Free Diet so as to deplete them for the vitamin A Test.

VITAMIN A FREE DIET.

Casein (Vitamin A Free) (2)	18%
Salt mixture (Osborne-Mendel or McCollum No. 185)	4%
Agar (finely ground)	2%

[1] The following well-balanced diet, rich in vitamins, has been found satisfactory as a Colony Diet:

COLONY DIET.

Wheat meal (entire kernel)	33.0%
Yellow corn meal (entire kernel)	33.0%
Whole milk powder	21.0%
Old process linseed oil meal	7.0%
Alfalfa leaf flour (green color)	2.0%
Liver (vacuum dried)	2.0%
Calcium carbonate ($CaCO_3$)	0.5%
Sodium chloride (NaCl)	0.5%
Cod liver oil (of high vitamin assay)	1.0%

The ingredients of all diets should be ground fine enough to insure a uniform mixture. The diet, with the exception of the whole milk powder and the cod liver oil, may be mixed in large quantities and the milk powder and cod liver oil should be added to such portions as will be consumed in about one week.

This Colony Diet must be supplemented daily by the addition of fresh green leafy material. An approximate allowance of about 5 Gm. daily per rat of this material should be sufficient. Boiled bone or other hard materials should be supplied occasionally for gnawing.

Yeast (dried) (1)	8%
Corn starch	63%
Hydrogenated vegetable oil (Vitamin A Free)	5%
Vitamin D (3)	

(1) The vitamin "B" value of the yeast should be such that not more than 150 mg. of the yeast is required for a daily-rat-weight recovery dose when animals are on the Sherman Basal Vitamin B Free Ration.

(2) Casein which will pass through a No. 60 sieve is treated with denatured alcohol "3A" (which is a mixture of 100 parts of ethyl alcohol and 5 parts of methyl alcohol).

Reflux 20 lbs. casein 1 hr. with 7 gals. 3A alcohol
Filter
Reflux 1 hr. with 5 gals. 3A alcohol
Filter
Allow casein to stand over night in 5 gals. 3A alcohol
Reflux 1 hr. with 5 gals. 3A alcohol
Filter
Reflux 1 hr. with 5 gals. 3A alcohol
Filter
Wash with 3 gals. 3A alcohol

Drain and dry the washed casein in a current of air for 16 hrs. at 120° F. in layers not over $^1/_4$ in. deep.

(3) In order to insure sufficient antirachitic activity one-fourth of the yeast should be irradiated before it is incorporated in the diet. To accomplish this the powdered yeast in a layer not exceeding one-sixteenth of an inch in depth is irradiated for fifteen minutes at a distance of 12 or 18 inches with a quartz mercury vapor lamp. The yeast should be stirred during exposure. If desired, the antirachitic factor may be supplied by other materials. Whatever material is used, it must be Vitamin A Free and its antirachitic potency should be such as will provide antirachitic activity in the diet equivalent to 3% of a cod liver oil having 100 vitamin D units per Gm.

VITAMIN A TEST.

The animals should be fed the Vitamin A Free Diet until there is either a decline in weight or a stationary weight for at least seven days. Preferably xerophthalmia should be manifest at this time but declining weight or stationary weight for seven days and definite eye conditions do not necessarily occur simultaneously. In any case, the weight criteria should be used for the administration of cod liver oil to the test animal. As a check, the control test rats must show both symptoms not later than 10 days after the administration of the cod liver oil to the test animals has begun. In order to insure more comparable conditions the beginning of the administration of the cod liver oil should preferably not occur before the 30th day or after the 45th day of the Vitamin A Free preparatory period.

The experimental animals should be divided into groups of six rats each, one group to serve as a control and the others to be treated with varying amounts of the cod liver oil under test, each animal within the respective groups being given the same dosage.

Cod liver oil being so potent should be diluted with a vitamin A and D free oil such as peanut or corn oil. These dilutions should be prepared as often as once per week. The total daily volume of the diluted oil for each rat shall be 0.1 cc. This diluted cod liver oil should be fed separate from the diet. The control animals should receive 0.1 cc. daily of the oil used as a diluent. The time for its administration should be judged by the same criteria as that for the cod liver oil.

