

## SUGGESTIONS FOR PHARMACOPOEIAL REVISION.

Several months ago the Chairman of the Revision Committee sent out a general request for recommendations for changes in the Pharmacopoeia to be considered during the next revision. The response has been generous and the comments are submitted herewith in abstract. Attention has been called to a few communications already published in pharmaceutical journals, but as these are available, they have not been duplicated. Several circulars, suggesting changes in the U. S. P., have been previously submitted to the Committee of Revision and will also be made available for the new Committee. The Chairman hopes that if any additional errors are discovered or other alterations are thought desirable they will be yet submitted for consideration.

CHARLES H. LAWALL, *Chairman*.

## U. S. P. REVISION METHODS.

*Dr. Torald Sollmann:* In general, I believe that it would be desirable, if possible, (a) to restrict the formal Revision Committee to the chairmen of the sub-committees, which also could be somewhat reduced; (b) to elect these directly for their positions at the Convention (*i. e.*, the Convention to vote directly for a chairman for sub-committee I, II, etc.); and (c) to let each of these appoint an auxiliary committee, subject to confirmation by the General Committee (the latter corresponding to the present Executive Committee).

*Prof. Henry Kraemer:* I hope that the members of the Committee of Revision and the Board of Trustees of the U. S. P. Convention can see their way clear to recommend a change in regard to the issuing of the U. S. Pharmacopoeia. I think it should be mandatory that the Pharmacopoeia be issued within one year after the meeting of the Convention. This can be accomplished if the present Committee prepares a revision in the form of a supplement, to be presented to the U. S. P. Convention in 1920. By following the general principle on publicity adopted by the Convention in 1910, all of the proposed changes could be made public for comment and criticism. These changes in descriptions and standards to be printed in a manner similar to that followed in the issuance of the U. S. P. IX and published not later than January 1, 1920.

The plan which I have in mind would enable us to work ahead. It would also enable all the interests represented at the Convention to discuss a work which was concrete and embodied definite principles and proposed standards. It seems to me that in issuing the "Digest of Comments" on the Pharmacopoeia, Dr. Rice must have had in mind the perfection of an organization so as to expedite the work of revision. Furthermore, in the excellent "Digest" of Motter and Wilbert, we have all of the basic materials required to expedite such a supplementary publication of the U. S. P. IX.

*Prof. Edward Kremers:* The revision of the entire volume as practiced in the past (even though 90 per cent. of the items are not in need of revision) to be replaced by card revision of the item that demands revision at once. If the Committee cares to consider the plan, I shall be pleased to give reasons for the change if they are not too apparent already to require enumeration, also to submit samples of cards such as the Wisconsin Pharmaceutical Experiment Station is now publishing. The present method is unscientific and costly.

*Dr. L. F. Kebler:* It is recommended that the interval between the date of issue of the Pharmacopoeia and the time of its becoming effective should be at least one year. It is clearly evident that a shorter interval of time is inadequate for the trade and analysts and others to adjust matters affected by the new publication. It would also relieve considerable responsibility from those who are required to enforce the laws affecting these commodities.

The reasons for this recommendation are very obvious. It requires considerable time for the trade to adjust itself to a new standard, and also requires time to dispose of the material on the shelf of druggists. It would hardly seem the proper thing to say that a drug made according to a standard of one Pharmacopoeia would immediately become worthless when another edition becomes effective.

It is recommended that instead of requiring volunteers to do the major part of the work, such work be done by paid workers. It does not seem quite fair to ask busy men to do the work gratis required to establish various standards, etc., to enable the Pharmacopoeial Committee to accumulate funds. It is not a business proposition.

The reason for the above proposal is very obvious. In addition to what has been said, experience shows that the busy workers do not always have the time to make the determinations

asked for, with the result that in many instances the work to be done is turned over to some one else. The results in some instances may be better than if based on the work of the best experience, but the probabilities are against such an outcome.

*George E. Éwe:* There should be a method of keeping the U. S. P. within easily handled size. The less potent, less important, and less used substances can be continued in the following revision, merely by reference to the previous revision, and adding any new standards or deleting or modifying any old ones. This is the practice adopted by the Secretary of the U. S. Treasury in announcing additions to or modifications of existing Treasury decisions.

#### HISTORICAL INTRODUCTION.

*S. L. Hilton:* Make the Historical Introduction as brief as possible, the saving of space thereby making the book smaller.

#### PREFACE.

**Abbreviations.**—*Dr. N. S. Davis:* The abbreviations in the Pharmacopœia are bad. An abbreviation should be easy to write and as short as possible. Tr. for tincture is all right. Why not Ex. for extract instead of ext. which is much harder to write? Also Fl. for fluidextract. When this last word was adopted by the former Revision Committee, it was assured that it was not two words but a new word. Fl. ext. is not at all easy to write. When it comes to drug names a short abbreviation seems to have been lost sight of. Might not for inorganic elements the chemical symbol be adopted? Both physicians and pharmacists know these. I think all these abbreviations should be thoroughly revised.

**Mil.**—*Dr. H. W. Wiley:* I believe that a mistake has been made in introducing the word "mil" for cubic centimeter. There is already an established measure of money known as the "mil." This name also means a thousandth of a dollar. Any expression of quantity, therefore, that denotes a thousandth may generically be known as a "mil." As long as the action has been made specific by an Act of Congress to denote the thousandth of a dollar, I do not think we should use it to denote a thousandth of a liter any more than we would to denote a thousandth of a gram. I am not prepared to suggest just now a shorter term than cubic centimeter, which I will admit is a cumbersome proposition. Just now it seems to me that "cubem" might do. It would be, however, more in harmony with established usage to write "c. c."

*Prof. Harold B. Meyers:* Substitution of term cubic centimeter for term milliliter. The basic reason advanced for the change made in terminology in the U. S. P. IX is debatable and not justifiable, considering the handicap it is placing on the introduction of the metric system among the members of the medical profession.

*Bureau of Standards:* It is recommended that either the complete word "milliliter" or the correct abbreviation "ml" be used.

**Definitions.**—*Dr. L. F. Kebler:* It is recommended that the definition for products be carefully formulated so that they will include exactly what is desired and nothing more. Such definitions become part of the test prescribed by the various food and drug laws. In the analysis of asafœtida, for example, if it is desired to exclude products other than those derived from the usual sources of asafœtida, some test should be introduced for detecting adulteration. If, on the other hand, the definition prescribes that the product should be derived from a given source, such definition would automatically exclude material not derived from the sources prescribed. It happens from time to time that on the basis of the definition a product may be declared adulterated. So far as practicable the tests prescribed for the product aside from the definition should cover adulteration and misbranding quite fully.

**Alcoholic Percentage.**—*George E. Éwe:* The Revision Committee of the U. S. P. IX found it impracticable to follow the recommendation of the Convention that a range of volume content of absolute alcohol be stated in the Pharmacopœia for each preparation containing alcohol. The H. K. Mulford Company offers its figures on all of the U. S. P. preparations which it has manufactured in accordance with the formulas of the U. S. P. IX to assist the Revision Committee in stating a range of volume content of absolute alcohol of each of the alcoholic preparations of the present U. S. P. which are carried over to the U. S. P. X.

*Dr. L. F. Kebler:* It is recommended that every effort possible be made to reduce the percentage of alcohol in medicinal products to the amounts absolutely necessary for extracting the

medicinal principles, for getting the medicaments in solution or preserving the preparations. There have been some of the alcoholic preparations deleted from the present Pharmacopoeia, and in some the percentage of alcohol has been reduced. There is no question whatever but that there are still a goodly number in the Pharmacopoeia containing alcohol in excess of what is absolutely necessary. It is a well recognized fact that alcohol in and of itself possesses very little medicinal value. The only reasons for its use are those indicated above. Public sentiment is against products that lend themselves well for beverages.

*Prof. L. E. Sayre:* The official alcoholic and hydro-alcoholic preparations should all be carefully reconsidered, in view of the prohibitory law, so that the Committee can with authority state in a prefatory manner in the U. S. P. that medicinal preparations containing alcohol contain only that amount of alcohol which is absolutely necessary for extracting the medicinal principles and for the preservation of the preparation.

#### BOTANY.

**Botanical Nomenclature.**—*Prof. Oliver A. Farwell:* Rules as laid down by the Vienna Congress should be adopted except where such rules prevent the adoption of the oldest names, beginning with the Species Plantarum, 1753, and the Genera, 1754. Article 20 on "Nomina conservanda" should be disregarded. Article 22 should be disregarded also. All "Family names" should end in "aceae" and affixed to the oldest "root" applied to the "family group." Recommendation X—decapitalization of geographical names should be disregarded. Article 54-2 and Article 55-2 should be disregarded. 54-2 refers to the rejection of so-called uninomial generic names and 55-2 refers to the rejection of the specific name when identical with the generic.

A stable nomenclature is a great desideratum. The rules above mentioned are exceptions, and exceptions (increased by each succeeding Congress) can never bring stability. Stability can only be obtained by rigid adherence to set rules designed to bring about that end.

**Capitalization.**—*Prof. Oliver A. Farwell:* Citrus medica Lin. and Smilax medica Cham. and Sch. as usually written are utterly wrong. Should be C. Medica, Lin. and C. medica, C. and S. In the former the specific name is geographical from ancient Media and in the latter it refers to medical properties.

*Miss Margaret Ritchie:* To "star" or mark in some manner the diagnostic characteristics of powdered drugs as an aid in their microscopic examination. The U. S. P. IX gives under each drug a short chapter on its Histology (*i. e.*, the appearance of the powdered drug under the compound microscope). While many pharmacists have no technical working knowledge of pharmacognosy, yet, if the official standard should emphasize the features which tend to identify the drug from all others, the average pharmacist with the aid of a textbook and a compound microscope would be in a position to fruitfully examine the powdered drugs which he buys, sells and dispenses.

An example of "starring" the diagnostic characteristics (*i. e.*, emphasizing the features of identity) would be in the case of Pink Root as follows:

\*—Parenchyma, with starch.

\*—Dark masses of epidermal tissue.

\*—Total absence of "cystoliths," "stone cells," and "long, white-walled bast fibers."

With a note that its most common adulterant, "Ruellia," contains white-walled bast fibers, stone cells, cystoliths, etc.

**Crude Plants.**—*George E. Ewe:* Market supplies require extreme care in selection because of the frequent presence of excessive and extraneous matter, such as inert stems, dirt, insects, whole roots where only the part is desired, wood where only bark is desired, leaves collected in the "dead" instead of "live" condition, "flinty" and "mushy" instead of "flexible" bulbs, foreign plants, fruits where only leaves are desired, moldy drugs, etc. It is suggested that a formal letter be addressed by the U. S. P. Revision Committee to the crude drug collecting, jobbing and grinding companies asking for coöperation in correcting this bad condition, or making the standards more practical. See report of Committee on Drug Market of Pennsylvania Pharmaceutical Association Annual Meeting 1919. It is my opinion that crude drug jobbers and collectors are not doing their share in the establishment of standards for crude plant drugs. In other words, they do not exercise a sufficient degree of scientific control.

*Dr. L. F. Kebler:* Limit test for ash, stems, wormy and infected material should be provided. It is recommended that the question of ash limits, etc., be carefully studied before limits covering these features be introduced in the Pharmacopoeia. It is a well recognized fact that the ash contained in a given plant product would vary materially, depending upon the nature of the soils on which it is grown. Unless the ash limits are carefully studied and the percentage of stems carefully specified, bearing in mind of course that certain stems contain a goodly proportion of active constituents, much injustice may be done the manufacturer or dealer or may enhance, unduly, the price of drugs.

*Miss Margaret Ritchie:* To establish, if possible, fixed botanical origin for official drugs. U. S. P. IX gives Saigon Cinnamon as being derived from an "unknown species of *cinnamomum*," "Rhubarb, from *Rheum officinale* Baillon, *Rheum palmatum* Linne, and the var. *tanguticum* Maximowicz and probably other species of *Rheum* grown in China and Thibet;" then *Cinchona Ledgeriana* Moens, *Cinchona Calisaya* Weddel, and hybrids of these "with other species of *Cinchona*," and Agar from *Gracilaria* (*Sphaerococcus*) *lichenoides* Greville and "other marine algae growing along the east coast of China, particularly several species of *Gelidium* or *Gloiopeltis*."

When a drug is of sufficient importance to justify its inclusion in the Pharmacopoeia and its botanical origin is in doubt, the small expense of sending a capable botanist to the scene of its habitat in an effort to rightly classify it would be but a trifle in comparison to bringing the U. S. P. that much nearer perfection.

