COMMITTEE REPORTS

REPORT OF THE COMMITTEE ON THE UNITED STATES PHARMACOPOEIA.

It is with much interest and satisfaction that the members of this Committee have perused the pages of the new U. S. Pharmacopoeia and have noted the various comments thereon that have appeared from time to time in the pharmaceutical press.

We are very glad to note that comments and reviews as have appeared are on the whole kindly and that this Ninth Revision continues to maintain for the U. S. P. the foremost position among the pharmacopoeias of the world.

With the increase in the magnitude of the work of revision, the time required must necessarily be greater and, owing to the rapid growth of our materia medica, it would seem that a revision at less remote intervals or at least a supplement would be desirable.

The admissions to the U. S. P. on the whole seem to be well chosen and conservative. Regret is expressed by some members of the medical profession that acetyl salicylic acid was not included in this list. Concerning the deletions there is a greater difference of opinion. Most physicians dislike to have a remedy that they are accustomed to use dropped from the official list, and such deletions do not seem to us to add to the usefulness and purpose of the U. S. P.

In the short time at the disposal of the Committee this year it has been impossible to cover seriatim the entire scope of the new book. The Committee does not desire to make any general or specific recommendations at this time. The following observations, however, have been made by the members and are hereby recorded for future reference.

NOMENCLATURE.

That the botanical names employed in the Pharmacopoeia should be in accord with the best knowledge and the best usage of botanists goes without saying. An article has been recently published by Mr. O. A. Farwell in the *Druggists Circular* for April 1917, criticising in detail the botanical nomenclature of the U. S. P. IX. Mr. Farwell's work has been done with intelligence and thoroughness, the majority of his criticisms pointing out needed changes. His article is timely and should open the way for more extended remarks and some lively discussions among the botanists.

It seems particularly unfortunate that the Pharmacopoeia should for any real or fancied reason adopt titles that may lead to confusion or to depart from an established custom as has been done in the following instances:

Ferri et Quininae Citras U. S. P. IX is entirely different from the *Ferri et Quininae Citras* of the U. S. P. VIII.

Ferri Phosphas U. S. P. IX is not really ferric phosphate and tends to confuse the ferric phosphate of the pharmacist with the ferric phosphate of the chemist.

Cascara Sagrada U. S. P. IX. What is the precedent for this change?

VEGETABLE DRUGS.

The following errors have been noted:

Cascara Sagrada. In the description of the sections (second paragraph, third line) the stone cells are described as being in the outer bark. They are usually considered as being in the middle bark, the cork being considered the outer bark.

Foeniculum. In the description of the sections (second paragraph, tenth line) the two vitae are on the commissural surface and not on the dorsal surfaces as stated.

Viburnum Prunifolium. The drug should be defined as the dried bark of the root since that is the article subsequently defined.

ASSAY PROCESSES.

We are pleased to note that the assay processes both organic and inorganic have been greatly improved and extended. The following points have come to our notice:

Acetonum. To insure accuracy, should read, "Partially fill with distilled water a stoppered weighing bottle and note the exact tare; then introduce about 1 mil of acetone, stopper and weigh accurately."

Acidum Aceticum Glaciale. In the assay the directions should read, "Introduce into a stoppered weighing bottle about 10 mils of distilled water and take the exact tare of the whole, add about 2.5 mils of glacial acetic acid and weigh accurately, etc." The text calls for simply a "tared flask" to which 10 mils of distilled water (weight deduced presumably from its measure and the stopper) comes in as an afterthought apparently.

Acidum Hydrochloricum and Acidum Nitricum. Comments similar to those under *Acidum Aceticum Glaciale* apply equally well to these.

Acidum Citricum. This is distinctly an efflorescent substance although the pharmacopoeias generally describe it as "permanent in the air" or at most as efflorescent at temperatures above 30° C. As long as it remains in translucent crystals it may be regarded as uneffloresced but when in powder this cannot be assumed and we know that the crystals in time become quite opaque from efflorescence unless kept in well closed containers. In the assay, therefore, the sample should always be rendered anhydrous before weighing, by drying at 100° C. to constant weight. The assay will then show in the dried salt not less than 99.5 percent of $C_6H_8O_7$. Each mil of normal potassium hydroxide V. S. will correspond to 0.06402 Gm. of $C_6H_8O_7$ and each Gm. of the dried acid will correspond to 15.56 mils of normal potassium hydroxide, V. S. (if pure, 15.62 mils).

Acidum Sulphuricum. After mixing 1 volume of the acid with 50 of distilled water, is it necessary to cool the mixture before titrating?

Acidum Sulphuricum Aromaticum. It has been shown that the use of a reflux condenser in the preparation of a sample for assay is a mistake. The proper procedure is to add to the acid three times its volume of distilled water and heat in an uncovered beaker on a boiling water bath for four hours to effect hydrolysis of the ester present. Titration will then show correctly the quantity of sulphuric acid originally present. The results obtained from the assay in the text are much too low.

Aconitum. Dr. H. Engelhardt points out that the assay processes for both the fluidextract and solid extract and possibly the tincture should be thoroughly revised, it being impossible to obtain concordant results when using cochineal as indicator. Methyl orange appears to give better results. A detailed report is forthcoming.