Any animal that dies from causes other than vitamin A deficiency in less than two weeks after the beginning of treatment should not be included in judging the results of the test. A record should be made three times a week of the body weight and the condition of the eyes during the test period. The condition of the eyes may be recorded as normal, watery, sensitive to light oedema, bloody exudate, pustules and opacity of cornea.

II. Vitamin D (Antirachitic).—Cod liver oil shall be assayed for its vitamin D content

by the following method. When so assayed the oil shall contain at least 100 vitamin D units per Gm.

This assay is based upon the estimation of the minimum amount of cod liver oil necessary to initiate a specific degree of recalcification in the leg bones of rachitic rats reared and fed under definite control as specified.

The vitamin D potency of cod liver oil shall be expressed in units per Gm. of oil, the unit to be the minimum average daily amount (in mg.) of cod liver oil required to produce, in sixty per cent of the animals in any one group, a degree of recalcification represented by a narrow continuous "line" across the metaphysis of the leg bones of the rats which have been kept and fed under the conditions as specified in the assay.

The vitamin D content per Gm. of cod liver oil is computed by dividing 1000 mg. (1 Gm.) by the determined minimum average daily amount of oil, in mg., required to induce the requisite degree of recovery. The average daily dose is understood to be the total amount of cod liver oil given divided by the length of the test period, ten days.

Method.—Experimental animals for vitamin D test, obtained from mothers which have been reared and bred on the Breeders' Diet, are fed the Vitamin Restricted Diet until they are twenty-eight to thirty-two days old and weigh fifty to sixty Gm. They are then fed the Steenbock Ricket-Producing Diet, No. 2965, or the McCollum Ricket-Producing Diet, No. 3143.

Steenbock Ricket-Producing Diet, No. 2965.		McCollum Ricket-Producing Diet, No. 3143.	
Whole yellow corn (freshly ground)	76%	Corn (yellow)	33%
Wheat gluten	20%	Wheat (soft winter wheat)	33%
Calcium carbonate ($CaCO_3$)	3%	Wheat gluten	15%
Sodium chloride (NaCl)	1%	Gelatin	15%
		Calcium carbonate ($CaCO_3$)	3%
		Sodium chloride (NaCl)	1%

During the period of preparation for the test and while on test the animals should receive distilled water.

After the experimental animals have been on the rachitic diet for a suitable period (18 to 20 days) examine four rats, by the "line test" as described later, to ascertain whether a satisfactory stage of rickets has been attained. If so, the remainder are considered as satisfactory for the test and should be divided into groups of seven animals each. It is desirable to have at least four groups, one as control and three for treatment with the cod liver oil in varying doses so that one can judge the potency of the oil above and below the unit value sought.

From the beginning of administration of the cod liver oil the rats should be kept in individual cages and a record should be made of the daily food consumption.

The cod liver oil should be diluted with a vitamin A and D free oil, such as peanut or corn oil so that the total daily volume of oil consumed by each rat shall be 0.1 cc. These dilutions should be prepared as often as once per week. The oil should be fed separate from the diet. A control group of representative animals should receive 0.1 cc. daily of the diluent.

The diluted cod liver oil (or the diluent) should be given for eight consecutive days. The rats are continued on the rachitic diet for two remaining days of the test period to allow for the latent effect of the cod liver oil.

Any animal which has lost weight continuously during the test period; has eaten less than two Gm. of food on two consecutive days; or has averaged to eat less than four Gm. of food per day should be excluded from the final interpretation.

At the conclusion of the tenth day of the test, the animals should be killed and the femur and tibia bones (or ulna and radius) removed from the right leg and preserved in formaldehyde (10%) for examination. When ready for staining the bones should be thoroughly rinsed in water, split, placed in acetone for three minutes, dried on a blotter, placed in silver nitrate (2%) three minutes, intensified under bright light until the "line" is clearly evident, placed in sodium thiosulfate solution (5%) for three minutes and examined under a microscope. Reserve the bones from one other leg in formaldehyde for possible confirmation test.