**Powdered Vegetable Drugs.**—*Prof. Albert Schneider:* It is recommended that the microscopic description of the U. S. P. IX be revised by a Committee of specialists. I believe a committee of three would be better than a larger committee. This is not to be construed as an adverse criticism of the work of the committee headed by Dr. Kraemer. The present descriptions can be reduced by more than thirty per cent. which would be a saving of both paper and ink, to say nothing of the resulting gain in clearness. All unnecessary verbiage should be omitted.

**Botanical Terminology.**—*Prof. Albert Schneider:* I can see no reason why the naming of plants should not be standard and up to date.

**Pharmacognostical Descriptions.**—*Prof. Albert Schneider:* The description of some crude drugs should be made to conform to the conditions prevailing in the United States, as for example, *Belladonna*.

#### SCOPE.

*Dr. William Fankhauser:* 1. Add descriptions of the pharmaceutical preparations, especially of such classes as collodions, fluidextracts and oleoresins, which pharmacists nowadays do not make themselves. How can they tell that the purchased products meet the U. S. P. requirements, and, in turn, the physician feel satisfied that he is obtaining standard preparations of correct composition, purity, and strength?

2. Add incompatibilities, of interest alike to pharmacist and physician. From the large mass of matter that has been published in the pharmaceutical press your Sub-committee could readily pick out those instances that have occurred or are apt to occur in prescriptions and where there is no doubt as to the incompatibility, physical or chemical—physiological incompatibility or antagonism I consider beyond the scope of a pharmacopoeia.

3. Add antidotes or antidotal measures, a matter of importance to druggists, to whom the public usually turns first for help in cases of poisoning, as well as to physicians who have little occasion to treat such cases.

4. Add therapeutic indications or action. A few words would answer; and I would suggest following the opinion of the American Medical Association as published in the "Epitome of the Pharmacopoeia of the U. S. and National Formulary."

5. Add a few typical formulas for making tablets, a common form of medication at the present day. This would give those physicians who prefer to write complete prescriptions for tablets just as they do for mixtures a chance of obtaining freshly made tablets of just the formula they want instead of ready-made combinations of fixed dosages of the several ingredients.

6. Amplify the alcohol content table on page 593 of the Ninth Revision so as to include all official preparations; or better still, add under each article in the body of the book a mention of its content in absolute alcohol, ether, and chloroform, besides the content of acetanilid, cannabis, opium, etc., per ounce av. or fluidounce of the preparation.

Adoption of the above suggestions would, in my opinion, considerably enhance the value of our Pharmacopœia and render it popular also among physicians where it is now wholly disregarded, yet where it should be a favorite work of reference.

*Benjamin A. Levinson:* It is recommended that an appendix containing a list of poisons, symptoms of poisoning and their antidotes be included in the U. S. P. X. Many pharmacies have no reference books other than the U. S. P. and National Formulary and such a list would be invaluable.

*Edward A. Wickham:* To include a chapter in the next revision similar to the chapter on Suppositories in the U. S. P. IX on the subject of Ampoules, giving detailed instructions for filling and sealing the ampoule and rendering the solution sterile. The ampoule is fast becoming the preferred means of conveying the important medicaments intended for hypodermic use. By use of the ampoule the physician can obtain the medicinal agent in a sterile solution of the proper dosage to suit the particular and individual case. It is most practical, for solutions can be prepared and the ampoule filled, sealed, and sterilized in the pharmacy just as any other prescription or preparation.

**Plans for Deciding Upon Additions to the U. S. P.—***Dr. L. F. Kebler:* It is recommended that the basis of including articles in the Pharmacopœia be the drugs prescribed by the medical profession generally, excluding, of course, the proprietary and secret preparations. A careful canvas should be made among the medical profession and prescriptions on file at drug stores to determine what drugs are generally used by the medical profession in the treatment of human ailments. The drugs in the Pharmacopœia are intended primarily for treating ailments. Such ailments are generally treated by physicians and therefore the demands of the physician are a fair criterion as to drugs to be included in the Pharmacopœia. It is true the laity may purchase drugs recognized in the Pharmacopœia, but usually on advice of a physician or because some lay person has suggested their use.

*George E. Éwe:* In the Case of Chemicals—Material for Decision. Lists of purchases of chemicals by the larger and more representative drug trade jobbers and pharmaceutical manufacturers should be obtained from the jobbers and manufacturers. (Note: The output of chemical manufacturers should not be included, unless the manufacturer supplies only medicinal chemicals or unless the manufacturer supplies a list containing only his output of medicinal chemicals.) The lists should include all U. S. P. and all important and widely demanded chemicals, and must be kept strictly confidential. Purchases of jobbers and pharmaceutical manufacturers are suggested, because these records are available, whereas output could not be obtained because of the diversions of a lot of chemicals to innumerable uses. A period of not less than two years should be considered as a basis of collection of data, as this is necessary to obtain an average.

**Basis of Decision.** The items on the individual list are placed in classes based upon the dosages of the U. S. P. chemicals in the list. Where the output or purchase of non-official chemicals is greater than the output of U. S. P. chemicals of the same general dosage, the non-official chemicals are placed in a class to be considered for admission to the U. S. P. Then the results of classification of all of the individual lists are harmonized and the chemicals thus selected should be seriously considered for admission to the U. S. P. The H. K. Mulford Company will offer data for this purpose upon request.

**In the Case of Crude Drugs.** Material for Decision. Lists of purchases of crude drugs by the larger drug trade jobbers and pharmaceutical manufacturers. (Note: The output of a collecting house should not be considered unless the output is solely for medicinal purposes or the list specifies only the part of the output which was diverted to medicinal purposes.) The lists should include all U. S. P. and all important and widely demanded crude drugs and must be considered strictly confidential. Purchases of jobbers and manufacturers are suggested for the same reasons as mentioned under chemicals. A period of not less than two years should be considered as a basis for collection of data, because some supplies of crude drugs are bought ahead of the time required for use.

**Basis of Decision.** As mentioned under chemicals, the H. K. Mulford Company will offer data for this purpose upon request.

**In the Case of Manufactured Products.** In my opinion, only those manufactured products with a single potent ingredient should be admitted. This limits admission to fluid, solid,

and powdered extracts, liquors, elixirs, syrups, ointments, powders, pill masses, etc., which represent only one drug. All formulas should be transferred to the National Formulary.

Material for Decision. Lists of purchases by jobbers and output of manufacturers.

(Note: The lists should include all U. S. P. and all important and widely demanded products, and must be considered strictly confidential).

Purchases of jobbers and output manufactures are suggested, because these records are readily available. A period of not less than two years is desirable, because the number of lots of any one preparation made up in one year is too small for average purposes.

Basis of Decision. Same as under "Chemicals." The H. K. Mulford Company will offer data upon request.

Source of Standards for New Additions to U. S. P.—*George E. Éwe*: Monographs submitted by the manufacturer or collector modified or approved by the user, as represented by pharmaceutical, chemical, physiologic, and botanical work, reported in various publications, particularly along lines of examination of market supplies. The scientific laboratories of the H. K. Mulford Company will be pleased to offer assistance to the Revision Committee in this respect, upon request.

#### ADDITIONS.

*The E. Clarke Company: Virgin Peanut Oil.* We suggest that Virgin Peanut Oil be recommended for the same purposes as Olive Oil. Virgin Peanut Oil is the pure oil of selected White Spanish Peanuts. After the peanuts are shelled, the red skins are removed and the oil pressed by a cold process from the kernels. No chemical treatment is required and the oil is ready for medicinal use or for food purposes after it is filtered either through cloth or paper. According to the U. S. Government Bulletin issued by the Bureau of Chemistry, Department of Agriculture, Virgin Peanut Oil is physiologically practically identical with Olive Oil, but it is about a half per cent. more digestible and it is much more palatable. Virgin Peanut Oil has not the oiliness of Olive Oil or other oils heretofore used to take the place of olive oil and will be more readily taken than any other oil because of its palatability.

*W. H. Stone and George E. Éwe: Fluidextract of Belladonna Leaves* should be included in the U. S. P. with assay method and standard. It has a tremendous sale. Satisfactory menstruum is dilute alcohol. Assay method like Fluidextract Belladonna Root, U. S. P. Standard—0.3 Gm. total alkaloids per 100 mils.

*George E. Éwe: Emetiné Bismuth Iodide* should be included in the U. S. P. X as it is widely used by mouth in the treatment of amebic dysentery. It is suggested that a monograph be adopted based upon the description in New and Non-official Remedies.

Crude Ammonium Sulphoichthyolate should also be included in the U. S. P. because of its vast use. It is likely that a standard for organically combined sulphur is most important, though physical characteristics should also be described.

Following are details of examination of some Crude Ammonium Sulphoichthyolate samples:

Sample No. 1. 10.2 per cent. total sulphur and 9.96 per cent. organically combined sulphur. Physical characteristics: Similar to original "Ichthyol."

Sample No. 2 assays 10.6 per cent.  $\text{NH}_3$ , 9.2 per cent. combined sulphur, ash 0.132 per cent., water 48.1 per cent. Physical characteristics: Similar to original "Ichthyol."

Sample No. 3. 9.043 per cent. total sulphur, 0.336 per cent. Ammon. Sulphate, 0.081 per cent. sulphur as Ammon-sulphate and 8.962 per cent. combined sulphur. Physical characteristics: Similar to original "Ichthyol."

Sample No. 4. Moisture 52.8 per cent.; total  $\text{NH}_3$ , 5.8 per cent.; total Sulphur, 13.5 per cent.; organic "sulphidic" sulphur, 2.56 per cent.; sulphur in Ammon. Sulphate, 3.976 per cent.; Ammonia in Ammon. Sulphate, 2.103 per cent.; Ammonia combined with organic sulphonic acids, 3.69 per cent.; Sulphur in organic sulphonic acids, 9.54 per cent.; Ammonium Sulphate, 16.43 per cent.; Sulphur present as "sulphonic" sulphur, 6.95 per cent. Answers all other New and Non-official Remedies requirements.

Sample No. 5. Total ammonia, 3.2 per cent.; water, 49.44 per cent.; total sulphur, 9.0 per cent.; ammonium sulphate, 7.07 per cent.; "sulphonic" sulphur, 4.3 per cent.; organic "sulphidic" sulphur, 3.0 per cent.; ammonia combined with organic sulphonic acids, 2.3 per cent. Answers all other New and Non-official Remedies requirements.

Sample No. 6. Water, 50 per cent.; total NH<sub>3</sub>, 2.57 per cent.; total sulphur, 7.02 per cent.; ammonium sulphate, 3.48 per cent.; organic "sulphidic" sulphur, 2.18 per cent.; organic (sulphonic acids) sulphur, 6.18 per cent.; ammonia combined with organic sulphonic acids, 2.13 per cent. Answers all other New and Non-official Remedies requirements.

Sample No. 7. Total sulphur, 6.3 per cent.; total NH<sub>3</sub>, 2.3 per cent.

Sample No. 8. Total sulphur, 8.3 per cent.; total NH<sub>3</sub>, 4.3 per cent.

Sample No. 9. Total sulphur, 8.13 per cent.; total NH<sub>3</sub>, 4.41 per cent.

Samples, No.....	10	11	12	13	14	15
Total sulphur.....	6.32	8.30	8.13	8.78	4.78	7.21
Total ammonia.....	2.30	4.35	4.14	2.02	1.84	3.64
Ammonium sulphate.....	3.39	10.5	10.3	.....	.....	5.66
Loss at 100° C.....	34.5	60.34	68.5	.....	.....	.....
Ash.....	0.179	None	None	.....	.....	None
Ammonia as ammonium sulphate.....	0.956	2.71	2.67	.....	.....	2.89
Sulphur as ammonium sulphate.....	0.830	2.54	2.50	.....	.....	2.71
Ammonia combined with organic sulphonic acids.....	1.344	1.64	1.47	.....	.....	0.75
Sulphur in sulphonic acids in oxidized state.....	2.53	3.08	2.76	.....	.....	1.41
Sulphur in organic sulphonic acids.....	5.49	5.76	5.62	.....	.....	4.50
Organic sulphidic sulphur.....	2.86	2.68	2.97	.....	.....	3.09
Miscibility with water.....	O.K.	O.K.	O.K.	O.K.	O.K.	O.K.
All other New and Non-official Remedies requirements.....	O.K.	O.K.	O.K.	.....	.....	O.K.

