EDITORIAL

E. G. EBERLE, EDITOR EMERITUS. 2215 Constitution Ave., WASHINGTON, D. C.

THE EXCISE TAX ON DISTILLED SPIRITS.—H. R. 6068.

DURING the last annual meetings of the AMERICAN PHARMACEUTICAL ASSOCIATION and the National Association of Retail Druggists, similar resolutions were adopted urging "the Federal and state governments to remove any excise tax from ethyl alcohol used in bona fide medicinal substances with such safeguards and penalties against abuse as may be necessary, in order that the cost of these to the sick may be more reasonable." Other organizations have since endorsed the proposal.

In the December, 1938, issue of the JOURNAL, reference was made to a hearing before the Undersecretary of the Treasury, John N. Hanes, in Washington, on November 10th.

Although it does not propose to eliminate the tax, it is encouraging to report that Mr. Knutson of Minnesota introduced into the House of Representatives, on May 1, 1939, the following bill, H. R. 6068, which was referred to the Committee on Ways and Means of which he is a member:

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That section 710 of the Revenue Act of 1938 (relating to the tax on distilled spirits) is amended by adding at the end thereof the following new subsection:

"(*f*) Provided, That upon all ethyl alcohol withdrawn and used for other than beverage purposes, the tax shall be $1.10 per proof gallon."—E. F. K.

INTERNATIONAL CONGRESS OF MILITARY MEDICINE AND PHARMACY.

THE TENTH CONGRESS and the first one to be held in the United States was convened in Washington, D. C., on May 7th and met there until May 15th, with a number of trips to places of interest. The sessions of the Congress were then transferred to New York where they were completed on May 19th with an official banquet. Surgeon General C. R. Reynolds, U. S. Army, served as president of the Congress.

In addition to the general business of the Congress which meets each two years, and a number of Scientific Programs, the following seven questions will be considered at separate meetings; the Organization and Function of the Medical Services in Colonial Expeditions; Probable Casualties in War and Methods of Calculation; Practical Procedures in Anesthesia and Analgesia in War Surgery; Organization and Function of the Military Chemico-Pharmaceutical Service; Emergency Treatment and Primary Apparatus for Fractures of the Jaws in War; Technical Specialization of Administrative Officers in the Medical Service; Oxygen Therapy and Its Practical Use with Troops on Active Duty.

The delegates will spend some time in sight-seeing, attending various social functions and in visiting the many medical facilities in and around Washington.

A number of delegates representing Pharmacy and Pharmaceutical Chemistry will attend and it is encouraging that Pharmacy has been given greater recognition in the Medical Department of the Army in advance of this important International Congress.

Dr. E. N. Gathercoal, former president of the ASSOCIATION, served as an honorary vice-president of the Congress.—E. F. K.

HOW MANY PRESCRIPTIONS TO A PATIENT?

EVERY PHARMACIST should be interested in the answer, but the answer cannot be forthcoming unless you help make it possible. Will you, therefore, as a retail pharmacist, do this for your own benefit as well as for retail Pharmacy in general? Please assign some one to the compiling of the following very simple record (which record when sent in will be combined with others from all states of the union for a national summary).

(1) The total number of new prescriptions compounded during June 1939. (2) How many patients presented one new prescription for compounding? (3) How many customers presented two new prescriptions for compounding? (4) How many customers presented more than two new prescriptions for compounding?

This report should clearly indicate the city and state in which it was made and must be signed. The identity of the store will be kept secret.

Will you also please make a second report which will help answer the question, "Is the Nature of Prescriptions Changing?" This second report can be made at the same time the first report is being compiled. It should be arranged in four parts, each part headed with one of the following captions:

(1) One ingredient prescriptions—nonproprietary; (2) One ingredient prescriptions—proprietary (a brand or trade name product); (3) Several ingredient prescriptions—nonproprietary; (4) Several ingredient prescriptions—proprietary; (5) Several ingredient prescriptions—mixture.

