mixture until the zinc is completely precipitated. After allowing it to stand for about one hour, filter the precipitated zinc sulfide and wash it a few times with water containing a little ammonium sulfide. Dissolve the precipitate of zinc sulfide from the filter by pouring over the edges of the filter hot diluted hydrochloric acid in small portions at a time. Wash the filter thoroughly with small quantities of hot distilled water, receiving the filtrate and washings in a tared porcelain dish. Evaporate the filtrate on the water-bath to about 2 cc. then add to it 3 Gm. of yellow mercuric oxide, previously mixed with about 15 cc. of distilled water. Evaporate the mixture to dryness and carefully ignite the residue under a hood to constant weight. The weight of the zinc oxide thus obtained, corrected for any non-volatile matter contained in 3 Gm. of the mercuric oxide, corresponds to not less than 19 per cent and to not more than 21 per cent of the weight of the Ointment taken for the assay.

REPORT ON THE UNITED STATES PHARMACOPŒIA, ELEVENTH REVISION.*

BY E. FULLERTON COOK, CHAIRMAN OF THE U. S. PHARMACOPŒIA COMMITTEE, ELEVENTH REVISION.

The work of revision upon the U. S. P. XI of necessity must soon come to a conclusion if the new Pharmacopœia is to appear within a reasonable time. The galley proofs, after an exacting review by the members of the Revision Committee, and the insertion of many alterations, have been sent back to the printer for issuance as page proof. While it will be necessary to make a few additional changes, these cannot be of a drastic character, since page proof, when once made up, does not permit of extensive revision.

This means that admissions and deletions are settled for this printing, although the Convention has authorized the admission of new titles, should this prove desirable, through the issuance of "Supplements."

The question of "Scope" always will be one of the major problems of the Revision. Members of the Sub-Committee responsible for these decisions have most earnestly and conscientiously studied this problem. Their deliberations cover about 500 pages of Bulletins, and, in a number of instances, they have called for information and advice from the Sub-Committee on Therapeutics, in which Committee's Bulletins will be found many more pages of discussion.

The Sub-Committee on Scope has proceeded on well-defined principles. Its objective has been to include as official in the Pharmacopœia, a comprehensive and dependable list of therapeutic agents meeting most of the needs of the medical profession. Insulin will be a striking example of omission, for, though approved, it could not be admitted due to its control by patent. As soon as this expires, it will promptly be admitted by the Supplement route.

The newly admitted substances are as follows:

ARTICLES ADDED TO THE U. S. P. XI.

Acriflavina	Ephedrina
Acriflavinæ Hydrochloridum	Ephedrinæ Hydrochloridum
Æthylenum	Ephedrinæ Sulfas
Æthylhydrocuprinæ Hydrochloridum	Erythrol Tetranitrate
Æthylis Oxidum	Extractum Hepatis
Antitoxinum Scarlatinæ Streptococcicum	Ferri et Ammonii Citrates Virides
Bismuthi et Potassii Tartras	Fluoresceinum Solubile
Calcii Creosotas	Histaminæ Phosphas
Calcii Gluconas	Hydrargyri Succinimidum
Calcii Hydroxidum	Iodophthaleinum Solubile
Carbo Activatus	Liquor Ergosterolis Irradiati
Carbonii Dioxidum	Liquor Hepatis
Chlorobutanol	Liquor Hepatis Purificatus
Digitalis Pulverata	Liquor Histaminæ Phosphatis
Emulsum Petrolati Liquidum	Liquor Parathyroidei

* Read at the 1935, A. PH. A. meeting, Portland, Oregon.

Liquor Sodii Hypochloritis
Merbaphenum
Neocinchophenum
Oleum Iodatum
Oleum Maydis
Oleum Morrhuæ Non-Destearinatum
Oleum Rosæ
Phenacainæ Hydrochloridum
Phenobarbitalum Solubile
Pulvis Chiniofoni
Serum Antimeningococcicum
Serum Antipneumococcicum
Sodii Perboras
Sodii Stearas
Stomachus
Tabellæ Glycerylis Trinitratis
Theophyllina cum Æthylenediamina
Theophyllina et Sodii Acetas
Tinctura Iodi Mitis
Toxinum Diphthericum Detoxificatum
Toxinum Diphthericum Diagnosticum
Toxinum Scarlatinæ Streptococcicum
Toxitabellæ Hydrargyri Bichloridi Parvæ
Tryparsamidum
Tuberculinum Pristinum
Vaccinum Rabies
Vaccinum Typhosum
Vaccinum Typhosum Paratyphosum

Interim Revisions.—There has been an increasing recognition within the past few years that decennial revisions were not adequate for official standards; that the U. S. P. policy of a ten-year change in the official requirements and scope greatly lessened the usefulness of the Pharmacopœia, and, in fact, established some standards which soon became inaccurate or incapable of enforcement due to advances in scientific knowledge.