Dr. John F. Anderson: It is recommended that *Anti-Pneumococcic Serum* be admitted to the next Revision of the U. S. P. Standards have been established for this by the U. S. Treasury Department. Under Guiding Principles of last Convention biological products for which there were governmental standards must be admitted to the Pharmacopoeia.

The same is true of *Anti-Meningitis Serum*.

Edward A. Wickham: To include *Acidum Acetyl-Salicylicum* in the next Revision, with a formula for its manufacture, and to employ the word "Aspirin" as the official synonym. The extensive use of this product justifies its inclusion in the official standard; if included, the public will be assured of receiving a product of a standard strength and purity. The word "Aspirin" as the official synonym would be added assurance, for it is by this name that the general public knows the product and many manufacturers thus designate it.

George E. Éwe: Acetyl-Salicylic Acid is used so extensively that it should have a place in the U. S. P. The requirements outlined in New and Non-official Remedies for 1919 are satisfactory as a basis for a U. S. P. monograph. These requirements can be met by the market products. Legal standards are advisable for purposes of uniformity and basis of comparison.

Corn Products Refining Company: We recommend *Corn Oil* to be introduced in the U. S. P. It is a natural edible oil of high quality which has been tried out with great success in many pharmaceutical preparations. Dr. Virgil Coblenz investigated this oil for us as to its value in pharmaceutical preparations and found that it worked better than cottonseed oil for ammonia emulsion, dissolved camphor much more rapidly than cottonseed oil and gave a better cold cream than cottonseed oil and worked well in plaster. Dr. Joseph P. Remington informed us some years ago that he preferred corn oil to cottonseed oil in making various pharmaceutical preparations, especially emulsions.

The chemical constants for the oil are approximately:

Specific gravity.....	0.9265	
Free Fatty Acid as Oleic Acid.....	0.05	
Saponification Number.....	189 to 192	
Iodine Number.....	118 to 125	
Titre Test.....	18.3° C.	
Cold Test {	Cloud.....	-8.3° C. to -6.7° C.
	Solidifying.....	-15.6° C. to -14.9° C.

Corn oil is exclusively a domestic product. It is an oil of high quality and free from odor, which, in several instances, is superior for the manufacture of pharmaceutical preparations to cottonseed, which is now introduced in the Pharmacopoeia.

*Carus Chemical Company:* It is recommended that *Chloramine-T* be admitted to the Pharmacopoeia because of its germicidal properties.

*Dr. Waller S. Haines:* A preparation of *digitalis* for hypodermic and intravenous use should be included in the next Pharmacopoeia. One of the most glaring defects in the present Pharmacopoeia is the absence of any preparation of *digitalis* that lends itself readily to hypodermic and intravenous use. When the physician wishes to administer *digitalis* hypodermically or intravenously, as he not infrequently does, he is obliged to resort to some proprietary article. Every teacher of materia medica in medical schools is constantly asked by his students what official preparation of *digitalis* can be conveniently used hypodermically. The answer is, "There is none; you must use some non-official article."

*Lucius L. Walton:* A new class of preparations should be introduced for which I suggest the name *Petrolata Medicata (Medicated Petrolatums)*. Zinc oxide petrolatum containing 20 per cent. of zinc oxide with petrolatum base. This is a particular case, but there may be other combinations such as phenol, menthol, camphor, capsicum, etc.

Nearly all large pharmaceutical manufacturers are selling such a product under the name of U. S. P. Zinc Oxide Ointment. Some of them make a practice of sending it out on all orders for "Zinc Oxide Ointment" which do not specify "U. S. P." One manufacturer claims "that this is a more satisfactory ointment than the official product." The petrolatum product may have equal merit with the U. S. P. ointment in some cases to which the article is adapted and the keeping qualities are in its favor, but there should be some way for physicians to distinguish the two products and indicate the petroleum product when they prefer it. The manufacturer who has really improved upon the U. S. P. product should be rewarded with an official title in the U. S. P. which he may use as a name for his product and avoid being particeps criminis in the violation of pure drug laws by dispensing pharmacists.

*American Drug Manufacturers' Association:* The Scientific Section of the American Drug Manufacturers' Association recommends to the Committee of Revision of the Pharmacopoeia of the United States that *Iron Glycerophosphate* be introduced into the next revision with the description, tests, and assay given in the National Formulary IV with the modifications quoted in the following report submitted to the Scientific Section of this Association by the Chairman of the Sub-Committee on Glycerophosphates, Mr. Gaston DuBois, of the Monsanto Chemical Works.

(a) Change the iron content from "not less than 14 per cent. nor more than 16 per cent. Fe" to "not less than 13 per cent. nor more than 15 per cent. Fe."

The reason for reducing the iron content is that we have found it practically impossible to produce iron scales containing 14 per cent. iron. Iron glycerophosphate is produced in two forms—as scales and as powder. The scale was used, I think, mostly in Europe. The powder, I should say, is the American product; it is better, inasmuch as it is cheaper to produce, more convenient to use, and has the same value. However, we have to consider the scales as it is a market product. We have found it very difficult in the case of scales to bring the content of iron in this product up to 14 per cent. If we dry it up to that degree, the product becomes brittle, a powder, and you do not have scales, and therefore if the scales have to be considered it is not practical to retain the present description in the National Formulary. If the powder alone is considered, then we can bring the iron content up to 14 per cent. or over very easily. But as this description would embody both powder and scales, we suggest that the iron percentage be reduced to 13, and instead of reading "14 to 16 per cent." should read "13 to 15 per cent."

The National Formulary is somewhat vague on the percentage of chloride and we have set the highest limits to 0.3 per cent., because we found that the market products contain only 0.2 per cent. of chloride and therefore we suggest a limit of 0.3 per cent. chloride as reasonable.

(b) In place of the qualitative test for chloride insert "An assay for chlorides by the U. S. P. method No. 5 (p. 588) shall show not more than 0.3 per cent. chloride as  $\text{FeCl}_3$ ."

(c) Add to tests the following for ferrous salts: "A freshly prepared solution of an alkali ferrocyanide (1 : 10) shall show no blue color (ferrous salts)."

We have in our report a list of analyses of iron glycerophosphate in powder form and in scale form and we find the product in powder form to test (about 10 products) from 14.2 to 16.3 per cent. iron, and from 0.03 to 0.14 per cent. iron chloride, etc.



This table shows that in the case of Iron Glycerophosphate scales, the National Formulary requirements are almost impossible to meet and would cause rejection of goods, which are otherwise perfect, on account of one or two-tenths per cent. iron.

The therapeutic value of Iron Glycerophosphate should, we believe, be equal if not superior to the therapeutic value of other glycerophosphoric acid salts, and it is for this reason that we suggest the iron salt be included in the next U. S. P. The above changes and conditions are prompted by facts.

Laboratory results on factory products furnish basis for contention (a) That content Fe be changed to read "not less than 13 per cent. nor more than 15 per cent."

Powder.	%.	Per cent. FeCl <sub>3</sub> . %.	Scales.	%.	Per cent. FeCl <sub>3</sub> . %.
Lot 410.....	16.3	0.14	Lot 127.....	12.8	0.18
Lot 409.....	16.8	0.07	Lot 132.....	12.8	0.18
Lot 261.....	15.6	0.08	Lot 112.....	14.8	0.44
Lot 262.....	14.3	0.04	Lot 168.....	12.5	0.22
Lot 265.....	15.5	0.03	Lot 182.....	13.7	0.34
Lot 271.....	15.5	0.05	Lot 260.....	13.3	0.22
Lot 272.....	14.4	0.05	Lot 264.....	13.4	0.25
Lot 276.....	14.7	0.09	Lot 342.....	13.9	0.21
Lot 280.....	15.2	0.08	Lot 359.....	13.8	0.12
Lot 285.....	14.2	0.07			
Lot 286.....	14.6	0.05			

(b) Above records indicate that 0.30 per cent. represents a fair limit for chlorides in both powder and scale form.

(c) Ferrous salts are very seldom found in the manufacture of Iron Glycerophosphate. Their presence forms a basis for rejection on account of being insoluble.

*American Drug Manufacturers' Association:* In the United States Pharmacopoeia, 9th Revision, Belladonna Leaves and Belladonna Root are made official. In the requirements for belladonna leaves the Pharmacopoeia allows the dry leaves and tops without the presence or admixture of more than 10 per cent. of the stems and other foreign matter and not less than 0.3 per cent. total alkaloids of belladonna leaves.

It is a well known fact, since the European War, supplies of belladonna from foreign sources have been cut off and the consumer of belladonna has been compelled to rely to a considerable extent on the American grown product; by the requirements of the Pharmacopoeia the growers of belladonna are confronted with the problem that a large portion of the plant is not official and in some instances this amounts to as high as 60 per cent. of the belladonna plant by the rejection of the stems of cultivated belladonna. It has been found that they contain an amount of alkaloid equal to and sometimes surpassing the requirements of the Pharmacopoeia, and with many cultivators, it has been found that a mixture of the dry stems and leaves exceeded in alkaloidal contents the Pharmacopoeial requirements. This latter is of considerable importance to the grower as well as to the consumer of the drug. To grow belladonna or other drugs requires the investment of considerable capital, the expenditure of a considerable amount of labor, and the rejection by the Pharmacopoeia of a considerable percentage of the crop containing alkaloid considerably above the requirements of the Pharmacopoeia materially increases the cost of the product. Considerable effort is now being made by the National Department of Agriculture, by the State Agricultural departments, and by private individuals to so conduct the cultivation of this and other drugs that this country will be independent so far as certain of its drug supplies are concerned.

The American Drug Manufacturers' Association respectfully suggests that Belladonna Herb, by which term it is intended to include the leaves and dry stems, should be made official in the Pharmacopoeia and allowed to be used for galenical preparations and in the manufacture of medicinal products. The suggestion is, that in addition to belladonna leaves and belladonna root, the following be inserted in the Pharmacopoeia:

*Belladonna Herb:* The dried stems, leaves, and flowering and fruiting tops of *Atropa Belladonna* Linné (Fam. *Solanaceae*), yielding not less than 0.35 per cent. of total mydriatic alka-

loids when assayed by the official process, and containing not more than 18 per cent. of total ash.

Stems hollow, cylindrical, or more or less flattened, green or brownish green, longitudinally furrowed, wrinkled, and finely hairy. Leaves much crumpled and having the characteristics given under *Belladonna Folia*.

The powder is either dull green or brownish green, somewhat hygroscopic, and reveals the same characteristics when examined with the compound microscope as given under *Belladonna Folia*.

*Belladonna Herb* may be used in the place of *Belladonna Folia* in the preparation of *Tinctura Belladonnae*, *Extractum Belladonnae*, and *Emplastrum Belladonnae*.

*American Drug Manufacturers' Association:* This Association also recommends the inclusion of *Hyoscyamus Herb* in the next revision of the U. S. P. and submits the following tentative standard:

*Hyoscyamus Herb:* The dried stems, leaves, and flowering and fruiting tops of *Hyoscyamus niger* Linné (Fam. *Solanaceae*), yielding not less than 0.065 per cent. of the alkaloids of *Hyoscyamus*.

Stems, hollow, cylindrical, flattened, longitudinally furrowed and wrinkled, grayish green and glandular pubescent. Leaves more or less broken and having the characteristics given under *Hyoscyamus*.

The powder is light grayish green and possesses the same characteristics when examined with the compound microscope as given under *Hyoscyamus*, with the exception that the woody fragments are more numerous.

*Hyoscyamus Herb* may be used in place of *Hyoscyamus* in the preparation of *Extractum Hyoscyami*, *Fluidextractum Hyoscyami*, and *Tinctura Hyoscyami*.

*American Drug Manufacturers' Association:* Acting on the advice of its Committee on Standards and Deterioration who have duly investigated the matter scientifically and have collated the experience of the firms in the membership, the American Drug Manufacturers' Association respectfully recommend to the Committee of Revision of the U. S. P. that:

A standard for *Belladonna and Capsicum Plaster* be established, viz., the plaster to contain 0.125 per cent. alkaloids of belladonna.

Heretofore there has been no authoritative standard for a *Belladonna and Capsicum Plaster*, manufacturers having, in part at least, followed the practice of making the *Belladonna and Capsicum Plaster* half the strength of the regular *Belladonna Plaster*, and, in order to make such a practice uniform, this Association makes the above recommendation as to alkaloidal strength, establishing the standard of this plaster as follows:

*Belladonna and Capsicum Plaster* to contain 0.125 per cent. alkaloids of *Belladonna*, and 5 per cent. of powdered *Capsicum*.