Alkaloids and Alkaloidal Drugs. In a few instances a rubric is given for the alkaloids and alkaloidal salts. This might well be extended to all of them since it is a well-known fact that many contain an excess of water and, etc. It is becoming more and more imperative to qualitatively examine the alkaloidal residues obtained in the assay of galenical preparations. Some attention to this is advocated for the U. S. P. X.

In several of the assay processes of the U. S. P. IX for fluidextracts and tinctures, purified oak sawdust is employed. This oak sawdust is not so easily obtained as one without experience might imagine. Dr. A. B. Lyons suggests that cheese cloth is a convenient substitute easily obtained and easily manipulated.

Alumen. Under the assay process the surprising statement is made that "the aluminum oxide obtained corresponds to not less than 99.5 percent of alum assayed." The meaning is that the aluminum oxide obtained corresponds to $AlNH(SO_4)_2 + 12H_2O$ or $AlK(SO_4)_2 + 12H_2O$ as the case may be, equal in weight to 99.5 percent of the alum taken for the assay.

Alumen Exsiccatum. Although it is required that the label state whether it is potassium or ammonium alum from which the exsiccated product is made, there is no intimation that one differs materially from the other. It requires that not more than 2.5 percent of the dried alum be insoluble in water. Of course if made from potash alum it would be wholly soluble. There seems to be no reason why an allowance of 3.5 percent for impurities sho uld be made in case a potassium alum is used. Query: Does the insoluble residue consist of Al_2O_3? If so, it should be strongly ignited before weighing. Then since the aluminum oxide constitutes something like 20 percent of the salt, the amount of impurity indicated will be much greater than seems to have been assumed in preparing the article on Exsiccated Alum.

Ammonii Carbonas. In the assay the reading should be, "Put into a stoppered weighing bottle about 10 mils of distilled water, ascertain the exact tare; add about 2 Gm. unaltered, translucent ammonium carbonate and weigh accurately. When the salt is dissolved, transfer the solution to a "suitable beaker or flask with the aid of about 40 mils of distilled water, add 50 mils of normal sulphuric acid, V. S., and titrate the excess of acid with normal potassium hydroxide, V. S. using methyl orange T. S. as indicator."

Aqua Ammoniae Fortior. It would be well to require that a stoppered weighing bottle be used in weighing the sample for assay, as in the case of water of ammonia, 10 percent.

Bismuth Salts. The method for the estimation of the bismuth oxide in these is a rather crude one. A convenient electrolytic method would be acceptable.

Caffeina Citrata. In the third line from the bottom of the assay, insert before "Citrated Caffeine" the word "dried."

Caffeinae Sodio-Benzoas. In the assay for sodium benzoate the statement should be made that "each mil of half-normal sulphuric acid V. S. used corresponds to 0.07202 Gm. of $NaC_7H_5O_2$. Each Gm. of the dried mixture corresponds to not less than 6.94 nor more than 9.50 mils of half-normal sulphuric acid V. S." Note that in the assay of sodium benzoate, p. 383, the salt is dried at 110° C., while in this case the drying is done at 80° C.

Hydrargyri Iodidum Rubrum. Only the electrolytic method is given. An alternate method would be acceptable.

Liquor Cresolis Compositus. A method for the assay of this preparation is needed, especially a method for the estimation of the amount of water in the product.

Liquor Potassii Hydroxidi. There is something puzzling about the expression at the top of page 253: "The solution shows not more than 5.5 percent of alkalinity calculated as KOH (carbonate)." The word "carbonate" should be deleted or else explained. As a matter of fact this test should form part of the assay process, which should be so performed as to show the presence of not less than 4.5 percent of KOH, and to limit the total alkali, including the carbonate, to the equivalent of 5.5 percent. This comment applies equally to *liquor sodii hydroxidi*.

Opium and its Preparations. A reduction in the amount of slaked lime used in the assay would seem feasible.

Resina Jalapae. In the determination of the solubility of the resin in chloroform and in ether, no account is taken of the amount likely to be absorbed by the filter paper. The evaporation of an aliquot part would give more concordant results.

Spiritus Ammoniae Aromaticus. An assay process is desirable since an appreciable loss of ammonia is liable to occur during the manufacturing process.

Tinctura Iodi. The heating of the evaporated tincture until the free iodine is expelled is liable to produce losses. It is much simpler to convert the iodine into halide by thiosulphate or preferably sulphite, titrating the total amount of halide, etc.

Zincum. In the electrolytic estimation of zinc it is recommended to use a nickel dish or a platinum dish upon which a thin layer of silver or copper has been previously deposited. Dr. H. Engelhardt points out that a mercury cathode cup gives just as good results and is even more rapid than the nickel dish method.

BIOLOGICAL ASSAYS.

The value of these has been officially recognized for the first time in the U. S. P. IX. This is a move in the right direction, but it is very unfortunate that the only compulsory standard, that of cannabis, should lack the essence of standardization, namely a standard for comparison. Why not have the United States Public Health Service establish the standard here as in the case of antitoxins?

PREPARATIONS.

But little comment on these is believed to be justifiable at this time.

Collodium Flexile. Some doubt is expressed as to the advisability of the substitution of camphor for Canada balsam.

Emplastrum Plumbi. Some experiments have indicated that it requires about five hours' boiling to complete the reaction in this preparation. Since constant stirring with a wooden spatula is also one of the requirements, this formula is not likely to become popular with the retail pharmacist nor to stimulate in him an interest in manufacturing pharmacy.

