SOME OF THE CHANGES MADE IN THE NINTH DECENNIAL REVISION OF THE UNITED STATES PHARMACOPŒIA.*

BY GEORGE M. BERINGER, A.M., PH.M.

On the eve of the appearance of the Ninth Decennial Revision of the United States Pharmacopœia, it is very appropriate that the changes made in this legal authority for drugs should be discussed by pharmacists.

The present revisions of the Pharmacopœia and of the National Formulary are the first editions of these books to appear since they were specifically named in the Food and Drugs Act as the standards for the identity and quality of drugs. To revise the Pharmacopœia so that its standards shall properly fulfil this added responsibility has been the paramount thought of the revisers. Hence it may be observed that the Ninth Revision will be noteworthy for this purpose and its consequent aim at scientific accuracy, and this purpose has been the primary cause for many of the changes that will appear in this revision.

From a therapeutic standpoint, the changes made in the strength of the galenical preparations are, as a rule, negligible. For the most part, they have been minor and not sufficient to affect either the action or dosage of the preparations. As most of the potent remedies were brought into harmony with the Brussels International Protocol by the Eighth Decennial Revision, radical changes, such as were then made in the strengths of Tincture of Aconite and Tincture of Veratrum, are not now necessary.

It was to be expected that the advances and the changes occurring in medical practice, and likewise the progress of our knowledge of the composition of drugs and their therapeutic actions, would demonstrate that the requirements of that Protocol must be revised. Absolute compliance with all of its provisions is already no longer possible. In the two revisions of the Pharmacopœia that have been made since the promulgation of the International Protocol, we have given ample evidence of our good faith and adherence to the principles to which our nation as a participant in the Brussels Conference and as a signator to the Protocol committed us.

A few of the variations between the requirements of the Protocol and those of the United States Pharmacopœia are cited as examples, and the reasons for the non-acceptance of the international requirements are given. The Protocol requires that Aconite shall be "the tubers of the current year." In America this has never been considered practicable, as *Aconitum Napellus* is not indigenous nor cultivated in this country, and, under the conditions existing during the past two years, it would have been absolutely impossible to have complied with this requirement. Moreover, it is an established fact that aconite, properly stored, retains its activity for a long period, and hence this requirement was considered as unnecessary and has not been adopted in our Pharmacopœia. The Protocol specifies that Belladonna is to be "only the dried leaf." The commercial article is the dried leaves and tops, and hence the U.S.P. very correctly so defines it. The Protocol contains no standards for the tincture or extract of Belladonna, except that the latter shall contain "about 10 per cent. of moisture." The U.S.P. provides alkaloidal standards for both. The same criticism applies to the absence of

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standards in the Protocol for the preparations of Colchicum and Hyoscyamus. The Protocol directs that tincture of Strophanthus shall be made from the seed and not de-fatted and with a menstruum of 70 percent alcohol. We know that the fat in strophanthus is exceedingly disagreeable and nauseating, and that this fat can be removed with purified petroleum benzin without the loss of strophanthin. Moreover, 70 percent alcohol will not extract the drug, and hence the U. S. P. improves on the international preparation by the preliminary de-fatting of the seed and the use of alcohol as the menstruum.

The use for which a preparation is commonly administered may, likewise, necessitate a deviation from the Protocol, as adherence to its provisions would possibly prove a menace to life. As examples: Bitter almond water is commonly administered in the United States as a vehicle or flavoring medium in fairly large doses, and hence it is directed by the U.S.P. to contain not more than a mere trace of HCN. The Protocol requirement is 0.1 percent of HCN, and to follow this in the dosage in which bitter almond water is, at times, directed as a vehicle in the United States would be dangerous. The U.S.P. Syrup of Ipecac is seven times stronger than that of the Protocol. As this preparation is commonly used in the United States as an emetic, it was not deemed advisable to so reduce the strength as to render it valueless as an emetic in croup and similar affections in which it is so commonly employed.

As examples of the more important changes of strength of galenicals may be mentioned Unguentum Hydrargyri Dilutum from 33 per cent. to 30 per cent. of mercury in order to comply with the Protocol, and Syrupus Acidi Hydriodici, changed from 1.19 Gm. HI in 100 Cc. to from 1.3 Gm. to 1.45 Gm. in 100 mils.