*American Drug Manufacturers' Association:* The following recommendation is made: That the Committee of Revision of the U. S. P. permit the use of *Mexican Scammony* and its resin in the Pharmacopœia in place of *Levant Scammony*; and that in U. S. P. formula, calling for *Scammony Resin*, they permit the use of *Mexican Scammony* as well. This recommendation is based on necessity, as there is practically none of the so-called *True Scammony* available in this country. This Association maintains that so far at least as pharmaceutical purposes are concerned, there is no detectable difference between the *Mexican* and the *Oriental Scammony*. The Committee of Revision is reminded also that *Mexican Scammony* is recognized in the British Pharmacopœia and therefore has the endorsement of a very important and careful body of representative men, whose judgment should be given due weight.

#### DELETIONS.

*George E. Éwe:* The lists of purchases and outputs obtained by me under the subject, "Plan for Deciding Upon Additions to the U. S. P.," should be carefully filed away and compared with new lists, obtained for the succeeding revision, in order to keep down the size of the U. S. P. Deletions can be freely made by continuing the old standards in the new revision by merely referring to the previous revision and adding any new standards or deleting or modifying any old ones.

*W. H. Stone:* As there is little or no demand for *Fluidextractum Granati*, it is recommended for deletion. The same is true of *Fluidextractum Aromaticum*.

*Thomas S. Blair:* *Arnica, Guaiacum, Mezereum, Veratrina, Taraxacum, and Viburnum Prunifolium* are recommended for deletion. *Arnica* is practically useless, no defined activity making it useful internally and it is apt to be harmful externally. *Guaiac* should be turned over to the laboratory and abandoned as a remedy. *Mezereum* is useless and employed only in the shot-gun sarsaparilla preparations. *Veratrine* is a mixture, uncertain and dangerous. *Taraxacum* is practically worthless. *Viburnum Prunifolium* has no defined activity.

*Edward A. Wickham:* It is recommended that either *Mistura Glycyrrhizae Composita* or *Pulvis Glycyrrhizae Compositus* be deleted. As these two preparations are so vastly different in composition and are used for such totally different purposes, it would seem that either one or the other should be dropped or else have its name changed.

#### MISCELLANEOUS RECOMMENDATIONS.

*S. L. Hilton:* Publicity of changes before publication of the book. This is not a new feature, as it was carried out in the last Revision. I believe it resulted in much good and should again be followed in the U. S. P. X.

*Prof. Robert P. Fischelis:* It is suggested that a sub-committee on publicity be appointed to have charge of publicity given to the work of revision, to both the professional and lay press, under the supervision of the Chairman, this committee to function throughout the work of revision and issue bulletins and collect clippings, so as to have a complete record of the publicity given to the work of revision. A committee of five is suggested, with a chairman who is familiar with publicity work and in active touch with the avenues that lead to publication of articles in the lay press; monthly bulletins to be issued to pharmaceutical and medical journals; monthly bulletins to be issued to newspapers, preferably Sunday editions, and to certain magazines; the monthly bulletins to lay press to be carefully worded and calculated to educate the public and cultivate public opinion in favor of the present method of revision in preference to a Government-controlled revision. Very few laymen know that there is such a thing as a Pharmacopoeia, and therefore do not realize just how pharmacists and physicians protect lives each day by insisting on drugs and preparations which come up to certain legal standards. Chemistry is fast becoming as favorably associated in the minds of laymen as medicine. This is due chiefly to the propaganda carried on by the American Medical Association and the American Chemical Society. There seems to be no good reason why pharmacy and the work of pharmacists should not also be in the public eye and the suggestions above would appear to me to be one of the best means to achieve such an end.

*The National Association of Drug Clerks:* U. S. P. methods are too complex. The work should be compiled upon more practical principles for the retail drug trade. Principles and methods should be as practical as possible, yet the standards should not be lowered, so as to encourage the retail drug trade to develop ethically the professional side of pharmacy by manufacturing, to a greater degree, within his own store all U. S. P. products.

In taking up constructive and educational work in the field during the past three years with the retailers and in covering fourteen states, it has been found that many retailers express themselves against the complexity of methods employed in the U. S. P. in the past for the manufacture of many of the simpler preparations. Some go so far as to state that their opinion was that the Revision Committee did not give retail drugdom the proper consideration hereon in the compilation.

*Prof. A. H. Clark:* It is recommended that the Committee of Revision publish as a separate volume all the technical scientific work such as assay methods, analytical operations, etc. (See THIS JOURNAL, January, 1919, p. 13.)

The scientific work could be brought to a much higher degree of perfection in such a volume, thus making it more useful to chemists and officials everywhere. The book of formulas, doses, etc., could be made more useful to pharmacists and physicians. Each volume would be smaller, less expensive, and more useful.

*Dr. N. S. Davis:* Would it not be well to indicate all drugs which have physiological and pathologic activity by printing their names in heavier type than the others which are almost or quite useless but still used?

Also in the same way indicate the one or two best liquid and solid preparations of those drugs. This will ultimately lead to the use of fewer preparations, but the best. Only one or two

preparations for pills and liquids are needed. The drugs which have genuine activity should be selected by the physicians of the Committee. The preparations to be preferred should be selected by a small committee, mostly pharmacists, but with a medical representative too. Of course, they should be able to get the advice of any others when needed.

*George E. Éwe:* Crude drugs, fluidextracts, and tinctures unstandardized. Extractive standards are desirable for purposes of uniformity. The H. K. Mulford Company offers its extractive standards.

*Edward A. Wickham:* It is suggested that working formulas for chemical compounds be included in the next revision. While it is true that but few dispensing pharmacists are inclined to manufacture their own chemicals (such as zinc stearate, sodium bromide, etc.), yet inasmuch as the U. S. P. is a "laboratory guide" it would seem right to give the few dispensing and the many manufacturing pharmacists the benefit of suggestive formulas. During the recent war, no doubt, many pharmacists had stocks of raw materials, say salicylic acid, but allowed patients to wander in search of sodium salicylate, not caring to prepare it from the acid, fearful that their finished product would not be true. Suggestive formulas, in addition to making the U. S. P. of more value to the dispensing and manufacturing pharmacists would make it of paramount value as a textbook to students of both medicine and pharmacy.

*Dr. L. F. Kehler:* If the present Pharmacopoeia provides a good standard or a good method for determining such a standard, they should not be changed unless better ones are available. Methods and standards should not be changed for individual reasons. Unless something of a definite character can be accomplished by the introduction of a new method, the old one should be retained. Frequent changes in methods and standards result in economic losses. They require manufacturers to adjust their products to the new basis. The analysts are compelled to spend time and money to become acquainted with the new elements involved.

It happens from time to time that a worker will develop a method which in his hands gives excellent results, but when actually tried out proves unsatisfactory. No one-man method should be included in the Pharmacopoeia because such method as a rule will not be productive of the best results. Every method proposed by an individual or laboratory should be carefully tried out and if it proves satisfactory, then, and then only, should be included.

It is recommended that only such methods of analysis be included in the Pharmacopoeia as give fairly concordant results in the hands of experienced workers. No methods should be considered for possible inclusion which in the try-out vary more than 20 per cent. in the hands of skilled operators. The reasons for this are self-evident. A method which does not give concordant results in the hands of skilled workers will only lead to confusion, trouble, and discord. None of these elements should find a place in Pharmacopoeial methods.

*Fineness of Powders.—Prof. Frederick J. Wulling:* I feel some attention should be given to the determination of more suitable degrees of fineness of powders for the preparation of fluidextracts, tinctures, and extracts. There appears not to be sufficient research result along these lines. The degrees of fineness to be decided upon should be determined or indicated more largely by the nature of constituents and cells and the density of resulting preparations. It appears that heretofore the general principle followed was based merely upon the results growing out of the practical experience of pharmacists and manufacturers and not out of scientific research.

It would be of advantage if by suitable research work a single degree of fineness of powder of each vegetable drug might be determined that would be suitable for employment of that powder in the preparations of fluidextracts, tinctures, and extracts. To make clearer what I have in mind I will enclose compilation based on the U. S. P. showing that most vegetable drugs are designated to be in more than one degree of fineness. Gentian is required to be in No. 20 powder for preparation of the extract, in No. 30 powder for the preparation of the fluidextract, and in No. 40 powder for the preparation of the tincture. Methods of preparation, of course, also have much to do with the selection of a suitable degree of fineness of powder. Everything else being equal, it costs less to grind a drug into a No. 20 powder than into a finer one, but I think this economic question could safely be put aside in favor of uniformity.

Some allowance should also be made on tailings of different degrees of fineness. Some research work ought to be done along these lines. In our extensive work in milling digitalis in

connection with the preparation of the tincture for the Government and in the milling of other drugs cultivated in our own medicinal plant garden, we have come across many evidences of the value of more systematic and scientific work along these lines. If our faculty and service force is increased in the near future, as I hope it will be, this College might be willing to undertake some original work of this kind. Our Dr. Newcomb has gained a valuable experience which the College would be glad to develop for the benefit of the revision. I cannot make any promises at present, but can say in a general way that the College would be willing to be helpful to the extent its facilities and resources would warrant.

TABLE SETTING FOR THE DIFFERENCES IN DEGREE OF FINENESS OF U. S. P. VEGETABLE POWDERS.

	Designated degree of fineness U. S. P. IX.			Oleoresins.
	Fluidextracts. No.	Tinctures. No.	Extracts. No.	
Aconite.....	40	60	60	
Belladonna Leaves.....	..	60	40	
Bitter Orange.....	20	40	..	
Cannabis.....	30	40	20	
Cascara.....	40	..	20	
Colchicum Seed.....	40	50	..	
Digitalis.....	30	60	..	
Gelsemium.....	40	60	40	
Gentian.....	30	40	20	
Hydrastis.....	40	60	40	
Hyoscyamus.....	40	60	40	
Rheum.....	30	40	40	
Zingiber.....	40	30	Pulvis Aromat.	No. 60
			60	
Physostigma.....	..	50	60	
Stramonium.....	..	60	40	
Capsicum.....	..	50	..	40
Podophyllum.....	40	..	..	Resin 60
Nux Vomica.....	40	40	20	
Scilla.....	20	20	..	

**Powdered Vegetable Drugs.**—*Prof. E. L. Newcomb:* There should be more uniformity in the degree of fineness of the same drug when used for making different preparations. The indicated degree of fineness for vegetable drugs to be based not only upon the physical problems to be met during extraction, but also upon the pharmacognostical character of the cells containing the active medicinal constituents.

A limit of residue or so-called gruffs or tailings should be specified for certain drugs.

There should be conferences between the chairman of the committee on Botany and Pharmacognosy and the chairmen of other committees having to do with preparations containing vegetable drugs.

Bale lots of official drugs should be ground to the different degrees of fineness required, under scientific supervision, and by the use of different types of mills. Standard sifting apparatus should be employed and figures on the percentage of middlings and tailings for first and second grind obtained from which reasonable limits of waste may be established. Many factors relative to the condition of the crude drug must be considered.

There are inconsistencies relating to this subject in the U. S. P. IX. Powdered drugs are less uniform in quality than they would be if limits for waste during milling were established. Drug millers are asking that such standards be included.

*Henry Paul Busch:* The Pharmacopoeia is now most important as a book of standards. On general principles, I believe that a standard once adopted, should not be entirely abandoned, though, of course, it may require modification or revision from time to time. However, many items have been dismissed from preceding revisions of the Pharmacopoeia and doubtless others will be dismissed in the future. I would therefore suggest that all old titles be included in their

proper alphabetical order in the body of the work, printed in a distinctive type (say *Italic* or *Extended*) with some brief note of their disposition. For example:

Deleted from X Revision.  
No Official Standard,  
or  
Deleted from IX Revision.  
See N. F. IV.

There are many reasons why it would be desirable to extend this idea to many titles deleted from earlier editions, though just where to draw the line I would leave to the Committee.

I would also like to suggest that there should appear in the body of the text in connection with each official title in small type (6-point or 8-point) some brief notes indicating when it was first introduced, and the time at which some material change was made in the strength or requirements for the article. I have in mind such very important changes as were made in the 8th Revision in regard to Tincture of Aconite, etc.

I would suggest further that immediately following each official title, or immediately preceding the purity rubric, there should appear a statement of the alcohol and narcotic content in the form required to be shown on the labels under the Food and Drugs Act. This would, of course, show alcohol—per cent., and the other articles in grains per ounce.