Unguentum Iodi. Although this ointment is not to be dispensed unless it has been recently prepared, a rapid absorption of the iodine takes place and experiments with vehicles other than lard are suggested.

EFFLORESCENT SALTS.

In the case of a considerable number of more or less efflorescent salts the new Pharmacopoeia has abandoned the principle of the "Rubric of Purity," heretofore consistently followed in dealing with nearly all mineral salts, and has established new standards essentially fallacious. The

fallacy depends upon the fact that assay processes are prescribed for such salts without requiring that they be rendered anhydrous, or at least that they be brought to a definite condition of hydration before the sample taken for assay is weighed.

The list of salts to which this criticism applies includes the following which will be discussed seriatim: Copper sulphate, ferrous sulphate, magnesium sulphate, sodium sulphate, zinc sulphate, sodium acetate, sodium arsenate, sodium borate, sodium phenolsulphonate, sodium phosphate, sodium thiosulphate, lead acetate, zinc acetate, zinc phenolsulphonate, zinc valerate, and potassium and sodium tartrate.

Cupri Sulphas. Crystallized copper sulphate, which is the official salt, contains 5 molecules of water of crystallization. Exposed to dry air at ordinary temperature, it loses by efflorescence 2 H_2O; at 100° C. the total loss amounts to 4 or 5 molecules of water leaving a monohydrated salt. It is in this condition that a sample should be weighed for assay, if a definite rubric is to be fixed. Instead the U. S. P. IX starts with the salt in the condition in which it happens to be. It may contain hygroscopic moisture or on the other hand it may have lost a part of its water of crystallization. The apparent "impurity" (calculating the salt as $CuSO_4 + 5H_2O$) may be high including water (hygroscopic) or it may be low (even a minus quantity), owing to loss of water of crystallization. The Pharmacopoeia determines in the sample taken, not $CuSO_4 + 5H_2O$ but simply $CuSO_4$ and proceeds to deduce a rubric standard. The salt contains, it says, not less than 62.97 percent of $CuSO_4$ corresponding to not less than 98.5 percent of the crystallized salt. One infers that this permits a maximum of 1.5 percent "impurity" in the salt. The fallacy becomes apparent when we attempt to reason in a similar manner from the maximum (66.79 percent) amount of $CuSO_4$ that may be permitted, since this would correspond with 104.48 percent of $CuSO_4 + 5H_2O$, showing a minus impurity of 4.48 percent. In fact, the assay has told us nothing about the presence of fixed impurities in the salt. In order to make this clear suppose that a sample of copper sulphate containing 0.5 percent of fixed impurity has lost by efflorescence 2 percent of water, the assay will show the presence of apparently 101.5 percent of $CuSO_4 + 5H_2O$. Or, suppose that a salt containing 2 percent of fixed impurities has lost by efflorescence 1 percent of water. Assay will show apparently nearly 99 percent purity.

Clearly the assay is of no value as a criterion of the real purity of the sample. It seems only to show whether or not the salt conforms to an arbitrary fixed standard whose significance is uncertain. It would be far more rational to make the requirement depend upon the amount of residual H_2O in the salt. A sample dried to constant weight at 110° C. must lose not less than —nor more than—of its weight. However, the only scientific plan is to establish as usual a rubric of purity and provide an assay process for determining the degree of purity, then if necessary there may be also provided a limit of permissible efflorescence.

The assay would then be made as follows: "Dissolve about 1 Gm. of copper sulphate, previously dried to constant weight at 110° C. (a tentative figure) and accurately weighed, in 50 mils of distilled water, add 4 mils of acetic acid and 3 Gm. of potassium iodide, and titrate the liberated iodine with tenth-normal sodium thiosulphate, V. S., starch T. S. being used as indicator. It shows in the dried salt not less than 99.5 percent of $CuSO_4 + H_2O$. Each mil of tenth-normal sodium thiosulphate, V. S., corresponds to 0.017766 Gm. of $CuSO_4 + H_2O$. Each Gm. of dried copper sulphate corresponds to not less than 56.00 mils of tenth-normal sodium thiosulphate V. S." If we wish to limit the permissible amount of efflorescence, direct to "weigh accurately about 1 Gm. of the copper sulphate and dry it to constant weight at 110° C. It loses not less than 9 percent of its original weight." It is doubtful however if multiplying the requirements of this kind is expedient. In the case of copper sulphate it seems particularly unnecessary to resort to a quantitative standard. If the official salt is in the form of crystals, as it may well be, efflorescence shows itself at once by a striking change in color. Only uneffloresced crystals should be dispensed. Even in preparing Fehling's solution, the official directions are merely to use "carefully selected small crystals of cupric sulphate" (Cupri Sulphas, U. S. P.) though, perhaps, a method of standardization would be desirable here; posological considerations, however, do not demand greater exactness than can be secured by attention to the physical properties of the salt.

Ferri Sulphas. The facts regarding this salt are closely analogous to those regarding copper sulphate. Its crystals have a distinctive color, strikingly changed by efflorescence. It loses all but one molecule of its water of crystallization at a temperature not much above 100° C. It differs from the copper salt in that it tends to absorb oxygen, while the latter is subjected rather to a partial deoxidation. The analysis of ferrous sulphate for fixed impurities, providing oxida-

tion has not taken place, may be made exactly as in the case of copper sulphate, and the description excludes an oxidized salt. The dried salt retains one molecule of water having, therefore, a molecular weight of 169.93.