The changes that have been made in the strength of the chemical products are, for the most part, such as were required by the commercial conditions and the quality of the products commonly dispensed as medicines. The principle of allowing for the proper variability of chemicals and for the natural variation in crude drugs has led to many modifications of the rubric requirements by which, instead of the fixed purity statements of the previous revision, there now appears in most of the monographs a variability allowance in accordance with determined conditions, and the limitations of such variability are officially defined. The following examples among the chemicals illustrate the desirability and practicability of this change, which, in many cases, has been only a rounding off of the requirements: The Eighth Revision required that Diluted Hydriodic Acid should contain not less than 10 percent HI; the Ninth Revision will state from 9.5 to 10.5 percent HI. In the Eighth Revision, Hydrochloric Acid was required to contain not less than 31.9 percent HCl; the Ninth Revision will state from 32 to 33 percent HCl. In the Eighth Revision, Ether was about 96 percent ethyl oxide; in the Ninth Revision it will be from 95.5 to 97.7 percent.

The purity of a few official chemicals has been increased. As examples: Ammonium Bromide, Potassium Bromide and Sodium Bromide have been each increased from 97 percent in the Eighth Revision to 98.5 percent of the respective absolute bromide. In a few cases the rubric is not so exacting as in the previous revision. The reasons for such modification are usually self-evident. As examples, Ferric Chloride is to contain 20 percent of Fe instead of 22 percent, and Thymol Iodide 43 percent of I instead of 45 percent.

A noticeable improvement is seen in the pharmacognostic descriptions. Here we have not only the microscopic appearance and structure of the drug described, but also descriptions of the powdered drug under the microscope. The purity rubric has been extended to the organic drugs, and these monographs commonly

give the percentage of allowable admixtures of other parts of the drug plants or other foreign matters. In the organic drugs and their preparations that permit of chemical assaying, limitations are likewise fixed for the variability naturally existing in the drugs and the personal equation or error introduced in the assay processes, and in each case the alkaloidal percentage is fixed by an upper and lower limit.

The assay processes introduce several changes, such as the use of purified saw dust as a distributing medium, and the adoption of the aliquot part method. Cantharides has a definite standard of cantharidin of not less than 0.6 percent, and an assay process is now given. In Nux Vomica, the percentage of total alkaloids is fixed at 2.5 percent in place of 1.25 percent strychnine, and the preparations of Nux Vomica are all assayed for total alkaloidal content. Opium must now contain not less than 9.5 percent *anhydrous* morphine instead of not less than 9 percent *crystallized* morphine, and the lime method of assay is adopted. This increase in strength is to be noted, and likewise the determination of morphine content in the anhydrous form instead of that of the crystallized alkaloid.

Assay processes have been extended to numerous preparations not previously assayed. Among such may be mentioned Benzoic Acid, Salicylic Acid, and Citrated Caffeine; and among preparations, Liniment of Camphor and Spirit of Camphor, for which a polariscope method for the determination of camphor is now introduced. Very few pharmaceutical laboratories have the expensive polariscopes required. Hence I fear that this test is more academic than practicable, and its observance in practice will be largely confined to the State Laboratories.

The Ninth Revision will be noted for the number of innovations in pharmacopœial revision. Among these may be mentioned "Electrolytic Determination," which is especially recommended as the method for assaying zinc and mercury compounds; official methods for the "Determination of Ash," "Saponification Values," " Acid Number of Resins," " Determination of Crude Fiber," " Volatile Extractive and Non-volatile Extractive," "Determination of Alcoholic Content," "Melting Points," "Boiling Points," and "Congealing Points," with a description of "Standard Thermometers, and Solubilities." The chapter on "Sterilization" should be carefully studied by every dispenser. The chapter on "Diagnostical Reagents and Clinical Tests" is an important addition to the U. S. P., in which the example of the later revisions of some of the foreign pharmacopœias, notably the German Pharmacopœia, is followed. This contains standard formulas for the reagents used in the examination of urine, gastric contents, blood, and microorganisms.