The following will illustrate the above ideas:

SPIRITUS FRUMENTI	Deleted IX.
Whisky	No official standards.
ACETUM OPII	Deleted IX.
Vinegar of Opium	v. N. F. IV.
ALCOHOL ABSOLUTUM	
Absolute Alcohol	v. Alcohol Dehydratum in this edition.
TINCTURA ACONITI	o
Tincture of Aconite	35 per cent.
Tr. Aconit.	Chemical Assay 10 per cent. VIII
Alcohol 66 per cent.	Biological Assay 10 per cent. IX.
SPIRITUS ÆTHERIS NITROSI	
Spirit of Nitrous Ether	
Sp. Aeth. Nitros. Sweet Spirit of Nitre.	
Alcohol 92 per cent. Ethyl Nitrite 15.25 grs. per fl.oz.	

*Dr. J. M. Francis:* When the completed revision of the U. S. P. IX was ready for sending to the printer, I protested most vigorously against the seemingly indiscriminate use of glycerin in all sorts of liquid preparations. I protested particularly against the use of glycerin in so many of the drug preparations.

The unexpected advent of the European War proved the truth of my contention that the indiscriminate use of glycerin would prove costly to the drug trade of this country, for, as you remember, glycerin became prohibitive in price and it is an undisputed fact that the drug trade, physicians and the patients of the United States were subjected to useless expense, amounting to untold thousands of dollars, for this one reason.

Now I am as convinced as ever that the Pharmacopoeia still contains many preparations having glycerin in the formula in which it is practically useless, and therefore an uncalled for item of expense; and there are various other preparations in the Pharmacopoeia which contain a quantity of glycerin that is excessive. I, therefore, hope that this matter will be directed to the attention of the proper sub-committees and will be given most careful study in the Tenth Revision.

NOTE: Dr. Francis' opinions are concurred in by *Mr. J. P. Snyder*, of the Norwich Pharmacal Company; *Mr. Howard T. Graber*, of the Digestive Ferments Company; the *Scientific Section of the American Drug Manufacturers' Association*; *Dr. F. B. Kilmer*, of Johnson and Johnson, and *Dr. John Uri Lloyd*, of Lloyd Brothers.

*Dr. Fred Kilmer:* Dr. Kilmer presented at the Annual Meeting of the New Jersey Pharmaceutical Association, 1919, constructive suggestions for Pharmacopoeial Revision. (SEE *American Journal of Pharmacy* for August, 1919.)

## ACETANILIDUM.

*Dr. Thomas S. Blair:* Reduce the average dose of Acetanilid to  $1\frac{1}{2}$  grains in place of 3 grains. Therapeutists are coming to the view that the dosage of acetanilid is entirely too high. An article in the *Journal of the American Medical Association*, some time ago, placed the proper dosage at  $1\frac{1}{2}$  grains. While out on detail for the U. S. Public Health Service last fall, during the influenza epidemic, I was deeply impressed with the fact, for it is a fact, that the coal-tar synthetics are used vastly to excess and the doses at present in vogue are doing so much harm that this useful class of drugs is threatened with a reaction against them that need not be if they are properly used and if the American chemical industry exploits them properly, which the Germans did not do, for they were interested only in sales and they suggested excessive dosage.

## ACIDUM BENZOICUM.

*Dr. Thomas S. Blair:* Approve only certain of the processes for making synthetic benzoic acid and benzoates, and exclude products made from the urine of herbivorous animals. There is much inferior benzoic acid on the market and I have observed depression to follow the use of benzoates of uncertain synthetic type.

*Dr. A. R. L. Dohme:* A more definite test for distinguishing between the natural and the synthetic acid should be given. The chlorine test which is usually applied for distinguishing between the natural and the synthetic acid is not reliable, because the process for manufacturing the synthetic acid has been so perfected that the acid can be made free from chlorinated products.

## ACIDUM HYDRIODICUM DILUTUM.

*Dr. A. R. L. Dohme:* The test for total solids should be revised. The residue left after evaporating and incinerating 5 mils of the acid is not potassium carbonate as is usually accepted, but is potassium iodide which volatilizes when too high heat is applied. Therefore, it should be stated that the heating should be carried out only at dull redness.

## ACIDUM HYDROCYANICUM DILUTUM.

*H. V. Farr:* Under the method of assay it is recommended that the material be cooled, ice cold and the portion for test be withdrawn with a pipette instead of by pouring as recommended in the present edition. In place of the present test for hydrogen chloride a direct titration of the total mineral acid with standard alkali and methyl orange indicator is recommended, as follows:

*Mineral Acid:* Into a small Erlenmeyer flask introduce exactly 5 mils of the acid to be tested and two drops of methyl orange T. S. Not less than 1 mil nor more than 2 mils of  $\frac{N}{10}$  sodium hydroxide solution should be required to change the red color to yellow.

Hydrocyanic acid is extremely volatile even from very dilute aqueous solutions so that in pouring the acid from a bottle, particularly in warm weather, considerable loss inevitably results. The acid can be safely drawn into a pipette by the use of a suction pump, and if it be previously cooled (ice cold) loss becomes negligible.

With regard to the test for mineral acid, having in mind the fact that traces of some mineral acid are necessary to the proper preservation of hydrocyanic acid, it seems desirable to establish a minimum as well as a maximum limit. The determination above suggested is very much more convenient than the present method, and, at the same time, is more accurate and reliable.

## ACIDUM SULPHURICUM AROMATICUM.

*Dr. A. R. L. Dohme:* Assay process should be changed. A process should be adopted similar to the one published by Penniman and Randall in the *Journal of Industrial and Engineering Chemistry* for October, 1919. The results obtained by the official method are too high, due to the reaction being reversible.

## ACONITUM.

*George E. Éwe:* It is suggested that the standard be reduced to 0.45 per cent. and a corresponding change be made in the physiological standard. The standard of 0.5 per cent. of ether-soluble alkaloids appears to be too high. Data for the establishment of a lower standard are herewith submitted. A lower standard would be desirable to accord with the market quality of aconite root. Furthermore, practical manufacturers of the fluidextract and tincture indicate

great difficulty in getting these preparations up to the present standards because of the present somewhat high standard of the crude drug.

Year.	No. of assays.	Lowest assay.	Highest assay.	Average.	Standard.	Number.	
						Above.	Below.
1911.....	15	0.372	0.965	0.577	0.5	7	8
1912.....	16	0.418	0.965	0.692	0.5	12	4
1913.....	10	0.272	0.800	0.433	0.5	2	8
1914.....	8	0.297	0.784	0.490	0.5	4	4
1915.....	5	0.360	0.626	0.497	0.5	2	3
1916.....	11	0.230	0.640	0.418	0.5	2	9
1917.....	12	0.360	1.048	0.622	0.5	10	2
1918.....	3	0.33	0.49	0.414	0.5	0	3
1919.....	5	0.371	0.693	0.549	0.5	4	1
Totals.....	85					43	42

*S. L. Hilton:* Chemical assay should be omitted unless a more accurate method be devised whereby the aconitine does not break down.

*American Drug Manufacturers' Association:* The Scientific Section of this Association suggests that the U. S. P. X include so-called Japanese Aconite Root, provided a study of the drug confirms our belief that it is as efficient as the present official variety of aconite root.

#### ADEPS LANAE.

*George E. Éwe:* The "alkalies and soaps" requirement appears to be difficult to attain. An upper limit of 0.3 per cent. ash instead of the present 0.1 per cent. and the dropping of the requirement that the ash be not alkaline to moistened litmus paper would not include any harmful products.

#### ADEPS LANAE HYDROSUS.

*Bertha Mueller:* It is recommended that a formula for making lanolin be made official. The following formula is submitted:

Liquid Petrolatum.....	10.00
Distilled Water.....	20.00
Anhydrous Wool-fat.....	70.00

Melt the anhydrous wool-fat at a low heat when liquefied, add the liquid petrolatum followed by water, and stir vigorously until the mixture thickens and assumes a creamy white appearance.

Inasmuch as lanolin was considered sufficiently valuable to be included in the Pharmacopoeia, and since its preparation requires neither more skill nor labor than does any one of the official ointments, it would seem that a formula for preparing it ought to be made official.

#### ALCOHOL.

*S. L. Hilton:* U. S. P. IX Standard for total solids is too high. The total solids in alcohol should not be more than 0.001 Gm. in 50 mls when dried at 110° C. There is no trouble to obtain alcohol well within this requirement. I suggest a test for furfural be added so that a means will be at hand to distinguish and differentiate alcohol made from grain from that made from cane or molasses; all molasses alcohol contains considerable furfural, while the amount obtained when made from grain is almost if not nil. Cane or molasses alcohol is frequently sold for grain alcohol.

#### AQUA DESTILLATA STERILISATA.

*Bertha Mueller:* It is recommended that the technic for closing the flask be modified in order to guard more effectively against contamination. Cut a piece of sterile gauze about 6-8 inches wide, unfold it and place one end of it over the mouth of the flask, then lay a pledget of cotton on top of it and gently push the cotton together with the gauze down into the neck of the flask, allowing sufficient cotton to extend over the rim to act as covering, then bring the free end of the gauze over the mouth of the flask and wrap tightly around the neck, fastening it with a pin. Then put the flask over to boil according to U. S. P. directions. The U. S. P. directions do not guard effectively enough against contamination. In order to reduce to a minimum all possible chance for contamination, the mouth and the neck of the flask should be carefully protected with



sterile gauze before the flask is put over to boil. Then again, if the cotton is not wrapped in sterile gauze, there is considerable danger of some cotton hairs getting into the sterile water and acting as a foreign body there.

#### ASAFÆTIDA.

*L. T. Andrews:* Assay for alcohol-soluble content. Place a cup-shaped, tared, filter paper (prepared by folding it over a cork) in a continuous extraction apparatus, add a weighed quantity of asafetida and warm on a water-bath until all alcohol-soluble matter has been extracted. Then dry the filter, weigh the residue, and calculate the per cent.

*Prof. Oliver A. Farwell:* The standard of strength for the powder should be the same as for the mass. The U. S. P. gives 60 per cent. alcohol-soluble constituents for the mass or 50 per cent. for the powder. Powdering the mass does not change the constituents or all percentages thereof.

#### ASPIDOSPERMA.

*George E. Éwe:* The U. S. P. prescribes no alkaloidal standard.

The U. S. P. method for cinchona is satisfactory and a standard of 1 per cent. total alkaloids is suggested based upon the assay of 5 samples during the past 7 years.

The following results of assays of *Aspidosperma* were abstracted from the Proceedings of the Annual Meetings of the Pennsylvania Pharmaceutical Association for the years mentioned:

Year.	No. of samples.	Lowest.	Highest.	Average.	Number.	
					Above Standard.	Below Standard.
1915.....	2	0.95	1.22	1.08	1	1
1916.....	1	1.09	1.09	1.09	1	0
1917.....	1	1.42	1.42	1.42	1	0

In addition to these we tested one sample in 1912 which assayed 0.97 per cent. total alkaloids.

*Alfred S. Burdick:* Include an assay process for *Aspidosperma*.

#### ATROPINÆ SULPHAS.

*Alfred S. Burdick:* The melting point of atropine sulphate, when free from hyoscyamine, is 194°, not 181–183° C.

#### BELLADONNA FOLIA.

*George P. Koch:* I recommend using the primary and secondary stems in conjunction with the leaves of belladonna, stramonium and hyoscyamus, as has been shown in the data presented: On Stramonium in the *American Journal of Pharmacy*, January 1919; on Hyoscyamus Niger in the *American Journal of Pharmacy*, February 1919, and on *Atropa Belladonna* in this JOURNAL, for May 1919. The stems can be used in conjunction with the leaves and the U. S. P. requirements met. The use of stems greatly facilitates and reduces the cost of harvesting these plants, as machinery can be used in harvesting, while if the leaves alone are employed, hand labor must be used. One can get a much greater yield per acre where the stems can be utilized.

*George E. Éwe:* The whole dried plant, exclusive of the root, should be made official instead of only the dried leaves and tops. Cost of U. S. P. belladonna would be reduced since the harvesting would be simplified.

#### BELLADONNÆ RADIX.

*Alfred S. Burdick:* In the assay of belladonna root and similar assays, the final chloroform extracts of the alkaloids should be filtered through a small filter paper before evaporating to dryness.

#### BENZOSULPHINIDUM.

*George E. Éwe:* The U. S. P. melting interval appears to be low. A melting interval of 224–226° C. is proposed. One lot melted at 225° C. but was otherwise U. S. P. Three other lots which we have examined were strictly U. S. P. but had melting intervals averaging 226, 228 and 225° C., respectively. It would appear that a higher purity is now being supplied.