This was strikingly true of products standardized by biological methods in which field tremendous strides were being made, but other influences such as new legislation, increased Governmental enforcement, and the introduction of new therapeutic agents all combined to force the issuance of supplements which became known as "Interim Revision Announcements."

There can be little doubt that if the Pharmacopœia of the future is adequately to serve the medical and pharmaceutical professions and to provide correct standards for governmental enforcement, that this policy will have to be continued and perhaps extended. One suggestion has been the issuance of an "annual supplement" but only time can determine the form which added titles and revised standards shall take to most effectively meet the changing and developing need for standards in medicinal products.

Fortunately the authority has been provided and the Revision Committee was prepared to meet the unusual situations of the past two years and thus prove that the revision machinery was sufficiently flexible and fully qualified to meet these new problems as they have arisen.

Vitamin and Anti-anemia Advisory Boards.—Among recent problems has been the necessity for the Pharmacopœia to assist in establishing standards for important new medicinal products. Here again the unique position of the Pharmacopœia has been demonstrated.

In the field of vitamins, the Committee by investigation has been able to bring into conference outstanding specialists in this field. The group includes those dealing with the subject as a pure science, mostly in University or Scientific Research, then the experts in Government laboratories, and, in addition, the technical experts associated with commercial organizations.

This group, coming together under Pharmacopœial auspices, sitting about one table, with their discussions reported in full and published, made it possible to establish a balanced judgment, eliminate special interests and reach wise decisions which ultimately were reflected in new U. S. P. standards for Cod Liver Oil.

To direct this program, the U. S. P. Vitamin Advisory Board has been established, having as members Doctors Mendel, Sherman and Nelson and a representative of the U. S. P. Board of Trustees and of the Committee of Revision. This Board is now directing an extensive study, with 26 laboratories participating, into methods of assaying vitamin B_1. A recent necessity for pharmacopœial standardization has been the newly admitted preparations for the treatment of pernicious anemia. To meet this need a new Board of experts in this field is being established. This Board will announce methods of assay and will evaluate clinical reports upon products which have been given official recognition.

Reference Standards.—It has become necessary for pharmacopœial authorities to establish and distribute certain reference standards for use as a basis of comparison in assays. This becomes a new function for the Pharmacopœia, although a similar service was rendered by the Food and Drug Administration during the past decade.

Among the reference standards will be the "Reference Cod Liver Oil" of known vitamin A and vitamin D potency, expressed in U. S. P. vitamin units; a "Reference Digitalis Powder" of known activity, expressed in terms of U. S. P. digitalis units; a "Reference Pepsin," having a proteolitic activity equivalent to 3000 times its weight of egg albumen; also the standard for Ergot, Ergotoxine Ethanesulfonate and perhaps several others.

Digitalis.—As already indicated, the potency of this drug and the two official preparations, the "Standardized Powder" and the "Tincture," will be expressed in terms of U. S. P. digitalis units. This U. S. P. unit is identical in potency with the International Digitalis Unit which is the activity of 0.1 Gm. of the International Standard Digitalis Powder. The potency of the official digitalis leaf shall be such that 0.1 Gm. shall possess an activity equivalent to not less than 1 U. S. P. digitalis unit.

Under the title for this drug will be found the statement "When digitalis is prescribed, 'Digitalis Pulverata' is to be dispensed." Under the title "Digitalis Pulverata" or "Powdered Digitalis" it is required that 0.1 Gm. shall possess an activity equivalent to not less than 1 and not more than 1.1 U. S. P. digitalis units, when assayed as directed under the Tincture.

In the Tincture of Digitalis the potency of 1 cc. is to be the equivalent of not less than 1 and not more than 1.1 U. S. P. digitalis units, in other words one-tenth of the strength of the powdered drug. And here will be found the details of the assay which retains the one-hour frog method. While a 10 per cent range of potency is indicated in the statement of standards, in both the powder and the tincture, at the end of the assay a tolerance is provided which states that owing to many variable factors in the assay which makes it difficult for different operators to obtain identical results, evidences of potency within 20 per cent above or 20 per cent below the standard are accepted.

The frog method of assay has been retained, since the Sub-Committee was not convinced of the superiority of any other method. An extensive investigation has been started, however, with clinical coöperation and to be participated in by the British Pharmacopœial Commission, in which a number of methods of assay will be compared on preparations distributed by the pharmacopœial committee and the investigation will include a comparison of the various assay methods and clinical results from the use of digitalis preparations which have been aged. When this study is completed it is expected that we shall have reliable evidence on many of the controversial points in digitalis assay.