These reports, coming from several cities in each state, should provide an excellent sampling of the national practice which, if it is not now the local practice, will soon become such. Each pharmacist should therefore be interested in the answer to the questions asked.

The month of June has been selected for two reasons. *First*, the reports will be made under like conditions, and *second*, will if mailed in immediately at the close of the month allow enough time for summarization into a report that can be presented at the annual convention next August in Atlanta.

Don't leave this very simple task "to some other pharmacist." It is your chance to help Pharmacy as well as yourself. Don't miss it.

These reports should be addressed to Prof. J. H. Goodness, Massachusetts College of Pharmacy, Boston, Mass. Should you wish, a penny postcard addressed to Professor Goodness will bring you mimeograph sheets with columns arranged to record the information for both reports.—E. F. K.

Papers to be submitted at the Atlanta meeting should be forwarded to the Secretary of the appropriate Section.

REFERENCE STANDARD AND ASSAY FOR THIAMIN CHLORIDE OR VITAMIN B_1.

The Sub-Committee on Scope in 1932 recommended the admission of Dried Yeast to the U. S. P. XI provided a suitable biological assay method could be provided for the standardization of its anti-pellagra activity. The U. S. P. Vitamin Advisory Board immediately undertook this study but were unable to offer such a test and yeast was not admitted to the new Pharmacopœia.

In the meanwhile, however, the vitamin B_1 factor of the vitamin B complex in yeast became increasingly important and the Vitamin Board was asked by the American Medical Association and by manufacturers to provide a Reference Standard for vitamin B_1 and also an assay method which could be endorsed by the Board.

In the initial study which required more than a year and involved many biological assays and a comparison of rat-growth, rat-maintenance, rat-curative and pigeon-curative methods as proposed by various authorities and with the coöperation of about twenty-five laboratories, the Vitamin Board decided upon the restriction of further studies to the rat-curative method. In the meanwhile the U. S. P. Board of Trustees, with the help of the Vitamin Board had provided a U. S. P. Reference Standard for vitamin B_1 for use in this country.

This U. S. P. Standard was identical with the International adsorbate standard and was prepared and standardized by Dr. C. P. Jansen of Amsterdam.

By this time crystalline vitamin B_1 had been synthesized by Dr. R. R. Williams and it became apparent that this definite chemical substance would ultimately replace the adsorbate as the vitamin B_1 standard. The Vitamin Board therefore immediately added to its investigation the potency of pure synthetic crystalline vitamin B_1 in terms of International Units and the same group of laboratories undertook the comparison of four suggested rat-curative assay methods. At the same time the comparative potency of the International standard and the crystalline material was determined. The Board of Trustees authorized the procuring of a considerable quantity of the synthetic crystalline vitamin B_1 from two independent sources and this was mixed, dissolved, recrystallized and packaged.

In the subsequent biologic tests by sixteen laboratories the majority of workers and also the U. S. P. Board decided upon the adoption for Pharmacopœial purposes of one of the methods being tried and also determined that the potency of the crystalline vitamin B_1, prepared for use as the new U. S. P. Reference Standard, was equivalent to 333 units in each mg. corresponding to 3 micrograms (3γ) = 1 International or U. S. P. Unit.

At approximately the same date the Biological Committee of the Health Organization of the League of Nations, who had been making similar tests announced the same value for the new International vitamin B_1 standard.

The following announcement was made by the League of Nations Committee.

"The International Conference on Vitamin Standardization, at its 1934 meeting, recommended that the potency of the existing vitamin B_1 standard, the standard adsorption product, 'should be tested relatively to that of the crystalline vitamin B_1 preparations then available with the aim of ultimately adopting pure crystalline vitamin B_1 as international standard.' During the past two years, this possibility has been brought nearer by the discovery, almost simultaneously in three different countries of methods for production of the pure vitamin by synthetic processes.