#### CALCII CHLORIDUM.

*Dr. A. B. Lyons:* If "calcium chloride" is taken to mean a salt containing approximately 25 per cent. of H<sub>2</sub>O (U. S. P. IX), it is quite certain that one part will dissolve in much less than

1.2 parts by weight of water. From one experiment I conclude that a solution of the salt saturated at 25° C. contains not far from 50 per cent. of  $\text{CaCl}_2$  equivalent to more than 66 per cent. of  $\text{CaCl}_2 + 2 \text{H}_2\text{O}$ . According to this, one part of the hydrated salt would require only about one-half of one part of water.

#### CALCIUM GLYCEROPHOSPHATE.

*American Drug Manufacturers' Association:* The Scientific Section of the American Drug Manufacturers' Association recommends that to the tests for Calcium Glycerophosphates there be added a titration method as follows:

Titrate about 3 Gm. of the dried salt, accurately weighed and dissolved in 250 mls of distilled water, first with half-normal  $\text{NaOH}$  V. S. and phenolphthalein T. S. as indicator, to a slight pink to determine presence of added acids, (1) then with half-normal hydrochloric acid V. S., using methyl-orange T. S. as indicator, to a slight yet distinct pink. Each ml of half-normal acid used corresponds to 0.10508 Gm. of  $\text{Ca}_3\text{H}_7\text{PO}_6$ . Each Gm. of dry calcium glycerophosphate corresponds to not less than 9.3 mls of half-normal hydrochloric acid C. S.

This is recommended as a rapid method of determining the purity of the product provided no organic acids have been added to the calcium glycerophosphate. While it was formerly the custom with some European manufacturers to add organic acids to their products, American manufacturers do not do so.

It is also recommended that the ash requirement of the U. S. P. for glycerophosphates—determined on the dry product—be reduced from 59.2 per cent. to 58 per cent. for the reason that manufacturers have found it impractical to manufacture a product having more than 58 to 59 per cent. ash. Since the  $\text{CaO}$  content, the titration, the solubility test, and the tests for chloride, sulphate and other impurities, give a definite indication of purity, while the ash seems to be a variable factor even in satisfactory products, both domestic and foreign, we suggest the above amendment.

*George E. Ewe:* The U. S. P. requirement of not less than 26.1 per cent. of  $\text{CaO}$  appears to be low. A standard for phosphorus content should be required. The four lots examined during the past two years assayed:

Sample No. 1.—33.2 per cent.  $\text{CaO}$  and 60.7 per cent.  $\text{Ca}$  pyrophos.

Sample No. 2.—30.0 per cent.  $\text{CaO}$  and 65.0 per cent.  $\text{Ca}$  pyrophos.

Sample No. 3.—38.18 per cent.  $\text{CaO}$

Sample No. 4.—28.0 per cent.  $\text{CaO}$

All of these samples answered all other U. S. P. requirements. The phosphorus content should be specified as it is by far the most important constituent.

#### CAMPHORA.

*C. L. Black:* The paragraph beginning "The specific rotation" is in conflict with the definition of specific rotation. Possibly the insertion of "observed" before "in a 200 mm. tube" would correct the error.

#### CANNABIS.

*H. C. Colson, Jr.:* 1. An impartial laboratory, *e. g.*, the Hygienic Laboratory, should be asked to prepare and distribute a standard Fluidextract of Cannabis to laboratories making physiological assays.

2. A revision of present biological standard doses for Cannabis preparations. The following doses represent the experience of this laboratory as to the degree of activity of standard Cannabis preparations, *viz.*:

F. E. Cannabis 0.10 mil per kilo dog

Tr. Cannabis 1.00 mil per kilo dog

Ext. Cannabis 0.04 Gm. per kilo dog

By having such standard Cannabis preparations on hand, it would tend to make the products of different manufacturers more uniform in strength and also the work of different laboratories would be more comparable. The present standards for Cannabis are entirely too high, as has been shown by tests in this and other laboratories. The present physiological test, as a whole, has been unsatisfactory and may be properly considered as little better than a qualitative test.

*W. A. Pearson:* See THIS JOURNAL, for October 1917.

## CAPSICUM.

*Dr. A. R. L. Dohme:* The percentage of ether-soluble oleoresin should be reduced. We have found that it is almost impossible to obtain capsicum with 15 per cent. of oleoresin. The average yield in oleoresin is about 12 per cent.

## CODEINA.

*Dr. A. R. L. Dohme:* Assay processes for the alkaloid and the sulphate should be given. An assay process is given for the phosphate, but not for codeine and codeine sulphate. Both at times are liable to vary in the amount of water present.

*Prof. Harold B. Myers:* Nomenclature of opium derivatives. It is confusing and inconsistent to list methyl-morphine under the heading codeine and to retain the scientific name for diacetyl-morphine.

## DIACETYLMORPHINÆ HYDROCHLORIDUM.

*Dr. Thomas S. Blair:* Delete from the Tenth Revision. Heroin has become a menace to society and anything possible should be done to remove the menace. In our work in the Bureau of Drug Control, heroin gives us more trouble than does any other drug, and for the reason that it is the favorite of the criminal addict. Addiction to it is very readily established. There is no question of the therapeutic usefulness of heroin properly employed. We wish that its manufacture and sale would be prohibited utterly; but its almost universal use by physicians makes this improbable. Its deletion from the U. S. P. would be a very proper first step in suppressing this dangerous drug.

*George E. Éwe:* The U. S. P. statement that diacetylmorphine hydrochloride is "insoluble in chloroform at 25° C." is not strictly correct. It is suggested that the statement be altered to read "soluble in chloroform at 25° C."

No. 1. A diacetylmorphine hydrochloride which melted at about 231° C. with slight darkening, yielded an unweighable ash upon ignition and answered all other U. S. P. requirements, was added to chloroform, which answered all U. S. P. requirements, in small portions with agitation of the mixture after each addition, with the result that the diacetylmorphine hydrochloride was obviously quite soluble in the chloroform.

No. 2. Another strictly U. S. P. diacetylmorphine hydrochloride was shaken with U. S. P. chloroform with the same result of obvious solubility.

No. 3. A third diacetylmorphine hydrochloride melting at 229° C. with slight darkening and answering all other U. S. P. requirements was added to U. S. P. chloroform in small portions. As much as 3 Gm. per 100 mils was dissolved in this experiment. The experiment was then stopped.

No. 4. A fourth diacetylmorphine hydrochloride, answering all U. S. P. requirements, was added to U. S. P. chloroform and shaken until a considerable portion of the salt remained undissolved. The mixture was then filtered and an aliquot part evaporated to dryness and the residue of diacetylmorphine hydrochloride was heated at 100° C. to constant weight. It was found that 100 mils of the chloroform solution contained 37.46 Gm. of diacetylmorphine hydrochloride.

## DIGITALIS.

*Prof. Frederick J. Wulling:* The methods of *physiological standardization* ought to be further studied with a view toward inclusion of a greater number of such standardizations into the coming revision. Coöperation should be had in this respect from medical men, especially from the pharmacologists of medical schools. When we were asked to prepare large quantities of physiologically standardized tincture of digitalis for the Medical Department of the Army, we naturally expected to standardize tincture of digitalis according to the U. S. P. method, but we were requested to use the cat method. At first we used Hatcher's ouabain cat method and later, upon further conference, we abandoned the use of ouabain in the end reaction. Out of this and some minor but related experience we have learned that physicians generally want the digitalis assayed by the cat method and not by the U. S. P. method.

*H. C. Colson, Jr.:* Under Digitalis, Strophanthus, and Squill substitute Houghton's 12-hour frog method for the one now recommended by the U. S. P. IX.

Strophanthin "K" and Strophanthin "G" should be investigated by the A. Ph. A. Committee on Physiological Assaying, with a view to recommending which is the better standard for biological assays. The investigation should deal with the chemical as well as the physiological phases of the problem.

Adoption of standard tables of doses and H. T. U. per mil for digitalis, strophanthus, and squill preparations. The experience of this laboratory (Sharp and Dohme) has shown the present methods to be unsatisfactory and such as do not give concordant results. See paper by Colson, THIS JOURNAL, January 1918, criticising the U. S. P. IX. 1-hour frog method.

Experiments by this laboratory show that the test period can be made 24 hours without materially changing the results and at the same time rendering the observation of the end-point more convenient for the average laboratory.

Houghton and others claim that Strophanthin "K" has an average M. L. D. of 0.000.001 Gm. per Gm. frog and hence contains an average of 100,000 H. T. U. per Gm. I have not been able to corroborate this claim. Many experiments made in this laboratory on different samples of strophanthin Kombe and employing the M. S. D., M. L. D. frog methods, as well as the M. L. D. cat method, have shown that by all methods Strophanthin "K" and Strophanthin "G" have practically the same toxicity and that the average M. L. D. for strophanthin "K" is 0.000.0005 Gm. per Gm. frog or an equivalent of 200,000 H. T. U. per Gm.

In this connection I would recommend that coöperative work be done by the members of the A. Ph. A. Committee in order to ascertain whether Ouabain or Strophanthin "K" should be made the standard for the biological assays of the heart tonics and also the average number of H. T. U. of each per Gm. frog.

	Standards: 24-hour 12-hour M.L.D. } or M. L. D. Method	H. T. U./mil
<i>Squill</i>		
Fluidextract U. S. P.	0.0012 mil/Gm.	80
Tincture U. S. P.	0.012 mil/Gm.	8
<i>Strophanthus</i>		
Tincture U. S. P.	0.00025 mil/Gm.	400
<i>Digitalis</i>		
Fluidextract U. S. P.	0.0012 mil/Gm.	80
Tincture U. S. P.	0.012 mil/Gm.	8

The above differs in some instances from the standards of Houghton, but the experience of this laboratory has shown that such changes are warranted.

#### ELIXIR AROMATICUM.

*S. L. Hilton:* Substitute Sugar 319 Gm. for 375 mils of Syrup. This is recommended because it is simpler and overcomes the making or using of syrup that has been made, eliminating thereby the introduction of spores.

#### ELIXIR GLYCYRRHIZÆ.

*W. H. Stone:* This elixir is recommended for deletion as there is no demand for it.

#### EMETINÆ HYDROCHLORIDUM.

*George E. Ewe:* A quantitative acidity test with a limit of 0.3 per cent. absolute HCl is preferable to the present requirement that a 1-in-20 solution be only "slightly acid" to litmus. See *American Journal of Pharmacy* for May 1919, pages 278-279. Excessively acid products are irritating upon injection.

A quantitative test for cephaeline with a limit of 3 per cent. is preferable to the present test. The test for cephaeline in the U. S. P. IX rules out the majority of the Emetine Hydrochloride on the market, which it reacts with, yet a material proportion of cephaeline is not present. A definite basis for comparison is necessary in order to prevent controversy.

#### EMPLASTRUM BELLADONNÆ.

*American Drug Manufacturers' Association:* Acting on the advice of its Committee on Standards and Deterioration, the American Drug Manufacturers' Association recommends that

the Pharmacopoeial standard for belladonna plaster be changed from that of the U. S. P. IX to that of the British Pharmacopoeia of 1914. This recommendation is based, first, on the scarcity of the drug belladonna; second, the difficulty of obtaining extracts of proper consistency and strength to make plasters; and, third, on the necessity of conserving the stock of belladonna for other important medicinal purposes.

The U. S. P. IX requires belladonna plasters to contain not less than 0.35 per cent. or not more than 0.40 per cent. of mydriatic alkaloids. The British Pharmacopoeia of 1914 established a standard of 0.25 per cent. of the alkaloid of belladonna.

In explanation thereof, it may be stated that the standard of belladonna plasters in the British Pharmacopoeia was 0.5 per cent., but not very long after its adoption the British Pharmaceutical Conference endorsed the standard 0.25 per cent. alkaloid, and the latter strength became the popular plaster, leading the British revisers of the Pharmacopoeia in 1914 to adopt the standard of 0.25 per cent. alkaloid. We may also call attention to the fact that in the Pharmacopoeia VII, the standard was approximately 0.3 per cent. alkaloid. It has been found in practice that a plaster containing this amount, 0.25 per cent. belladonna alkaloid, will give satisfactory therapeutic results. While the manufacturers of medicinal plasters have adopted this standard as an emergency war standard, they believe it should be adopted also as a practical standard in the U. S. P. In so doing there will be secured uniformity with the British Pharmacopoeia, thus covering the greater part of the world where belladonna plasters are sold.