Ergot.—Here again uncertainty prevails, notwithstanding the recent extensive studies concerning ergot constituents. Apparently no better assay than the cockscomb method, for determining the fact that the Fluidextract is potent, has been presented, at least the present state of knowledge is such that the question is still in flux. The Fluidextract, however, is to be prepared from drug of prime quality, by the Type C Method, without heat, and 1000 cc. is to be made from 1000 Gm. of drug. There is to be no subsequent adjustment of volume but the product must have a known minimum potency, per cubic centimeter, equivalent to that of not less than 0.5 mg. of ergotoxine ethanesulfonate—but no upper limit.

Should a Fluidextract fail to meet this standard it would indicate a product which was not official even though it could be shown to possess some potency by another type of assay but which probably evaluated a different constituent.

Sulfur vs. Sulphur.—"Sulfur" or words derived from sulfur, such as sulfite, sulfate, thiosulfate, etc., all will be spelled with an "f" in place of the "ph" in the new Pharmacopœia.

Tincture of Ginger.—Only recently it has been found practically necessary to omit Tincture of Ginger from the Pharmacopœia. This is due to the action by the Internal Revenue Bureau which places it in the same status as alcoholic liquors. As now regulated, this tincture can be prepared only by one holding a permit to make it and having a rectifier's license. It could then be sold and kept only in the original container which had the license number of the rectifier blown in the glass of the bottle.

Inasmuch as no rectifier has taken out a license to manufacture it, there is no legal Tincture of Ginger available to-day in the United States. Anyone having it in stock or making it by the official method is subject to severe penalties.

The Fluidextract will be retained and is directed in the formula for Aromatic Sulfuric Acid and will be available for therapeutic use when needed.

Distilled Water.—"Distilled Water" has replaced "Water" in the formulas of the Pharma-

copœia. This is in conformity with the practice of practically all pharmacopœias of the world and was adopted only after a wide survey of the water supplies in many parts of the country indicated that the available water in many communities was unfit for use in medicinal products. This fact, of course, had been generally recognized and careful pharmacists and manufacturing pharmacists have long been using nothing but distilled water in medicinal solutions and preparations.

Activated Charcoal.—U. S. P. X Wood Charcoal is being replaced by an "Activated Charcoal" which is required by test to have adsorbent qualities of a high order to insure superior therapeutic efficiency. By one test a methylene blue solution must be decolorized, by another test strychnine sulfate is adsorbed from solution while by a third test hydrogen sulfide gas is adsorbed. The U. S. P. will state that when Carbo Ligni is prescribed Carbo Activatus may be dispensed.

Solution of Potassium Arsenite.—Fowler's Solution has been modified so as to have only a slight alkalinity and the Compound Tincture of Lavender has been replaced by alcohol, thus making a colorless solution. This simplification of the formula is in harmony with scientific improvement. The old solution was simply an imitation of one of the oldest known proprietary medicines. The pharmacist and the doctor must, however, know of changes of this type as soon as possible.

Solution of Sodium Hypochlorite (4 Per Cent).—This solution has replaced Chlorinated Lime in the preparation of Dakin's Solution and also can be used advantageously as a disinfectant and deodorant in those cases where chlorinated lime was formerly employed.

A solution of this type is now widely used in the home and is readily available at small cost but usually under a trade-marked name. It should now be made available under the official title.

Solution of Magnesium Citrate.—The U. S. P. IX formula has been adopted with 33 Gm. of citric acid instead of 35 Gm. This reduction in acid is satisfactory when the Magnesium Carbonate used does not contain the equivalent of Magnesium Oxide in the maximum amount permitted. In fact, precipitation on long standing will occur unless the oxide equivalent is controlled at the lower limit. A note is introduced suggesting that for greater stability the amount of Magnesium Carbonate taken shall be the equivalent of 15 Gm. of 39.2 per cent oxide. If the oxide equivalent of the carbonate is stated on the package, this adjustment is readily possible. Sterilization is also suggested as a means of improving the stability of the solution.

Variations Permitted.—The new Pharmacopœia will specifically authorize variations in a few products. A blanket clause provides for the increase or decrease in the degree of consistence in ointments, but without altering the character or percentage of medication or the nature of the fatty vehicle. This is to meet varying climatic conditions.

In the Emulsions of Cod Liver Oil and of Liquid Petrolatum, other emulsifying agents are permitted, provided the general character of the finished product is not changed.