"Through the good offices of Sir Henry Dale, 70 Gm. of synthetic vitamin B_1 hydrochloride were generously provided by the following four firms: Messrs. Merck and Company, Rahway, N. J.; Messrs. E. Merck, Darmstadt; Messrs. F. Hoffmann-La Roche, Basle; and Messrs. I. G. Farbenindustrie, Elberfeld. The samples were mixed and the whole recrystallized by Dr. A. R. Todd at the Lister Institute. The final sample, 55 Gm., gave satisfactory criteria for purity as follows:

"*Vitamin B_1 (aneurin) hydrochloride:* Colorless monoclinic plates m. p. 246–247° (de comp.). *Picrate:* Yellow needles, m. p. 208° (decomp.). *Picrolonate:* Dimorphous, (*a*) Yellow needles, m. p. 165° (decomp.). (*b*) Yellow prisms, m. p. 226° (decomp.).

"Specimens of this material and of the present acid clay standard were distributed from the National Institute for Medical Research to twenty-two laboratories for examination and biological and chemical determination of the potency of the crystalline vitamin in terms of the present standard. Seventeen reports have been received, comprising thirty-one separate comparative experiments."

The new U. S. P. crystalline vitamin B_1 Reference Standard therefore is available now for research or for use in the standardization of vitamin B_1 preparations and may be obtained through the office of the Chairman of the Committee of Revision, at 43rd and Woodland Ave., Philadelphia, Pa.

The following instruction for use has been provided by the Vitamin Advisory Board.

SUGGESTIONS FOR USING THE U. S. P. REFERENCE STANDARD FOR VITAMIN B_1 (THIAMIN CHLORIDE).

Before preparing a solution dry the standard crystalline vitamin B_1 to constant weight in a desiccator over phosphorous pentoxide.

Precautions to Be Taken in the Preparation of Solutions.—The pure vitamin B_1 hydrochloride, if completely desiccated by exposure to vacuum at a high temperature, is very hygroscopic. In the form adopted for the standard preparation, containing approximately 1 molecule of water of crystallization, it is much less hygroscopic, but still gains weight if exposed to ordinary, moist air. It is preferable, therefore, to transfer the quantity required for a test to a small glass-stoppered weighing bottle, in which it can then be weighed on a microbalance, or an ordinary balance, according to the number of tests for which the sample is being taken. Even without such precautions, however, exposure to the air during weighing will not cause an increase in weight of more than about 0.6 per cent, if the operations are completed within five minutes.

Neutral and alkaline solutions of the standard are unstable, and aqueous acid solutions are readily infected by molds, which inactivate the vitamin. It is recommended, therefore, that stock solutions ($^1/_2$ mg. per cc. is a convenient strength) should be prepared in 25 per cent, aqueous ethyl alcohol to which hydrochloric acid is added to make the solution approximately $N/500$ HCl. This solution is stable if kept at about 4° C. Solutions of suitable strength for animal dosage (20 to 100 micrograms per cc.) must be made at least twice weekly from the stock solution by dilution with distilled water. Such dilutions must be kept at a low temperature and examined daily for molds.

The details of the bio-assay method proposed for inclusion in the Second U. S. P. XI Supplement are as follows:

BIO-ASSAY FOR DETERMINING THE POTENCY OF VITAMIN B_1.

Method of Assay for Thiamin Chloride (Vitamin B_1).

The assay of U. S. P. products for vitamin B_1 potency shall be by comparison with the U. S. P. vitamin B_1 Reference Standard, by assay procedure conforming in all respects to the following specifications:

The vitamin B_1 assay, comprising the recording of observations of rats throughout specified periods of their lives while being maintained on specified dietary regimens and the interpretation of such data, is as follows:

Preliminary Period.—Throughout the preliminary period each rat shall be raised under the immediate supervision of, or according to directions specified by, the assayer. Throughout the preliminary period the rats shall be maintained on a dietary regimen which shall provide for normal development in all respects, except that the vitamin B_1 intake may be restricted.