The directions for the assay would be: "Dissolve about 0.6 Gm. of ferrous sulphate, previously dried to constant weight at 115° C. and accurately weighed, in about 25 mils of diluted sulphuric acid and titrate with tenth-normal potassium permanganate V. S. until a permanent pink color is produced. It shows not less than 99.5 percent of $FeSO_4 + H_2O$. Each mil of tenth-normal potassium permanganate, V. S., corresponds to 0.016993 Gm. of $FeSO_4 + H_2O$; each Gm. of the dried salt corresponds to not less than 58.5535 mils (100 percent = 58.8478)." (Of course, any ferric salt would be included in the impurities thus determined.) It hardly seems necessary to add a quantitative test for loss of water by efflorescence. The statement in the text (first paragraph of fine print) is sufficient.

Note that in the Dried Ferrous Sulphate no attempt is made to ascertain the "purity" of the salt. The granulated salt is of necessity free from such fixed impurity but should be freshly prepared.

Magnesii Sulphas. Here again we have a salt whose crystals when heated to 150° C. lose all but one molecule of their water of crystallization. The suggested assay would be: "Dissolve about 0.6 Gm. of magnesium sulphate, previously dried to constant weight at 150° C., in 100 mils of distilled water, etc." (See U. S. P., p. 265.) "The weight of magnesium pyrophosphate obtained corresponds to $MgSO_4 + H_2O$ amounting to not less than 99.5 percent of the weight of the dried salt taken for assay. Each Gm. of the dried salt corresponds to not less than 0.80057 Gm. of magnesium pyrophosphate (pure = 0.80459). Each Gm. of magnesium pyrophosphate corresponds to 1.118583 Gm. of $MgSO_4 + H_2O$." The question of what degree of purity should be required for magnesium sulphate is open for discussion. The B. P. permits of 2.3 percent impurity which certainly seems large. The U. S. P. VIII permitted only 0.3 percent which certainly is too stringent. German and Swiss Pharmacopoeias provide a dried magnesium sulphate containing 23.69 percent of water, corresponding approximately to the formula $MgSO_4 + 2H_2O$. This is to be dispensed whenever magnesium sulphate in powder is required. Although this plan seems preferable to the requirement that the salt shall not have lost by efflorescence more than a certain percent of water (to be ascertained by a time-consuming quantitative operation), it does not seem advisable to confuse retail dealers with an alternative form of magnesium sulphate which they are to remember to dispense in place of the familiar epsom salt. It is to be remembered that this is a drug most frequently self-prescribed and sold very commonly in rural districts by persons not professional pharmacists. All things considered, it seems sufficient to describe the official salt as consisting of "crystals which are translucent" and add that "if they have become opaque by efflorescence they should not be employed for any pharmaceutical use, except after recrystallization." If any limit is to be prescribed for the permissible amount of efflorescence, the determination should be made by drying a sample of the salt at a temperature of 150° C., when the loss in weight should be not less than, say, 8 percent.

Sodii Sulphas. This salt effloresces very rapidly in dry air. Moreover the proportion of water of crystallization it contains (10 molecules = 55.91 percent) is very large. Since it loses the whole of this water by drying at 100° C., determination of absolute purity in the salt is a simple enough matter. A purity rubric of 99 percent in the anhydrous salt is, perhaps, reasonable and should be described as follows: "Assay: Dissolve about 0.5 Gm. of sodium sulphate, previously dried to constant weight at 120° C. and accurately weighed, in 100 mils of distilled water, and etc.," following the language of the text, but making the statement that "it indicates in the dried salt not less than 99 percent of Na_2SO_4. One Gm. of $BaSO_4$ = 0.60859 Gm. Na_2SO_4. One Gm. of dried sodium sulphate = 1.6267 Gm. $BaSO_4$ (pure = 1.64313 Gm.). The comments above on Magnesium Sulphate apply more pertinently to Glauber's salt which is not now often prescribed for human patients. The maintaining of a limit of permissible efflorescence seems to be wholly impracticable. Of course, the direct determination of the residual water, by drying the sample to constant weight, is much to be preferred to the determination of the sulphuric radical as now proposed in the Pharmacopoeia. It would be better to make the completely effloresced salt official if it is found that this is not too hygroscopic. In such case a dried salt of definite composition, having little tendency to absorb or give up water, might be substituted for the dehydrated salt, just as in the U. S. P. VIII ordinary crystallized sodium carbonate was replaced by the more

permanent monohydrated variety. It is to be noted that the German and Swiss Pharmacopoeias have a dried sodium sulphate (similar to dried magnesium sulphate).

Zinci Sulphas. This salt is similar in constitution and behavior to the sulphates of iron (ferrous) and magnesium. A rubric of purity should be provided, and the assay should be made on a sample, dried to constant weight at 120° C. before weighing, having, therefore, the composition of $ZnSO_4 + H_2O$. This yields in the assay an amount of ZnO corresponding to 99.5 percent of $ZnSO_4 + H_2O$ in the dried salt. One Gm. ZnO = 2.2054 Gm. of $ZnSO_4 + H_2O$. One Gm. $ZnSO_4$ dried = 0.45116 Gm. ZnO (pure = 0.453426). The comments under magnesium sulphate apply to zinc sulphate.