The Association also recommends that the U. S. P. VIII process for assaying belladonna plaster be adopted by the Committee in place of that of the 9th Revision. Experience has shown that the process of the 9th Revision is unreliable in the hands of chemists generally. They have been troubled by emulsions with which have come variations that have run into material amounts, in some cases sufficiently great to vitiate the accuracy of the work.

On the other hand, the method of the 8th Revision in the hands of chemists generally has given results as nearly concordant as those obtained on the average with assay processes of other substances.

#### EXTRACTUM ACONITI.

*George E. Éwe:* A reduction in alkaloidal standard to 1.6 to 2.0 and a corresponding change in the physiological standard is suggested. (See Aconitum, above.)

*H. C. Colson, Jr.:* Preparation of a standard extract, a standard fluidextract, and a standard tincture of aconite by an impartial laboratory, *e. g.*, the Hygienic Laboratory, and the distribution of samples thereof to laboratories making physiological assays is recommended.

Substitution of a 24-hour test period for the present 12-hour guinea pig test is also recommended.

Seasonal variations, or the difference in susceptibility of various lots of guinea pigs should be ascertained and allowed for by the use of aconitine, a standard sample of which should also be distributed by a designated laboratory.

A standard table of doses for each type of aconite preparation should be incorporated in the description of the physiological assay of aconite. These tables should be worked out by Committee on Physiological Testing of the American Pharmaceutical Association.

Such preparations would be of great service in biologically standardizing aconite preparations. With such standards on hand, the preparations of different manufacturers should be approximately uniform in strength.

The results of many aconite assays made in this laboratory (Sharp and Dohme) have shown that a 24-hour test period gives practically the same per cent. activity as does the present 12-hour period, and furthermore, the former period is a more convenient one for the average laboratory to use.

In comparative tests, or in coöperative work by the various laboratories these recommendations, if carried out, would tend to give more reliable and concordant results than can be obtained by present methods.

#### EXTRACTUM HYDRASTIS.

*W. H. Stone:* A reduction of standard to 8 to 9 per cent. is suggested. It is practically impossible to get an extract of 9 to 11 per cent. strength and it is sometimes necessary to fortify the extract with hydrastine alkaloid. A standard of 8 to 9 per cent. can be maintained on a practical scale.

*George E. Ewe:* The standard of 8 per cent. alkaloids is suggested. The standard of the fluidextract is 1.8 to 2.2 per cent. The solid extract should be four times the strength of the fluidextract. It is more difficult to make a solid extract of present U. S. P. strength than a fluidextract of present U. S. P. strength.

#### EXTRACTUM PHYSOSTIGMATIS.

*George E. Ewe:* U. S. P. method has not given reliable results in my hands. A more reliable method is proposed. See THIS JOURNAL, p. 1006, December 1919.

#### FERRUM REDUCTUM.

*George E. Ewe:* Practically all reduced iron on the market contains sulphides in excess of the U. S. P. allowance, yet we have never received a complaint of annoying eructations of H<sub>2</sub>S following the use of this material. A quantitative test should be included in the U. S. P. based on the BaSO<sub>4</sub> method. See p. 99 of "Commercial Laboratory Notes," Petty. A maximum allowance of sulphur should be included in the U. S. P. based on what manufacturers have found to be acceptable to the trade and practical to adhere to. The U. S. P. test appears to be too stringent or the market quality needs improvement.

#### FLUIDEXTRACTUM ACONITI.

*George E. Ewe:* A reduction in alkaloidal standard to 0.4 to 0.5 Gm. per 100 mils and a corresponding change in the physiological standard is suggested. See Aconitum above.

*H. C. Colson, Jr.:* See comments under Extractum Aconiti.

#### FLUIDEXTRACTUM ASPIDOSPERMATIS.

*George E. Ewe:* It is suggested that this fluidextract be directed to be assayed and that the standard be 1 per cent. total alkaloids. An assay similar to that for fluidextract of cinchona would be satisfactory. We have had no difficulty in maintaining the standard of 1 per cent.

#### FLUIDEXTRACTUM CASCARÆ SAGRADÆ.

*Bertha Mueller:* It is recommended that the formula of the U. S. P. VIII replace the present formula. The present formula is not workable. It is a physical impossibility to extract cascara with water, as it will not percolate through the drug, but causes an undue swelling of the same with a corresponding clogging, and eventually fermentation sets in. It is most unfortunate that the formula of the Eighth Revision was not retained, as it is workable and yields a highly satisfactory product.

#### FLUIDEXTRACTUM CASCARÆ SAGRADÆ AROMATICUM.

*Bertha Mueller:* It is recommended that the formula of the U. S. P. VIII, with the technic somewhat simplified, replace the present formula. Mix the cascara, licorice root, and magnesium oxide thoroughly, moisten with the menstruum given in the U. S. P. VIII. Allow to macerate for 48 hours and extract according to the U. S. P. VIII directions.

The present formula is not workable for the same reason as that given under fluidextract of cascara sagrada. If it is deemed advisable to use saccharin for the purpose of sweetening, though it does not seem necessary, the amount used should be reduced. The present official preparation is altogether too sweet.

#### FLUIDEXTRACTUM CIMICIFUGÆ.

*W. H. Stone:* Change of menstruum from U. S. P. alcohol to a mixture of alcohol 3 parts and water 1 part is suggested. This menstruum will easily exhaust the drug and will reduce the cost of manufacture.

#### FLUIDEXTRACTUM COLCHICI SEMINIS.

*W. H. Stone:* It is suggested that the yield be obtained by direct percolation. The drug is easily exhausted if properly powdered and the application of heat to the extra percolate is liable to decompose the alkaloids that may be present.

#### FLUIDEXTRACTUM ERGOTÆ.

*John K. Thum:* It is recommended that the use of hydrochloric acid, or any acid for that matter, in the menstruum for extracting this drug be dropped. The presence of acid prevents its use for hypodermic purposes. The extraction of this drug by the use of chloroform as

recommended in the N. F. for the making of the aqueous extract of ergot, or ergotin, shows that an acid is unnecessary, as this preparation gives evidence of all the therapeutic properties characteristic of this drug. Physicians often have need to give this drug hypodermatically and the fluidextract offers a ready means so to do as its high content of alcohol assures its being sterile, but the presence of an acid makes its administration very painful to the patient.

#### FLUIDEXTRACTUM GLYCYRRHIZÆ.

*Bertha Mueller:* It is recommended that the formula in the U. S. P. Seventh Revision replace the present formula. Though the formulas given in the U. S. P. VIII and in the present U. S. P. may be workable in the hands of large manufacturers who have the necessary equipment for forcing the directed menstruum through the drug, such is not the case with retail druggists. The formula is not workable for the same reason as that given in connection with fluidextract of cascara.

*Dr. J. M. Francis:* Any one attempting to produce this fluidextract in accordance with the instructions of the U. S. P. cannot but be impressed with the fact that it is "an utter pharmaceutical abomination."

The drug contains such a large amount of extractive matter of several different kinds that when extracted with water as prescribed, the resultant fluidextract will be almost as heavy as ordinary glycerin and moreover, it will contain a floating precipitate which makes the fluid exceedingly unsightly.

If one attempts to age the fluid so as to permit of this precipitated matter settling out, the final result is that the pharmacist will throw away about 50 per cent. of the total fluidextract, as the precipitated portion, amounting to about half the liquid, will not clear up, and moreover it cannot be filtered. I am calling attention to this matter, as it is one of the subjects which should receive preferred attention at the hands of the proper committee on revision.

#### FLUIDEXTRACTUM GRANATI.

*W. H. Stone:* It is recommended that this fluidextract be deleted as there is very little demand for it.

#### FLUIDEXTRACTUM HYOSCYAMI.

*Prof. A. R. Bliss, Jr.:* The Pharmacopoeia directs that 25 mils of the sample be used and the directions for assaying fluidextract of belladonna root be followed. The latter method recommends that after measuring out 10 mils of fluidextract of belladonna root, 10 mils of water, and 2 mils of ammonia, water be added, followed by the shaking out process with chloroform. While these amounts of water and ammonia water are sufficient to precipitate the resins and alkaloids in the belladonna assay where only 10 mils of the sample are used, they are insufficient to throw them out in the case of 25 mils of fluidextract of hyoscyamus. The results of this method as described in the U. S. P. are usually incorrect and often furnish the basis for controversy. In revising this method, the amounts of water and ammonia water should be increased sufficiently to bring about complete precipitation. With this change the writer believes the method will be satisfactory.

#### FLUIDEXTRACTUM PODOPHYLLI.

*W. H. Stone:* A menstruum of 4 parts alcohol and 1 part of water is suggested. This menstruum effectually extracts the drug and results in a reduction of cost of manufacture.

*George E. Éve:* An assay process and standard is suggested. The following method, based on the U. S. P. process for the assay of podophyllum, is suggested:

Assay for resin. Sample 10 mils. Evaporate in a 200 mil beaker until reduced to the consistency of a thin syrup. Pour 10 mils of ice water containing 0.1 mil of concentrated hydrochloric acid into the syrupy concentrated sample of fluidextract and stir until all lumps are broken up. Immediately filter off the precipitated resin while still ice-cold on a counterpoised filter, using suction and washing the beaker, resin and filter thoroughly, using not more than 25 mils of ice water. Dry the resin in the filter to constant weight at 100° C. Standard 3 per cent. dry resin.

NOTE: The drying of the resin in the air is a tedious and long drawn out procedure. It is better to dry the filter and resin in the oven at 100° C. This will not necessitate a change in the standard, as air-dried podophyllin resin contains but little moisture. To prove this we al-

lowed 5 lots of U. S. P. resin from different sources to remain spread out and exposed to the air, but protected from dust by 2 layers of cheese-cloth, for 2 days, and then determined the amount of loss at 100° C. The respective losses were 3.64 per cent., 4.00 per cent., 4.02 per cent., 4.03 per cent., and 4.08 per cent.

While this method is satisfactory if a standard of 3 per cent. dry resin is adopted, it does not give the full yield of resin like the "shake-out" method proposed by Parke, Davis & Company, when the present U. S. P. was in process of formation.

While we have had no great experience with the shake-out method we have determined that it gives higher yields of resin. The resin answers all U. S. P. requirements. The method yields more concordant results in different hands. (This is because the precipitation method involves precipitating and washing partially water-soluble resins in the presence of water.)

#### FLUIDEXTRACTUM SABAL.

*W. H. Stone:* It is suggested that the fresh, ripe berries be used instead of the partially dried ripe fruit and that U. S. P. alcohol be used as a menstruum. Fresh berries make a preparation superior to the dry berries. U. S. P. alcohol must be used in order to properly extract the fresh berries and keep the fluidextract clear and bright.

#### FLUIDEXTRACTUM SENEGÆ.

*Bertha Mueller:* It is recommended that the senega, previous to extraction, be treated with boiling water; that diluted alcohol be used as menstruum; that the acidity of the finished product be ascertained and the amount of the neutralizing agent be gauged accordingly.

The following formula is submitted:

Senega in No. 30 powder . . . . .	1000 Gm.
Boiling Water . . . . .	2000 mils
Potassium hydroxide . . . . .	
Diluted Alcohol to make . . . . .	1000 mils

Pour 2000 mils of boiling water upon the drug, mix thoroughly, cover up tightly and allow to stand for a period of 6 to 8 hours. Then dry at a moderate heat, and exhaust the drug with diluted alcohol. Neutralize the finished product with the required amount of potassium hydroxide, ascertained by titration.

The present U. S. P. formula yields an unstable preparation, and the syrup prepared from it is equally unsatisfactory because of its instability. It is quite impossible to neutralize fluidextract of senega with any degree of accuracy unless the acid content of the preparation has been ascertained, because the acidity varies with different lots of the drug. Inasmuch as diluted alcohol exhausts the drug quite as completely as a stronger alcoholic menstruum, there appears to be no good reason for using the latter.

#### FLUIDEXTRACTUM SCILLÆ.

*Dr. A. R. L. Dohme:* The manufacturing process should be revised. See paper by Messrs. Grantham and Colson, THIS JOURNAL, November 1918.

*H. C. Colson, Jr.:* The present method for manufacturing fluidextract of squill is cumbersome, and it has been found that a simplified process (see THIS JOURNAL, November 1918) yields a product which is physiologically and chemically the equal of one obtained by the present U. S. P. method.