SOURCES AND SPECIFICATIONS FOR MATERIALS USED IN THE PREPARATION OF EXPERIMENTAL DIETS RECOMMENDED BY THE VITAMIN ASSAY COMMITTEE FOR THE VITAMIN A AND D ASSAY OF COD LIVER OIL.

Agar—Parke, Davis & Co., Detroit, Michigan.—Specifications: To be requisitioned as Powdered Agar No. 826256 for A. D. M. A. (Emmett). A special lot has been set aside for this year's investigations.

Alfalfa Leaf Meal—The Garten Feed Co., 515 South Senate Avenue, Indianapolis, Indiana.—Specifications: Alfalfa Leaf Meal Triple Ground No. 1 Meal. Protein 17 to 20%-Fibre 18 to 20%.

Casein—The Casein Manufacturing Company of America, Inc., 205 East 42nd Street, New York, N. Y.—Specifications: D-3 Brand; Acidity 2.5%; Moisture 10%, Ash 4%, Fat 2%.

Corn Starch—Stein, Hall & Co., Inc., 285 Madison Ave., New York.—Specifications: Special material for vitamin studies.

Gelatin—American Agricultural Chem. Co., Michigan Carbon Works, Detroit, Michigan.—Specifications: Finely ground No. 431.

Gluten, Wheat—The Pure Gluten Food Co., 90 W. Broadway, New York.—Specifications: Dry Basis.

Ether Extract	1.99
Ash	1.54
Protein	81.08 (equal to 14.22% Nitrogen)
Starch not over	0.11
Crude Fibre	0.40
Nitrogen Free Extract	14.99

Hydrogenated Vegetable Oil—Purchase locally.—Specifications: Crisco.

Linseed Oil Meal—The Garten Feed Co., 515 South Senate Avenue, Indianapolis, Indiana.—Specifications: Old Process Linseed Oil Meal—34% Protein.

Liver—The Wilson Laboratories, 4221 South Western Avenue Blvd., Chicago, Illinois.—Specifications: (1) The kind of liver to be used—hog liver; (2) Liver to be dried in a vacuum of not less than $27^1/_2$" and a circulating temperature of 170° F.; (3) The product is not to be defatted or treated in any way; (4) The product to be ground to about 40 mesh.

Milk Powder, Skim—Milk Powder, Whole—The Borden Company, North Franklin Street, Syracuse, N. Y.—Specifications: A sufficient quantity of these products will be reserved by the Borden Company to meet the needs of all members of the Committee.

Peanut Oil—Welch, Holme & Clark Co., Inc., 563 Greenwich St., New York.—Specifications: Acid less than 0.05%, fire about 665° F., flash about 570, Cold Test about 35°, Saponification number about 190 and iodine number about 89.

Salts—Purchase of any reputable manufacturer.—Specifications: C. P. or U. S. P.

Wheat Flour—Frank T. Caughey, Detroit, Michigan.—Specifications: Ground soft winter wheat—entire kernel—preferably white (ground superfine to pass a 20-mesh sieve or finer). Attention: Mr. Bauman.

Yeast—Northwestern Yeast Company, 1750 North Ashland Avenue, Chicago, Illinois.—Specifications: Pure Dehydrated Yeast—99% must pass through a No. 60 sieve.

Yellow Corn—Frank T. Caughey, Detroit, Michigan.—Specifications: Ground yellow corn—entire kernel (ground superfine to pass at least a 20-mesh sieve). Attention: Mr. Bauman.

Officers American Historical Society.—*President*, Prof. Carl Becker, Cornell University; *First Vice-President*, Prof. Herbert E. Bolton, University of California; *Second Vice-President*, Charles A. Beard, New Milford, Conn.; *Secretary*, Prof. Dexter Perkins, University of Rochester; *Treasurer*, Constantine E. McGuire, Washington.

The next annual meeting will be held in Minneapolis.

INDIA CINCHONA CULTIVATION.