Potassii et Sodii Tartras. It is doubtful if this salt is sufficiently efflorescent to make it necessary to provide a limit of permissible water of crystallization. It occurs in the market, however, most commonly in the form of powder which is recognized as official. For assay, transparent crystals (powdered and pressed between folds of filter paper) may be weighed without further drying. The powder cannot be dealt with quite as satisfactorily. It may be recrystallized, it is true, but in doing so a considerable amount of the impurities will be left behind in the mother liquid. The alternative is a cautious drying of the salt to constant weight at a temperature raised gradually to 215° C., being careful not to carbonize it to any degree. Probably the desiccation can be facilitated by adding repeatedly small quantities of alcohol. Assuming that a satisfactory way can be found to accomplish the desiccation without injuring the organic salt, the further procedure for determining the purity of the salt will be obvious. If we are to rely upon weighing the transparent crystals as $KNaC_4H_4O_6 + 4H_2O$, the assay will be conducted as in the text, but the statement will be: "It shows not less than 99 percent of $KNaC_4H_4O_6 + 4H_2O$. Each mil of half-normal sulphuric acid, V. S., used corresponds to 0.07055 Gm. of $KNaC_4H_4O_6 + 4H_2O$. Each Gm. of potassium and sodium tartrate corresponds to not less than 14.033 mils of half-normal sulphuric acid (pure = 14.1743 Gm.)."

Sodii Arsenas. This salt loses the whole of its water of crystallization (40.41 percent) at 150° C. It should be thus dried to constant weight before weighing to determine purity. For the assay take about 0.3 Gm. of the dried salt accurately weighed. The statement will be: "It shows not less than 98 percent of Na_2HAsO_4 in the dried salt. Each mil of tenth-normal sodium thiosulphate, V. S., used corresponds to 0.009298 Gm. of Na_2HAsO_4. Each Gm. of dried sodium arsenate corresponds to not less than 105.39 mils of tenth-normal sodium thiosulphate, V. S. (pure = 107.544 mils)." It does not seem necessary to fix a limit of permissible efflorescence for this salt. The description calls for the uneffloresced salt (transparent) which is to be preserved in well closed containers. Then, if a product assumably uniform in strength is desired. we find provided the exsiccated salt. It is really not desirable that both of these forms should be official, one nearly double the strength of the other. The dried salt is the one that should be retained. As long as there are two, errors in dosage are sure to occur. It is interesting to note that the International Pharmaceutical Congress adopted $Na_2HAsO_4 + 7H_2O$ as sodium arsenate.

Sodii Acetas. At 120° C. it loses all of its water of crystallization (39.72 percent). The salt should be dried accordingly before weighing. It shows not less than 99 percent of $NaC_2H_3O_2$ in the dried salt, etc. Each mil of dried sodium acetate corresponds to not less than 24.14 mils of half-normal sulphuric acid (pure = 24.384 mils). (If any efflorescence limit is prescribed it may well be required merely that the salt lose, in drying to constant weight at 120° C., not less than 32 percent of its weight.) The description of the official salt should include only colorless transparent crystals. Then if the salt is preserved in well-closed containers it will not effloresce sufficiently to affect the dosage materially.

Sodii Boras. When dried thoroughly and the residue heated to redness it becomes anhydrous, losing, if pure, 47.14 percent of water. Instead of reducing the salt to an anhydrous condition before weighing a portion for assay, it is better to powder about 15 Gm. of the sample and weigh out separately two portions, one of about 5 Gm. the other of about 1 Gm., both to be weighed accurately. Dry the smaller portion and heat it to the point of igneous fusion. From the loss in weight of this sample, determine the weight of the larger sample in anhydrous condition. Use this portion for the assay as directed in the text, changing the reading to: "It shows in the anhydrous condition not less than 99 percent(?) of $Na_2B_4O_7$. Each Gm. of sodium borate (weighed

in anhydrous condition) corresponds to not less than 9.704 mils of normal hydrochloric acid V. S. (if pure, 9.802 mils.) Preferably, take for the assay about 1 Gm. of the undried salt, and use for the titration tenth-normal hydrochloric acid. The equivalent for 1 Gm. of the fused salt will then be 97.04 mils of the volumetric acid. As limit of efflorescence, 1 Gm. of the salt when dried and heated to fusion must lose not less than 40 percent (42 percent) of its weight. Only colorless crystals should be official. In such cases it should suffice merely to require that the salt be kept in well-closed containers.

Sodii Phenolsulphonas. Dried at 120° C. the salt loses the whole of its water of crystallization (15.52 percent if pure). It should be thus dried before it is weighed for assay. It shows in the dried salt not less than 99 per cent of $NaC_6H_5O.SO_3$. Each Gm. of dried sodium phenolsulphonate corresponds to not less than 201.93 mils of tenth-normal bromine, V. S. (if pure, 203.97 mils). The official salt should consist of colorless transparent crystals and then if kept in well-closed containers it should not lose water sufficiently to affect the dosage.

