THE PHARMACOPŒIA OF THE UNITED STATES AND THE FEDERAL FOOD AND DRUGS ACT.*

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The primary purpose of a pharmacopœia is to present a list of approved medicinal agents which have been standardized as to identity, purity and strength, so that the same title shall always apply to a substance of the same properties and potency. Even a layman can understand the danger to human life if the title "Tincture of Aconite" referred to a preparation of one strength in Portland, Oregon, and to one of a different strength in Portland, Maine.

In all of medicine and pharmacy there is probably no matter of greater importance than the principle that drug preparations dispensed under the same title shall always possess the same essential properties and be of the same potency. Accordingly in every country having a national pharmacopœia it is the custom to consider that the official title of a drug, unqualified by other words, always refers to a drug having the identity, strength, quality and purity prescribed in the pharmacopœia of that country. If this were not true the primary purpose of a national pharmacopœia would be defeated.

Practically every civilized nation has an official pharmacopœia governing the character and strength of the medicinal agents dispensed on physicians' prescriptions within its own territorial limits. In countries other than the United States the committees which revise their several pharmacopœias are appointed by some political department of their respective governments, whereas the Committee of Revision of the Pharmacopœia of the United States is elected by a convention of physicians and pharmacists, and of other professional and scientific men who are in some way concerned with the production or use of drugs and medicines.

ORIGIN AND METHOD OF REVISION OF THE PHARMACOPŒIA OF THE UNITED STATES.

The Pharmacopœia of the United States belongs to and is under the absolute and complete control of the United States Pharmacopœial Convention, a society which has had a continuous existence of one hundred and fifteen years, in which period it has issued ten revisions of the Pharmacopœia, the Eleventh Decennial Revision being now in process of printing.

The United States Pharmacopœial Convention originated as a voluntary national association of physicians in 1820, and continued as a voluntary association, first of physicians only, and later of physicians and pharmacists, for eighty years. In 1900 the Convention was incorporated under the laws of the District of Columbia, and its membership now includes not only physicians and pharmacists, but also representatives of numerous scientific institutions and societies, and societies of law enforcement officials.

At the last assembly of the Convention in Washington in 1930 its membership included delegates from the American Medical Association, the AMERICAN PHARMACEUTICAL ASSOCIATION, the American Chemical Society, and from four other national societies relating to medicine, pharmacy or chemistry; from four national societies of officials who are charged with the duty of enforcing either

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national or state food and drug laws; from six departments or divisions of the U. S. Government which are concerned with medicine or with the enforcement of Federal drug laws; from forty-five medical colleges and university medical departments; from fifty-five colleges of pharmacy and university departments of pharmacy, and from twelve other colleges and universities. In addition to delegates from colleges and universities there were representatives from sixteen state medical societies; from thirty-six state pharmaceutical societies, and from eighteen other institutions and societies having to do with the medical sciences.

Of the more than four hundred delegates present at the 1930 meeting of the U. S. P. Convention, only nine represented societies directly connected with trade or industry, so that the influence of commercial interests in the making of the Pharmacopœia may be regarded as practically nil.

This Convention of Delegates has absolute control of the affairs of the Pharmacopœia in every particular. It elects and instructs the Board of Trustees and the General Committee of Revision, and every act of these two bodies is subject to revision or disallowance by the next assembly of the Convention.

The General Revision Committee of fifty members in turn elects a smaller Executive Committee which directly handles the revision work, all decisions of the latter being subject to approval by the General Committee.

The members of the Board of Trustees, which handles the financial and business affairs of the Pharmacopœia between assemblies of the Convention, receive only their actual traveling and clerical expenses incurred in the service of their office. Any profit from sales of the Pharmacopœia must be devoted to research work upon pharmacopœial subjects, and cannot be diverted to any other purpose.

Thus while the U. S. P. might be technically defined as private property, its purpose and its services are of a most decided public character.

The standing of the U. S. P. among pharmacopœias of the world is indicated by the fact that it has been translated into the Chinese language and is used as the official standard of the Republic of China. The Spanish translation has been adopted as the official pharmacopœia of the governments of the Philippine Islands and of the Island of Porto Rico, and is officially recognized by the independent Republics of Cuba and Costa Rica. The Spanish edition also has a wide distribution throughout the other Spanish-speaking nations of the Western Hemisphere.