#### FLUIDEXTRACTUM SUMBUL.

*W. H. Stone:* U. S. P. alcohol is suggested as the menstruum. My experience shows that U. S. P. alcohol is a better means of exhausting the drug than the mixture of alcohol, 4, water, 1, now prescribed.

#### FLUIDEXTRACTUM TRITICI.

*W. H. Stone:* A temperature of not over 120° F. should be specified during evaporation of the aqueous percolate previous to the addition of the alcohol. The aqueous percolate contains



a large quantity of caramelizable substances and if a temperature above 120° F. is employed it is liable to become scorched, thus giving a bad odor, taste and color. A superior preparation is attainable.

#### FLUIDEXTRACTUM UVAE URSI.

*W. H. Stone:* Diluted alcohol is better for exhausting the drug than the present menstruum. Practical experience bears out this statement.

#### FLUIDEXTRACTUM ZINGIBERIS.

*W. H. Stone:* Yield by direct percolation is suggested. Concentration of extra percolate results in great loss of active constituents. Careful direct percolation to 1000 mils yields practical exhaustion. Time and labor of manufacture are reduced.

*George E. Éwe:* A standardization is recommended. The following method has given excellent results in these laboratories (H. K. Mulford and Company): Sample 15 mils. Place on 10 Gm. of oak-sawdust contained in a 6-inch evaporating dish, mix well and allow to dry spontaneously for about 6 hours or until the odor of alcohol is eliminated. Place the impregnated sawdust in a bottle; add 10 mils of ether. Shake for four hours. Filter off an aliquot of 50 mils. Place the aliquot in a tared 250 mil beaker. Allow the ether to evaporate on the steam-bath and dry at 110° C. to constant weight. Correct the weight of non-volatile ether extract by subtracting that found in the oak-sawdust by a blank determination. This blank determination should be made on a large lot of oak-sawdust and the assayed oak-sawdust then reserved for this assay.

Regarding standard, we have found all of the fluidextracts which we have made to range between 2.00 and 3.2 Gm. non-volatile extract soluble in ether, but the standard for the fluidextract should correspond to that of the drug so that the most suitable standard would be not less than 2 Gm. per 100 mils. Standardization is desirable for purposes of uniformity of commercial preparations.

#### GAMBIR.

*George E. Éwe:* Much of the gambir offered is soft and not friable as required by the U. S. P. Softness is due to moisture. The U. S. P. should describe the two conditions of gambir. A maximum moisture content of 12 per cent. should be prescribed for friable gambir.

Soft gambir should be described as follows: Irregular pieces of various sizes, externally pale grayish brown to reddish brown, more or less dull and porous; internally soft and of a light grayish brown or dull earthy color; sometimes with a hard friable exterior of varying thickness; inodorous; taste bitterish and very astringent. (Microscopic examination as in U. S. P. IX.)

Macerate 1 Gm. of gambir, etc. (U. S. P. IX, not less than 75 per cent. of soft gambir is soluble in water and not less than 70 per cent. in alcohol).

Ash not more than 8 per cent.

NOTE: Soft gambir may be used in place of friable gambir, using 1 per cent. more of the soft gambir for each per cent. of moisture which it contains over 12 per cent.

The following table shows the results of examination of 7 lots of soft gambir and 10 lots of friable gambir examined since September 1916.

GUM GAMBIR				
SOFT.				
Moisture.	Alcohol-soluble.	Water-soluble.	Ash.	All other U. S. P. requirements.
....	86.6	....	....	O.K.
....	83.4	....	....	O.K.
....	80.7	....	....	O.K.
Excessive				
....	85	....	....	O.K.
41.1	87.9	96	4	O.K.
....	77.8	....		O.K.

## FRIABLE

....	....	....	3.5	O.K.
....	....	....	2.0	O.K.
....	58	....	....	O.K.
....	55	....	....	O.K.
....	72.5	80.5	6.5	O.K.
....	74.1	81.1	5.6	O.K.
....	58	65.6	4.59	O.K.
....	83.9	....	....	O.K.
....	76.1	....	....	O.K.
....	60.15	58.63	6.03	O.K.

Unfortunately the figures corresponding to the blank spaces in the table were not recorded by the analysts.

Also see "Note on Soft Gambir" in "Laboratory Notes" by George E. Éwe and Chas. E. Vanderkleed, presented at the annual meeting of the American Pharmaceutical Association in 1914.

In lieu of adopting standards for soft gambir, the Revision Committee should seek the coöperation of the jobber in placing none but friable gambir on the market.

Friable gambir is preferable, but since the jobber finds it necessary to offer the soft variety, standards should be set for the soft variety by the Revision Committee.

## GELSEMIUM.

*Alfred S. Burdick:* Include an assay process for Gelsemium.

## GUAIACOLIS CARBONAS.

*C. L. Black:* It has been found that pure specimens may fail to give the test for guaiacol, U. S. P. IX, page 211, through the interference of minute quantities of acid taken up by the ether specified for the extraction. It is necessary to wash the ether and pass through a dry filter, or better still, use chloroform for the extraction.

## GUAIAACUM.

*George E. Éwe:* It appears to be difficult to obtain guaiac with an alcohol solubility of 85 per cent. It is recommended that this requirement be reduced to 80 per cent. See L. J. Lipman's contribution to Committee on Drug Market, Proceedings Pennsylvania Pharmaceutical Association 1919, p. 86. A reduction is warranted, owing to the present market quality.

## HEXAMETHYLENAMINA.

*L. T. Andrews:* Suggested method of assay. Add 35 mils of  $\frac{N}{1}$  H<sub>2</sub>SO<sub>4</sub> V. S. to 1 Gm. of Hexamethylenamine, boil on an open flame for five minutes and neutralize the excess of sulphuric acid with  $\frac{N}{1}$  NaOH V. S., using methyl-orange T. S. as indicator. The amount of  $\frac{N}{1}$  H<sub>2</sub>SO<sub>4</sub> V. S. taken, less the amount of  $\frac{N}{1}$  NaOH V. S. required, multiplied by 0.035, indicates the per cent. of absolute Hexamethylenamine.

## HYDRARGYRI SALICYLAS.

*Dr. A. R. L. Dohme:* The assay process might be simplified. Treat a weighed amount of salt with sulphuric acid and nitric acid and titrate the solution thus obtained with potassium sulphocyanide as directed under mercury.

## HYDRASTINA.

*Alfred S. Burdick:* The reaction of a saturated solution of hydrastine in alcohol is practically neutral to litmus paper, not alkaline.

## HYDRASTIS.

*George E. Éwe:* The standard of 2.5 per cent. ether-soluble alkaloids appears to be low. Data for the establishment of a higher standard is submitted. Results obtained upon assay are as follows:

Year.	No. of assays.	Lowest assay.	Highest assay.	Average.	Standard.	Number.	
						Above Standard.	Below Standard.
1911.....	11	2.884	4.850	3.740	2.5	11	0
1912.....	5	3.80	4.850	4.197	2.5	5	0
1913.....	6	2.90	4.09	3.41	2.5	6	0
1914.....	2	3.22	3.42	3.32	2.5	2	0
1915.....	5	3.16	3.98	3.63	2.5	5	0
1916.....	10	2.15	5.59	3.83	2.5	9	1
1917.....	9	2.65	3.86	3.29	2.5	9	0
1918.....	2	3.94	4.47	4.20	2.5	2	0
1919.....	10	2.97	4.06	3.64	2.5	10	0
Totals.....	60					59	1

A higher standard appears to be desirable to accord with the market quality of this drug.

HYOSCYAMUS.

*George P. Koch:* See recommendations under *Belladonna Folia*.

*George E. Éwe:* The whole dried plant either with or without the root harvested in the flowering or fruiting stage and before the plant has matured and dried should be made official instead of only the leaves and flowering and fruiting tops. Cost of U. S. P. *hyoscyamus* would be reduced since the harvesting is simplified. An increased supply is made available.

LINIMENTUM CAMPHORAE.

*I. Lewyn:* I recommend the use of peanut oil in place of cottonseed oil. Prepared with peanut oil I have obtained a very clear stable product, whereas with Cottonseed oil it often turns turbid or leaves a sediment; furthermore, cottonseed oil, as obtained in the market, is quite often mixed with other oils. Peanut oil is also more economical, and I believe the body absorbs it more readily.

*Dr. A. R. L. Dohme:* The limits of the requirement should be more liberal, considering the difficulties which are encountered in the assay process. We recommend the following procedure for assaying the liniment:

The liniment is first polarized directly. Since, however, in controlling the quality of the camphor used in making the preparation a 20 per cent. alcoholic solution rotates less than a 20 per cent. solution of camphor in cottonseed oil, the ratio being 1 : 1.19, a factor has to be applied. The percentage of camphor in the liniment can be calculated by applying the following formula:

$$\frac{4.15 \times R_1 \times 2.032}{R_{11}}$$

in which 4.15 equals the reading in a 100 mm. tube, a solution of 10 Gm. of official camphor in q. s. alcohol to make 100 mils.

$R_1$  is the reading of the camphor liniment in a 100 mm. tube.

$R_{11}$  is the reading of a 10 per cent. alcoholic solution *w/v* of the camphor obtained from the liniment.

The present assay process is tedious and reliable only within certain limits.

LINIMENTUM CHLOROFORMI.

*I. Lewyn:* I recommend the use of peanut oil instead of soap liniment. It is more economical and more stable and can be prepared instantly, thus preventing the evaporation of the chloroform.

LINIMENTUM SAPONIS.

*I. Lewyn:* I recommend the use of camphorated oil (prepared with peanut oil as per my suggestion) in place of soap and camphor:

Camphorated Oil.....	250 Gm.
Oil of Rosemary.....	700 mils
Alcohol.....	700 mils
Water, q. s., to make.....	1000 mils

Shake the mixture until it is thoroughly clear.

This process is simple and is more economical since the price of Castile soap has advanced..

## LINIMENTUM AMMONIAE.

*I. Lewyn:* I recommend the use of peanut oil instead of sesame oil. Sesame oil is more expensive and it does not keep so well. Peanut oil is a home-product.

## LINIMENTUM CAMPHORÆ.

*Edward A. Wickham:* It is recommended that olive oil be used in place of cottonseed oil. Olive oil does not get "gummy" as cottonseed oil has a tendency to do. It can as safely be rendered sterile and would, no doubt, serve as well for hypodermatic use.

## LIQUOR ARSENI ET HYDRARGYRI IODIDI.

*Dr. A. R. L. Dohme:* The total arsenic as well as the arsenic in the arsenous state should be determined also. It has been stated that the arsenic in the arsenous state is easily oxidized to arsenic in the arsenic state.

## LIQUOR CRESOLIS COMPOSITUS.

*Dr. A. R. L. Dohme:* A method for determining the water in this preparation should be given.

*Bertha Mueller:* It is recommended that cottonseed oil be substituted for linseed oil, and that the technic for making the solution be simplified.

Dissolve the caustic potash in hot water in a container that will retain heat. When solution has taken place, add the oil followed by the alcohol. Stir until saponification has taken place, then allow to remain undisturbed for about a half hour to insure complete clarification. Then add the cresol with occasional stirring until a clear solution is obtained.

Cottonseed oil is less expensive and has a more agreeable odor than linseed oil. The present U. S. P. directions are unnecessarily complicated.

*The Barrett Company:* Omit alcohol from formula and cut down excess of potassium hydroxide used. Use 60 Gm. of potassium hydroxide in place of 80 Gm. or 43 Gm. of sodium hydroxide in place of 54 Gm. The quantity of potassium hydroxide given in the formula is a decided excess and is both unnecessary and harmful. The revised figure still leaves a slight excess of hydroxide over the amount necessary to saponify the linseed oil. The sodium hydroxide figure is changed in proportion to the potassium hydroxide. The use of alcohol in this compound is unnecessary and should be omitted.

*S. L. Hilton:* To overcome the tedious process of making soap from linseed oil and the saving of time, this solution can be made extemporaneously.

Cresol.....	500 Gm.
Oleic Acid.....	226 Gm.
Sodium Hydroxide.....	35 Gm.
Water q. s. to make.....	1000 mils

Weigh the oleic acid in a tared flask or bottle and add the cresol, mix well, then add the sodium hydroxide previously dissolved in 100 mils of water, shake thoroughly and add water to make 1000 mils.

This is a very much simpler process, is less expensive, and makes a much better preparation.

(To be continued.)

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The greatest skill is not in enlisting the services of men but in enlisting their interests, their best efforts and their loyal support.

Criticizing the work of organizations is a simple matter but criticism often rushes in where construction fears to tread.