Sodii Phosphas. This is really a very efflorescent salt. For assay as to purity, it may be dried to constant weight at 110° C. (if pure it loses 60.35 percent). Weigh about 0.2 Gm. of the dried salt and proceed as in the text. It shows in the dried salt not less than 98 percent of Na_2HPO_4. Each Gm. of the dried salt corresponds to not less than 206.97 mils of tenth-normal silver nitrate, V. S. (if pure, 211.19 mils). The official salt must consist of clear crystals showing not more than traces of efflorescence. The effloresced salt is not to be dispensed unless first recrystallized.

Sodii Phosphas Exsiccatus. "It is a poor rule that does not work both ways," says the proverb. Sodium phosphate is keen to get rid of its water of crystallization. Equally eager is the exsiccated salt to attract to itself moisture from the air. In this case the U. S. P. IX requires that the former salt shall not be gratified in its self-abnegation beyond a certain narrow limit. In the other no objection is made to the acquisition of the water by the exsiccated salt, except that interposed by a well-closed container. However, there would seem to be a better plan than that of providing two forms of sodium phosphate so diametrically opposed in their behavior. There is an intermediate phosphate containing 7 molecules of water instead of twelve that is satisfied with its allotment of that compound. Why not make this one the official compound? Perhaps the simplest plan would be to dry the ordinary crystals until they had lost approximately 25 percent (25.145 percent) of their weight, requiring that when further dried to constant weight this salt shall lose approximately 47 percent (47.03 percent) of its weight. The assay for the determination of the purity would be the same as that for the present official salt and, for that matter, for the exsiccated sodium phosphate as well.

Sodii Thiosulphas. The crystallized salt when pure contains 36.29 percent of water of crystallization. Whether it can be brought to the anhydrous condition without decomposition is doubtful, but, if so, it is an easy matter to determine the purity of the sample by drying and titrating the residue with tenth-normal iodine, V. S.

If the plan of drying to constant weight is impracticable, the salt can still be brought to the form of sulphate and its weight compared with the theoretical yield of that salt. Only crystals should be official. These, when kept in well-closed containers in a cool place, are not liable to change materially.

Plumbi Acetas. It is stated that lead acetate loses its water at 40° C.; whether it also loses some acetic acid is not stated. Precaution would have to be taken against absorption of CO_2 if dehydration of the crystals should be attempted. Granted that this is practicable, the assay of the present text may serve for the determination of purity of the salt (rubric). The dehydrated salt being used, it shows in the dried salt not less than 99.5 percent (rather rigid) of $Pb(C_2H_3O_2)_2$. Each Gm. of the dried salt corresponds to not less than 61.20 mils of tenth-normal oxalic acid, V. S. (if pure 61.51 mils). The description calls for crystals of crystalline masses. If the crystals are transparent or translucent, showing not more than traces of efflorescence (or required to) and dissolve in recently boiled distilled water to a clear, or a most slightly opalescent solution, it seems hardly necessary to fix a limit of permissible efflorescence. It should be noted that the assay assumes complete solubility of the sample since the solution is not filtered before adding the oxalic acid, V. S.

If carbonate is present it counts in the assay as acetate. This is why care must be taken in drying the sample to exclude CO_2.

Zinci Acetas. The salt is somewhat unstable as shown by its acetous odor. It is doubtful whether it can be deprived of its water of crystallization without material loss of acetic acid. The assay may be based upon the uneffloresced crystals, the salt being recrystallized if necessary. The water of crystallization is only 16.42 percent so that it hardly seems necessary to establish a maximum of permissible efflorescence. An article which is in uneffloresced crystals and conforms to the description given should be satisfactory. If the crystals have effloresced, the salt may be recrystallized from water containing some acetic acid.

Zinci Phenolsulphonas. The salt is said to give up the whole of its water of crystallization at 125° C. (25.94 percent, if pure). If the dried salt is used for assay, the amount of zinc oxide obtained corresponds to not less than 99.5 percent of the dried salt. Each Gm. of the dried salt corresponds to not less than 0.1967 Gm. of ZnO (0.1977, if pure). The salt should be used in uneffloresced condition. A standard of admissible efflorescence is not advisable, but it would be well in this case as in similar cases to ascertain what quantity of water the salt will normally lose under ordinary conditions, and, if necessary, make the official salt a "dried" salt not liable to undergo much change if kept under ordinary conditions.

Zinci Valeras. It is noticeable in the case of this salt that nothing is said about drying the sample before weighing. There is an obvious reason for this but if the assay is to mean anything, the official salt should at least always be in the crystallized form, and it would seem that under the circumstances (possible presence of notable quantity of moisture) a requirement of the equivalent of 99 percent of the crystalline salt is too stringent. An arbitrary requirement like this may be made but it does not call for a 99 percent "purity" of the salt.

SUMMARY.

The method of dealing with efflorescent salts adopted in the U. S. P. IX is faulty in several particulars.

I.—It appears to supply for such salt a rubric of purity but in fact does nothing of the kind. The words "Corresponding to not less than—percent of the crystallized salt" should in each instance be deleted as false and misleading. With this change the text furnishes a standard of "strength," which possibly is better than none.

II.—The exact limit for permissible loss of water of crystallization by efflorescence may seem in theory a desirable thing; in practice it can accomplish little good, while it is liable to abuse in the hands of over-zealous inspectors. The permitted loss in each case is approximately 5 percent so that a general statement in the introductory notices of the U. S. P. similar to that with regard to limitation of hygroscopic moisture (page xlvi near the bottom) would suffice.