SHOULD THE PHARMACOPŒIA BE DELETED FROM THE FEDERAL FOOD AND DRUGS ACT?

Some of those who have been confused by the alleged private property status of the United States Pharmacopœia, and also by the controversy over the inclusion or non-inclusion of a so-called variation clause, have somewhat hastily reached the conclusion that the Pharmacopœia should be deleted entirely from the Federal Food and Drugs Act, which would lead to the rather strange result that only official drugs and medicines would then be exempt from the requirements of the Federal law. Under such a situation all other drugs and medicines, including patent medicines, would be required to conform to certain standards of purity, quality and strength, and to be truthfully labeled and advertised, while official drugs and medicines could be adulterated, to any extent, and still be admissible to interstate commerce without let or hinderance from either Federal or other authority.

Legally the crime of adulteration exists when the qualities of a substance differ from those of a recognized standard. If there is no recognized standard then there is no ground upon which a charge of adulteration can be legally sustained.

Surely those who have advocated that reference to the Pharmacopœia be omitted from the Federal Act have not fully considered all the consequences of such deletion.

SHOULD REFERENCE TO THE U. S. P. IN THE FEDERAL FOOD AND DRUGS ACT BE COUPLED WITH A VARIATION CLAUSE?

Another conclusion stoutly defended by some students of the subject is that the U. S. P. (along with the other named authorities) should be included in the Federal Food and Drugs Act, but should not be coupled with a variation clause.

(By a "variation clause" we understand any clause or provision in the law which permits variation from the otherwise prescribed standards upon condition that the products are so labeled as to prevent their confusion with those which profess to comply with such standards.)

Those who contend that no variation from pharmacopœial standards should be permitted under any circumstances exclaim, with apparent logic, "What is the use of having a legal standard, if compliance with it is purely voluntary, and if manufacturers and dealers may follow some other standard by merely stating that fact upon the label?"

The writer agrees with the thought implied in this question in so far as it applies to drugs dispensed upon physicians' prescriptions or which are sold under their official titles for medicinal purposes, but as will be seen on further study, there are numerous cases where the practical necessities of interstate commerce, as well as other considerations, require that departure from official standards be permitted under certain circumstances, provided no deception is attempted or accomplished, and provided also that the facts are truly and clearly stated upon the label.

In the first place it should be remembered that a Federal Food and Drugs Act is based upon the constitutional powers of Congress to regulate interstate commerce and, therefore, applies exclusively to foods and drugs while they are the subjects of interstate commerce. Before they enter into or after they have left the domain of interstate traffic, the regulation of their further distribution rests solely with the police powers of the states in which they are located. Except in places under exclusive Federal jurisdiction, as the District of Columbia, any Federal law regulating the distribution of untaxed drugs, on prescription or otherwise, after they have left the domain of interstate commerce, would be null and void, and of no more legal effect than the utterance of any private citizen.

The first part of the definition for drugs as it appears in the Copeland Bill[1] [S. 5, Sect. 201, paragraph (*b*)] reads as follows: "(*1*) *All substances and preparations recognized in the United States Pharmacopœia, Homeopathic Pharmacopœia of the United States, or National Formulary, or any supplement to any of them.*" It will be noted that this definition does not apply merely to substances and preparations intended for medicinal use, but to every substance and preparation bearing a name

[1] The following discussion is based upon the Copeland Bill, which with or without further modification will probably soon supersede the Act of June 30, 1906.

mentioned in any one of the three stated official compendiums, or in any supplement thereto, whether intended for medicinal or other purposes.

Again one of the definitions of an adulterated drug, Sect. 401, paragraph (*b*), provides that a drug shall be deemed to be adulterated "*If its name is recognized in an official compendium*[1] [*i. e.*, U. S. Pharmacopœia, Homeopathic Pharmacopœia or National Formulary], *or if it purports to be a drug the name of which is so recognized and it differs from the standard of strength, quality or purity as determined by the tests or methods of assay set down therein,*" *etc.*

And finally, under the provisions for misbranding [Sect. 402, paragraph (*h*)] it is declared that a drug shall be deemed to be misbranded, "*if its name is recognized in an official compendium, or if it purports to be a drug the name of which is so recognized and it is not packaged and labeled as prescribed therein, unless exempted under (1) of this Section.*"

From these definitions it seems clear that unless a variation clause be included in the Federal Act it will be unlawful to ship in interstate commerce any drug named in the U. S. P. unless it fully complies with standards of strength, quality and purity, and the methods of labeling and packaging prescribed therein.