The report of the Bengal Cinchona Department for 1929–1930 indicated an area under cultivation of 2877 acres. The bark harvested in Bengal amounted to 1,130,400 pounds. About 29,000 pounds of crude quinine sulphate, 15,700 pounds of cinchona febrifuge powder and 4350 pounds of cinchona febrifuge tablets were produced. (Vice-Consul Dorsey G. Fisher, Calcutta.)

PHARMACOPŒIAL VITAMIN CONFERENCE.

(ABSTRACTED FROM A REPORT BY CHAIRMAN E. FULLERTON COOK.)

A conference of experts in vitamin investigation was held under the auspices of the U. S. Pharmacopœial Board of Trustees and Revision Committee on Thursday, May 7th, at the Hotel Pennsylvania, New York City. There were present, at the invitation of the Committee of Revision, Dr. Lafayette B. Mendel of Yale, the discoverer of vitamin A; Dr. E. V. McCollum of Johns Hopkins University, the discoverer of vitamin D; Dr. H. C. Sherman of Columbia University, chairman of the American Chemical Society Vitamin Committee and Dr. Alfred B. Hess of New York City, both pioneer investigators in this field. Dr. E. M. Nelson, representing the Food and Drug Administration of the Department of Agriculture; Dr. W. H. Sebrell, of the Public Health Service, National Institute of Health, Washington; Dr. Arthur D. Holmes, Chairman of the A. D. M. A. Vitamin Committee, were also in the conference. The following additional workers were also present:

Dr. C. B. Benjamin, Dr. Charles E. Bills, Dr. Archie Black, Dr. John Dorsey Craig, Dr. Adolph G. De Sanctis, Dr. R. Adams Dutcher, Dr. Walter T. Eddy, Dr. A. D. Emmett, Dr. M. S. Fine, Dr. Arthur D. Holmes, Dr. William J. Horn, Dr. Charles W. Hooper, Dr. James H. Jones, Dr. Robert L. Jones, Dr. Henry T. Mason, Dr. Carl Nielsen, Dr. L. S. Palmer, Dr. H. W. Rhodehamel and Dr. H. C. Sherman.

Chairman E. Fullerton Cook, of the U. S. P. Committee of Revision, presided. Those at the Conference were all members of a Vitamin Committee organized some months ago as an auxiliary Committee of the U. S. P. Revision which includes the following additional workers in vitamin standardization:

Dr. John F. Anderson; Dr. J. H. Burn, Director of the Biological Laboratories, Pharmaceutical Society of Great Britain, London, England; Dr. Harriette Chick, Lister Institute, Chelsea Gardens, S. W. 1; Dr. Katharine H. Coward, Pharmacological Laboratories, Pharmaceutical Society of Great Britain, London, England; Prof. J. C. Drummond, University College, London, England; Mr. C. H. Hamsphire, Secretary, British Pharmacopœia Commission, London; Dr. E. Mellenby, Chairman of Accessory Food Factors Committee (Vitamin) of British Medical Research Council and Chairman of Vitamin Standards Sub-Committee of Biological Standardization of Health Committee of League of Nations, Sheffield, England; Dr. A. Graeme Mitchell, University of Cincinnati; Dr. Earl R. Norris, University of Washington, Seattle; Prof. E. Poulsson, Norway; Dr. Floyd K. Riggs, Rutgers University, New Jersey College of Pharmacy; Dr. Harry Steenbock, University of Wisconsin, Madison, Wisconsin.

Sixteen subjects were discussed. The agreements reached at this meeting will be formulated by an interim committee to consist of Doctors Sherman, Mendel, Nelson, Bills, McCollum, Holmes and Steenbock. This Committee will meet, if possible, before some of the members sail for London to attend the conference called by the Health Organization of the League of Nations and will agree upon a presentation of the conclusions of the American Conference for presentation in London. The London meeting will convene on June 17th and it is known at the present time that Dr. McCollum and Dr. Steenbock will be American delegates, although possibly other members of the Committee may be able to attend.