III.—There seems to be a better plan. In nearly every case if the official salt is in crystalline form the efflorescence is readily discernable and it is easy to declare that only the uneffloresced salt is to be dispensed (or a salt showing not more than traces of incipient efflorescence).

IV.—In the exceptional cases where efflorescence is rapid and results in loss of more than 5 percent of the weight of the salt a different plan must be adopted. It may be that the salt can be induced to crystallize with a smaller proportion of water of crystallization, showing in that form a little or no tendency to effloresce. We have already substituted in the U. S. P. the monohydrated salt for the exceedingly efflorescent crystals of ordinary sodium carbonate, a capital improvement. It is possible that a sodium phosphate containing only seven molecules of water of crystallization may with equal advantage replace the present official salt.

V.—However that may be, it is certainly possible to substitute for the troublesome efflorescent salt the already effloresced salt. Of course, it would be necessary to fix a standard to which manufacturers would have to make their product conform. Such product would undergo but little change if kept in well-closed containers. Some of the European pharmacopoeias have made official a "dried salt" to be employed in the place of the crystals in mixtures in powdered form, *e. g.*, *Natrium Sulphuricum Siccum* and *Magnesium Sulphuricum Siccum* of the German Pharmacopoeia. Of course, the dried salt is very much stronger than the crystals, so that the one should not be substituted for the other, Gm. for Gm. This would not solve our problem, indeed, we have already exsiccated forms of sodium phosphate and ferrous sulphate but these again do not fill the bill. The exsiccated sodium phosphate, for example, is as greedy to absorb moisture as the crystallized is eager to part with it. The suggestion of an effloresced salt to take the place of both the other forms is at least worthy of consideration.

VI.—Finally there should be provided for each of the salts in question a true "Purity Rubric."

DELIQUESCENT SALTS.

Calcii Chloridum. A purity rubric for this salt is wanting. The only requirement is that "the salt without previous drying shall show the presence of not less than 75 percent of $CaCl_2$." The salt is described as "very deliquescent" and yet it is required to show on assay more $CaCl_2$ than it would contain if but one percent of hygroscopic moisture were present, the salt otherwise consisting of pure $CaCl_2 + 2H_2O$. A better requirement is that of the British Pharmacopoeia, *viz.*, "when dried at 200° C. the salt shall lose not more than 5 percent of moisture." Preferably establish a purity rubric perhaps of 99 percent. For the assay direct that the salt be dried at 200° C. before weighing, every precaution being taken to prevent absorption of moisture during the weighing. Proceed as in the text but the statement will read: "It shows in the dried salt not less than 99 percent of $CaCl_2 + 2H_2O$. Each mil of tenth-normal silver nitrate, V. S., corresponds to 0.007351 Gm. of $CaCl_2 + 2H_2O$ and each Gm. of calcium chloride corresponds to not less than 134.68 mils of tenth-normal silver nitrate, V. S. (if pure, 136.036 mils)." (Include also test like the B. P. limiting hygroscopic moisture.)

Calcii Bromidum. This case is closely analogous to that of calcium chloride, except that a somewhat larger percentage of impurity (presumably chloride) has to be tolerated. Probably a rubric of 98.5 percent would be reasonable. Then the assay would be conducted as in the case of calcium chloride, drying the salt at 200° C. before weighing. Then, "the assay will show in the dried salt not less than 98.5 percent of $CaBr_2 + 2H_2O$. Each mil of tenth-normal silver nitrate, V.S., corresponds to 0.011797 Gm. of $CaBr_2 + 2H_2O$. Each Gm. of calcium bromide corresponds to not less than 83.495 mils nor more than 85.536 mils of tenth-normal silver nitrate V. S. (if pure, 84.767 mils). (Also when dried to constant weight at 200° C. the salt loses not more than 4 percent(?) of hygroscopic moisture.)

Lithii Bromidum. It is very doubtful if it is practicable to dry this salt without loss of bromine. If it is, a rubric of purity may be fixed as in the case of calcium chloride, otherwise we may be contented with merely determining the percentage of lithium bromide as in the text, but only extraordinary precautions will prevent further absorption of moisture so that the salt will sooner or later fail to fulfil the U. S. P. requirement. Note that the text permits the presence of nearly 1 molecule of water (one molecule = 17.18 percent).

Zinci Chloridum. A purity rubric is perhaps impracticable owing to the tendency of this salt to form oxychloride. The present assay may, therefore, be accepted as sufficiently safeguarding the purity of the product. Possibly 95 percent is too high a requirement. At all events it is evident that care must be exercised in selecting a fair sample for weighing. Instead of taking 0.3 Gm. as the text prescribes, we should start with a much larger sample, not less than 2.5 Gm., of which, after dissolving and making up to a definite volume, an aliquot corresponding to 0.3 Gm. of the original sample may be taken for assay.

MISCELLANEOUS COMMENTS.

Ammonii Iodidum. It is stated in the text that the salt soon becomes yellow or yellowish brown on exposure to air and light, but nothing is said of its unfitness for use in this condition, or of any remedy. It would seem that merely drying it at a temperature of 110° C. should render it fit for dispensing.