For the first time in the history of pharmacopœial revision, the methods for the biological assaying of drug products have been recognized. Chapter 23, in Part II, is devoted to this subject, and official processes are described by which the following drugs and their preparations *may be* assayed: Aconite, Digitalis, Strophanthus, Squills, and Dried Suprarenals, and Cannabis *must be* assayed by the official biological process. The standard adopted for the latter drug is that "Cannabis, made into a fluidextract in which one hundred mils represent one hundred grammes of the drug when assayed biologically, produces incoördination when administered to dogs in a dose of not more than 0.03 mil of fluidextract per kilogramme of weight."

The titles added to the list of pharmacopœial substances are only 66 in number. Some of these have been added because of their use as medicines necessitating standards. Among such may be mentioned: Ethyl Morphine Hydrochloride,

Diacetyl Morphine and Diacetyl Morphine Hydrochloride, Sodium Cacodylate, Calcium Glycero Phosphate, Sodium Glycero Phosphate, Creosote Carbonate, and Phenolphthalein.

Commercial conditions necessitated several changes. As examples: Virgin scammony not being now obtainable, scammony root was introduced as the source for making the official Scammony Resin, and Sodium Cyanide replaces Potassium Cyanide. The high price of potash salts, due to the war, has been recognized, and permission is given to substitute the sodium carbonate in place of the potassium carbonates in Solution of Magnesium Citrate, Rhubarb preparations, etc.

Several of the additions became necessary because they are ingredients in the formulas of the Pharmacopœia. Among these may be mentioned Glucose, directed as a diluent for solid extracts; Purified Siliceous Earth as a filtering medium, Oil of Sesame as an ingredient in liniments, and Sodium Indigotindisulphonate, introduced as a coloring for Poison Tablets of Corrosive Mercuric Chloride, which are to be "tablets of an angular shape (not discoid), having the word 'POISON' and the skull-and-crossbones design distinctly stamped upon each, and to contain 0.45 Gm. to 0.55 Gm. corrosive sublimate, and the tablets to be colored blue."

The preparations added have not been numerous, the tendency being to leave to the National Formulary the providing of formulas for preparations. Milk of Bismuth and Milk of Magnesia are two of the popular remedies, however, that have been given pharmacopœial standing.

Pharmacists will be pleased to learn that the list of powdered extracts has been greatly extended, and in several instances formulas for both the pilular extract and the powdered extract of the same drug are very properly given. The instructions of the Pharmacopœial Convention to adopt general formulas wherever possible has been partially carried out by the introduction of general instructions in the aromatic waters, and by general formulas and classifications in the fluidextracts and tinctures.

Two hundred and forty-two titles have been dismissed from the Pharmacopœia. Thirty-eight of these were fluidextracts, seven were pills, and ten were tinctures. A majority of these preparations have been included in the revised National Formulary, and so the National Formulary will relatively become more important because of these deletions from the Pharmacopœia.

Twenty-nine changes in the Latin titles have been made, and 28 changes in the English names. As examples: Alcohol Absolutum is now Alcohol Dehydratum; Aqua Hydrogenii Dioxidi is now Liquor Hydrogenii Dioxidi; Cardamomum is now Cardamomum Semen, the decorticated seed being the official drug; Elixir Adjuvans is now Elixir Glycyrrhizæ; Hyoscinæ Hydrobromidum is now Scopolaminæ Hydrobromidum; Rhamnus Purshianæ is now Cascara Sagrada.

One of the minor changes that has attracted, nevertheless, a great deal of attention is the adoption of the word "milliliter" in place of "cubic centimeter," and the word "mil" in place of "Cc." In this we have followed the example of the British Pharmacopœia and accepted the authority of the United States Bureau of Standards for the sake of absolute accuracy.

Synonymy will not be treated through the Index as in the Eighth Revision, but following each Latin title will be the official English title and the more commonly used synonyms. In addition to this, there will be official abbreviation printed in heavy type, with the hope that physicians will adopt these official abbreviations in prescription writing, so that there will be an official authority for the abbreviations for the official titles commonly used in prescriptions.