In some cases, as under Syrup of Ferrous Iodide, where there are standards, tests and assay, a formula is given but this is preceded by a statement, such as, "Syrup of Ferrous Iodide may be prepared by the following formula." This is in harmony with the principle that when adequate tests are provided for chemical substances, the chemical process may be varied if the resulting products are identical.

Color Standards.—The permissible intensity of color in Cod Liver Oil, and the degree of color permitted under many chemicals when subjected to the action of sulfuric acid, are now controlled by comparison with color standards. These color standards are those proposed by Professor Arny and his associates many years ago and the various "matching fluids," as they are officially termed, are prepared by mixing specific proportions of standard colorimetric solutions of cobaltous chloride, ferric chloride and cupric sulfate. This is an important advance and removes the uncertainty of meaning always introduced by descriptive color terms for which there is no color standard.

Reagents.—It will be of interest to chemists to know that the Pharmacopœia has elaborated many of the texts for reagents, bringing them in most instances into harmony with standards established by the American Chemical Society.

Coöperation.—The spirit of coöperation and the enormous amount of time-consuming labor from members of the Revision Committee and also from volunteers is perhaps unparalleled in work of a similar character elsewhere.

It is this interest from members of the pharmaceutical and medical professions which makes possible so unique a program as that which established our Pharmacopœia and which now main-

tains its prestige among similar publications. The unselfish and scientific character of pharmacopœial work must be maintained if Pharmacy is to merit this rich heritage, and our generation must look well to the spirit with which we approach the forthcoming Pharmacopœial Convention. The eyes of the coöperating scientific world are upon us and we who love our profession must zealously guard the essential standards.

With the limited time allotted for this presentation it is possible to touch only a few outstanding features of the revision. Detailed changes, in abstract, in many departments are being published in the A. PH. A. JOURNAL during the next two months and will provide an opportunity for many to obtain information concerning the changes.

THE TESTS FOR REDISTILLED WATER IN THE NATIONAL FORMULARY VI MONOGRAPH.*

BY R. S. ADAMSON, R. K. SNYDER, E. N. GATHERCOAL.

The tests in the N. F. VI monograph for redistilled water are as follows:

Tests for Purity.—Evaporate 100 cc. of Redistilled Water to dryness on a water-bath, and subsequently dry the residue in an oven to constant weight at 100° C.: not more than 0.0005 Gm. of *residue* remains.

Separate portions of 10 cc. each of Redistilled Water are not affected by the addition of barium chloride T.S. (*sulfate*); silver nitrate T.S. (*chloride*); ammonium oxalate T.S. (*calcium*); hydrogen sulfide T.S. (*metals*).

Redistilled Water shows not more than a faint yellow color when 0.1 cc. of alkaline mercuric potassium iodide T.S. is added to a 100-cc. potion (*ammonia*).

Add 10 cc. of calcium hydroxide T.S. to 5 cc. of Redistilled Water: the mixture remains clear and transparent (*carbon dioxide*).

Heat 100 cc. of Redistilled Water to boiling, acidulate with 10 cc. of diluted sulfuric acid, and subsequently add 0.1 cc. of twentieth-normal potassium permanganate: the color of the liquid is not completely destroyed by boiling for 10 minutes (*oxidizable substances*).

Test for Sterility.—Follow the general methods given on pages 24 to 26 for the Testing of Ampul Solutions for Sterility. If the sample to be examined is in a bulk package, follow Section D; plant 10 fermentation tubes with 1 cc. of the sample in each: if growth appears in any of the fermentation tubes, the test may be repeated. If growth appears in any of the second lot of fermentation tubes, the water in the bulk package shall not be used in any product intended for parenteral use. If the sample to be examined is taken from ampuls, follow Section E; if growth appears in any of the fermentation tubes planted, the test may be repeated. If growth appears in any of the second lot of fermentation tubes planted, the whole lot of ampuls shall be discarded.

QUANTITY OF WATER REQUIRED FOR THE TESTS.

Considerable objection has been raised to the use of a large quantity of Redistilled Water (when in ampuls) for making the tests for purity. In U. S. P. X, about 725 cc. of distilled water is required to make the purity tests. Therefore, in the redistilled water monograph, the 100 cc. quantities have been reduced to 10 cc. for the tests for *sulfate*, *chloride*, *calcium* and *metals*, and a 5-cc. quantity for *carbon dioxide*. The 100-cc. quantities are retained for determining the *residue*, *oxidizable impurities* and *ammonia*. This requires a total of 345 cc. of redistilled water.

THE TESTS FOR SALTS.

A solution was prepared as follows:

Sodium Chloride	1.0 Gm.
Sodium Sulfate, anhydrous	1.0 Gm.
Calcium Oxide	5.0 Gm.

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* Scientific Section, A. PH. A., Portland meeting, 1935.