Antimonii et Potassii Tartras. The salt is efflorescent, therefore it should be rendered anhydrous for the assay by drying it to constant weight at 110° C. The dried salt shows not less than 98½ percent(?) $K(SbO)C_4H_4O_6$. Each mil of tenth-normal iodine, V. S., is equal to 0.016167 Gm. of $K(SbO)C_4H_4O_6$. One Gm. of the dried salt requires 60.93 mils of tenth-normal iodine, V. S. (if pure, 61.856 mils).

Ferri et Ammonii Citras. In this and in the next item, the description "Ferric citrate rendered more readily soluble by the presence of ammonium citrate" is objected to. It seems hardly true to say that the product is ferric citrate when it is really a chemical compound (no doubt), of which ferric citrate is a constituent. It is true that the new compound is more soluble (in water) than ferric citrate alone and that pharmaceutically this gives it an advantage over the less soluble salt, but the definition is surely faulty—still more so in the case of *ferri et ammonii citras*, where the term "iron citrate" is used instead of ferric citrate. Is not iron and quinine citrate in itself a chemical individual, which is converted into a more soluble group by the further combination with ammonium citrate?

Ferri Phosphas. The comments on *Ferri et Ammonii Citras* apply equally well here.

Zingiber. It would be advisable to refer to the pages in the Pharmacopoeia where the special method for determining non-volatile extracts are given.

Tinctura Zingiberis. The following criticisms have been received: The requirements for tincture of ginger are open to the following criticisms: First, contrary to pharmacopoeial usage in case of fluid preparations, the assay is based on a weighed instead of a measured quantity of the tincture. Ten mils, rather than 10 Gm. of the tincture should be taken and the weight of the residue should not exceed 0.165 Gm. (corresponding closely enough with 2 percent). Second, a minimum requirement as to extractive is at least as important as a maximum, for reasons quite obvious. Third, the expression "when treated with 20 mils of cold distilled water" is too vague. The directions should be to "stir the residue with a glass rod during five minutes with 20 mils (or 16 mils as the case might be) of cold distilled water. Decant the water into an evaporating dish and rinse the residue with two mils of distilled water without further stirring. Evaporate to dryness and dry to constant weight at 100° C. or, perhaps better, dry the residue once more and determine the loss." Twenty percent, is suggested as a more reasonable allowance than fifteen in any case. Perhaps after all a requirement that 90 percent of the alcoholic extract should be soluble in ether would probably be more to the point than the requirement as to water solubility.

CAUTIONS AGAINST INJURIOUS EFFECTS OF PHARMACOPOEIAL ARTICLES.

Dr. A. B. Lyons submits the following comments: The Pharmacopoeia deals with many poisonous and corrosive substances. Is it in place to point out the dangerous properties of drugs? It seems only right that a book like this should keep before the minds of those who use it the distinction between active poisons and drugs of little potency. The former should surely be kept by themselves under lock and key and this should be specifically required in each instance. Such a practice is recommended in a number of the pharmacopoeias of other countries and should be universal. Our pharmacopoeia avoids mention of the word "poison." It does not even indicate the maximum permissable dose of such a potent agent as strychnine, an omission not less than criminal.

It does now and then, however, print in italics a cautionary sentence interpolated usually in the descriptive paragraph. Under Phosphorus, for example, it is stated that the drug *"has a distinctive and disagreeable odor and taste but should not be tasted except in very dilute solution."* Italics are those of the text. (Imagine a greenhorn taking a bite of phosphorus to find out how it tastes!) Mention is made of the spontaneous ignition of phosphorus on long exposure to the air and instructions are given to preserve the drug under water in strong well-closed containers in a secure and moderately cool place, but the words are not italicized or given prominence in any way. One would look for some such expressions standing out conspicuously on the page as "dangerously poisonous" or "exceedingly poisonous and extremely inflammable, liable to spontaneous ignition if not kept under water, producing burns exceedingly painful and difficult to heal." We find under Sodium Arsenate, "great caution must be used in tasting it and then only in very dilute solution." (Will someone please parse that sentence?) There is, however, no word of caution under Arsenic Trioxide or even under Solution of Potassium Arsenite.

It is said of Phenol (not italicized) that when undiluted it cauterizes the skin and mucous membrane, language which fails to convey an adequate warning against the deadly effects of this insidious poison.

There are cautions against carelessness in handling calcium hypophosphite and other hypophosphites and so with potassium chlorate where italics are used, but nothing is said of the reaction with strong mineral acids; potassium permanganate "when in solution or in the dry condition must not be brought into contact with organic or other readily oxidizable substances." The idea seems to be merely that the permanganate would be decomposed, with no suggestion of anything like an explosion.

The scope of my criticism is that cautionary expressions are employed in rather a haphazard way. They should be reduced to a system. My idea is to have a definite place under each title for a statement regarding the poisonous character of the drug (if poisonous) characterizing it as: "An exceedingly potent poison," "an active poison," or "a poison," and in each case, preferably inserting a descriptive adjective as "narcotic," "irritant," "corrosive," etc.

The introductory notices should define the uses of the terms "potent" and "active." Similarly, I would, when necessary, introduce a cautionary note with regard to any special care required in handling the article. This naturally would come in connection with the directions "in well-closed containers," etc.

L. D. HAVENHILL, *Chairman.*