Depletion Period.—A rat shall be suitable for the depletion period when the age of the rat does not exceed thirty (30) days, and if the body weight of the rat does not exceed 50 Gm. and if the animal manifests no evidence of injury or disease or anatomical abnormality which might hinder growth and development. Throughout the depletion period each rat shall be provided with the vitamin B_1 test diet and water (U. S. P.) ad libitum, and during this period no other dietary supplement shall be available to the animal. Throughout the depletion period and until the assay shall have been completed the rats shall be kept in cages provided with a wire cloth bottom, each mesh of which shall be not less than $^1/_3$ inch.

Assay Period.—A rat shall be suitable for the assay period provided that the depletion period shall not have exceeded 75 days, and provided that the rat shall manifest evidence of vitamin B_1 deficiency characterized by acute polyneuritis. Throughout the assay period each rat shall be kept in an individual cage and provided with the vitamin B_1 test diet compounded from the same lots of ingredients, and water (U. S. P.) ad libitum. On the day beginning the assay period there

shall be administered to each rat a single dose of the reference standard of such size that it will produce in individual animals a curative period of not less than 5 days and not more than 15 days. All of the rats used in any one assay shall receive the same quantity of the reference standard. Each rat shall then be observed for the cure of and recurrence of polyneuritis, and when polyneuritis reaches the same acute stage observed when the reference standard was administered, a single dose of the assay product shall be administered. The animals shall then be observed to determine if polyneuritis is cured, and if so, observation shall be made of the duration of the period. Each assay shall include successive administrations of the reference standard and assay product to not less than eight rats. The assay product may be administered orally or parenterally but in any one assay the reference standard shall be administered in the same manner as the assay product, and the quantity of the assay product administered to each rat shall be the same.

Recording of Data.—On the day beginning the depletion period and at intervals of not more than seven (7) days during the depletion period, a record shall be made of the body weight of each rat. On about the twenty-fifth (25) day and each day thereafter for the remainder of the depletion period, each rat shall be observed for symptoms of polyneuritis. The following dates shall be recorded:

1. The day on which the reference standard is administered.
2. The day on which cure of polyneuritis is observed following the administration of the reference standard.
3. The day on which acute polyneuritis recurs and the assay product is fed.
4. The day on which cure of polyneuritis is observed following the administration of the assay product.
5. The day on which acute polyneuritis recurs after the administration of the assay product.

Vitamin B_1 Potency of the Assay Product.—In determining the vitamin B_1 potency of the assay product the duration of the curative period following the administration of the reference standard and the assay product shall be considered. The dose of assay product administered contains an amount of vitamin B_1 equal to or greater than that contained in the dose of the reference standard administered if that quantity promotes in the assay animals a total curative period (the sum of the number of days of the curative period of each of the animals) equal to or greater than the total curative period produced by administration of the reference standard.

Definitions.—As used herein, unless the context otherwise indicates the term "acute polyneuritis" means that stage of vitamin B_1 deficiency in which the animal regains control of the voluntary muscles, as evidenced by standing or walking, a few seconds after extreme muscular contraction, which has been induced by twirling the rat by its tail. (Onset of acute polyneuritis is invariably accompanied by loss in body weight); the term "assay period" means the interval in the life of a rat between the last day of the depletion period and the final observation following the administration of the assay product; the term "assay product" means a product under examination for its vitamin B_1 potency; the term "curative period" is the interval of time between the administration of vitamin B_1 and the subsequent recurrence of acute polyneuritis after a complete disappearance of polyneuritic symptoms, and the duration of the curative period is expressed as the number of days in that interval; the term "cure of polyneuritis" means the complete disappearance of polyneuritic symptoms and is invariably accompanied by increase in body weight; the term "depletion period" means the interval in the life of a rat during which its food intake is only the vitamin B_1 test diet and water (U. S. P.); the term "preliminary period" means the interval in the life of a rat prior to the depletion period; the term "reference standard" means the U. S. P. vitamin B_1 reference standard, distributed by the Board of Trustees of the U. S. Pharmacopœial Convention, and which contains one U. S. P. unit of vitamin B_1 in each 3 micrograms; the term "vitamin B_1 test diet" means a uniform mixture which has not been compounded for more than seven (7) days of the following food materials and in the proportions designated:

VITAMIN B_1 TEST DIET.