The international agreements reached at the London Conference will in turn be brought to the attention of the American Committee at another Conference planned for next Fall. Members of the American Conference have already agreed that the decisions of this second American Conference will be given a thorough and practical trial in a number of American laboratories for a period of one year before the conference makes its final recommendations for Pharmacopœial adoption.

When these recommendations are finally presented to the Committee of Revision it is recommended that the Revision Committee publish these as the Pharmacopœial standards, to go into effect within a reasonable time without waiting for the appearance of the U. S. P. XI. This policy of issuing modifications of U. S. P. Standards in the period between revisions is one which is well established and for which there has been ample authority and precedence in all recent revisions. In the U. S. P. X, in the General Principles adopted by the 1920 Convention, is found the following authorization: "It is recommended that the Committee of Revision be authorized to prepare supplements to the Pharmacopœia, or lists of admissions or changes at any time they

may deem such action desirable." The Pharmacopœial Convention of 1930 adopted an exactly identical clause.

Two outstanding difficulties attend the modification of an official standard in the interim period; first of these is *the necessity of the utmost care in the preparation of a new standard* and this is being amply protected in the case of the vitamins. A second difficulty is *the lack of necessary publicity;* the old standards being those always easily available in the printed book, but it is believed that again ample publicity can be secured for a subject so important as the vitamins.

PHARMACEUTICAL SERVICE IN THE U. S. ARMY.

A conference, participated in by officers of the Medical Department of the Army, including Surgeon General Merritte W. Ireland and Colonel Robert U. Patterson,[1] who will succeed General Ireland as Surgeon General when the latter goes on the retired list on May 31st, and representatives of the AMERICAN PHARMACEUTICAL ASSOCIATION, was held in Washington on May 22, 1931.

During recent months, other conferences between the groups have been held with the object of working out legislation, satisfactory to the Army authorities and to the pharmaceutical representatives, for the improvement of the pharmaceutical service in the Army, including the commissioning of pharmacists—as a part of a general plan being developed to improve the Medical Department. It has been agreed that improvement and extension of the pharmaceutical service in the Army is essential to such a plan. The question still open is how this can best be done to accord with the military organization and the views of pharmacy.

The recent conference was for a further consideration of this question and also to acquaint Colonel Patterson with the progress already made toward agreement between the two groups.

A complete report of these conferences will be made by the Committee on Pharmacy Corps in the U. S. Army at the Miami meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION which will be attended by Colonel A. D. Tuttle as the representative of the Medical Department and of the Surgeon General.

Colonel Tuttle will discuss the legislation now pending before Congress for improving and extending the pharmaceutical service in the Army and will explain the plans which the Medical Department considers as essential to effective military operation from the standpoint of experience with the public health professions in the Army. Colonel Tuttle has taken great interest in these plans and is well qualified by professional training and army experience to discuss them from the military and professional points of view.

[1] Now in office.

NETHERLANDS INCREASES IMPORTS OF QUININE AND QUININE SALTS FROM JAVA AND MADURA.

Exports of quinine and quinine salts from Java and Madura to the Netherlands have doubled during the last three years. According to statistics of the two islands, 30 metric tons went to the Netherlands, as compared with 20 tons in 1929, and 15 tons in 1928. China purchased an average of 11 tons annually, while exports to Japan decreased to 3 tons in 1930, as against 5 tons in 1929, and 11 tons in 1928. British India bought about 3 tons yearly during the above period. (Trade Commissioner Richard P. Hendren, Batavia.)

CINCHONA EXPERIMENTATION IN PHILIPPINES.

The Philippine Bureau of Forestry has been experimenting with the production of cinchona on a small scale in the Province of Bukidnon, Mindanao, for a number of years. On March 27th, on recommendation of the Malaria Control Board, Acting Governor-General Butte approved an appropriation of $7500 annually to be used by the Director of the Bureau of Forestry in the furtherance of this work. Information from Forestry officials is to the effect that 12,000 trees are now growing successfully and that 50,000 cuttings are ready for planting. (Trade Commissioner E. D. Hester, Manila.)