Sucrose	60.25 per cent
Casein (1)	18.00 per cent
Salt mixture (2)	4.00 per cent

Autoclaved yeast (3)	5.00 per cent
Autoclaved peanuts (4)	10.00 per cent
Purified liver extract (5)	0.75 per cent
Cod liver oil (U. S. P.)	2.00 per cent

(1) The casein shall be free from demonstrable traces of vitamin B_1.

(2) The salt mixture shall be either salt mixture No. 1, described on page 479,* or a salt mixture having essentially the same proportions of the elements.

(3) Dried yeast which has been autoclaved in steam at 15 pounds pressure for 5 hours with the yeast spread in a layer not more than $^1/_4$ inch in depth and then dried at a temperature not exceeding 65° C.

(4) Unroasted shelled No. 1 grade Virginia peanuts are crushed in a food chopper, autoclaved in steam at 15 pounds pressure for 5 hours with the ground peanuts spread in a layer not more than $^1/_2$ inch in depth, and then dried at a temperature not exceeding 65° C. This preparation may be incorporated in the basal diet by grinding with the requisite quantity of sucrose.

(5) One hundred grams of Extract of Liver, U. S. P., are dissolved in 200 cc. of water. One thousand cubic centimeters of 95 per cent ethyl alcohol, followed by 1200 cc. of ethyl ether, are added with constant stirring. After precipitation is complete (usually five to fifteen minutes) the material is filtered through paper, reasonable care being taken to prevent loss of ether. The residue is redissolved in 200 cc. of water and precipitation and filtration are repeated as above. The solution of the residue and precipitation is repeated a third time. The final residue, after drying at a temperature not exceeding 65° C., constitutes the purified liver extract. Drying may be facilitated by evaporating a water solution of the final residue on a small quantity of vitamin B_1-free casein. One hundred grams of Extract of Liver, U. S. P., will yield approximately 75 Gm. of purified liver extract.

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It is further expected that synthetic crystalline vitamin B_1, under the title Thiamin Chloride will become official in the Second U. S. P. XI Supplement but no bio-assay will be required for the pure chemical since the physical and chemical tests available will adequately control its quality and if it meets these specifications it is believed that its therapeutic activity will be uniform.

E. FULLERTON COOK,
Chairman of the Committee of Revision of the U. S. Pharmacopœia.

Released April 17, 1939.

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE. PROGRAM OF PHARMACY SUB-SECTION N-2 OF THE MEDICAL SCIENCES SECTION.

A SYMPOSIUM ON THE VITAMINS WITH PARTICULAR REFERENCE TO THEIR STANDARDIZATION.

Tuesday, June 20th, 10:00 A.M. (first session).

The Vitamin B Complex

1. Vitamin B_1, Thiamin, by Aaron Arnold, Ph.D. (30 minutes).
2. Riboflavin, by P. H. Phillips, Ph.D.(30 minutes).
3. Nicotinic Acid, by C. A. Elvehjem, Ph.D. (30 minutes).

Tuesday, June 20th, 2:00 P.M.

4. Chick Antidermatitis Factor and Vitamin B_6, by W. D. Woolley, Ph.D. (30 minutes).
5. Vitamin A, by A. Black, Ph.D. (30 minutes).
6. Vitamin E, Mrs. F. P. Dann (30 minutes).

GLENN L. JENKINS, *Chairman Program Committee.*

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* U. S. P. XI.