It is true that a prefatory notice in the U. S. P. specifically states that its standards "*are intended to apply solely to substances which are used for medicinal purposes and when professedly bought, sold or dispensed as such,*" but this limitation is nullified by the language of the Bill, which makes "all substances and preparations recognized in the U. S. P." subject to the requirements of the Act.

Now it happens that one hundred and forty or more of the substances named in the Monographs and List of Reagents of U. S. P. X are the names of agents, many of them belonging to the class commonly known as heavy chemicals, which are more largely employed in the arts and industries than for medicinal purposes.

Among such chemicals we readily call to mind hydrochloric, nitric, sulphuric, acetic and phosphoric acids, the salts of iron, copper, zinc and manganese, the fixed alkali hydroxides, many salts of the alkalies and alkaline earths and numerous other agents, the uses of which in the arts and industries far exceed their employment for medicinal purposes. While a few hundreds or a few thousands of pounds of some of these agents would satisfy the strictly medicinal requirements of the United States, their employment in dye and paint manufacture, in metallurgy, in the manufacture of soaps, paper, fertilizers, textiles, leather, insecticides, fungicides and in the production of numerous other largely used commodities amounts to many thousands or even hundreds of thousands of tons in a single year. To require that these vast quantities of chemical should always meet the high standards of quality, strength and purity prescribed for them when employed medicinally would be prohibitive of their commercial and industrial uses. To make the U. S. P. the standard for drugs in the arts and industries would be to thrust upon it a duty which it is entirely unfitted to discharge, and which it expressly disclaims in its prefatory notes.

Putting aside the opinions of lawyers and appealing to our own common sense, is it conceivable that the United States Congress would knowingly adopt or

[1] By definition, Sect. 201, paragraph (*m*), "official compendium" is understood to refer to any one of the three: United States Pharmacopœia, Homeopathic Pharmacopœia or National Formulary.

that the Federal Courts would sustain the validity of such a rigid and unreasonable requirement?

From these considerations it seems clear that the necessities of commerce practically compel the insertion of a provision in the law which will permit the interstate transportation of drugs of other than pharmacopœial quality when labeled so as to indicate their true character.

VARIATION CLAUSE NECESSARY TO PERMIT IMPROVEMENT IN PHARMACEUTICAL SUBSTANCES.

Another reason for the presence of a variation clause is that it is necessary in order to permit improvement in official drugs and preparations in the interim between decennial revisions of the U. S. P. and between the issuance of supplements thereto.

That the qualities prescribed for U. S. P. drugs and preparations are not beyond improvement is shown by the fact that the specifications for many of them are altered with each succeeding revision of that volume—changes in the percentage of active constituents, in solvents and menstrua, in solubility, melting and boiling points and other physical constants, in the purity rubric, in methods of packaging, etc., etc. The necessities for these changes are not discovered all at once on the eve of a new issue of the Pharmacopœia, but come to light from time to time during the entire decade within which a given issue is in effect.

Unless the law provides some proper form of variation clause no improved product could be transported in interstate commerce until a new issue of the Pharmacopœia, or of a supplement, recognized such change. The improvement might be of the highest importance to human health and life, yet the producer could not ship his product across state lines by mail, express or freight, or carry it in person—even with the most elaborate precautions of labeling to show that the preparation did not purport to comply with Pharmacopœial standards, and specifically designating the particulars in which it differed therefrom.

His only recourse would be to market it as a proprietary specialty, under a coined name, which he would be perfectly free to do, and thus the absence of a proper variation clause would act as a direct encouragement to the further multiplication of a variety of preparations of which we already have too great a surplus.

VARIATION CLAUSE IN RELATION TO THE DELEGATION OF LEGISLATIVE POWER.

The presence of a variation clause in the Food and Drugs Act is also closely tied up with the judicial doctrine that legislative bodies cannot delegate to others the legislative powers vested in them by a written constitution.

The United States Constitution (Article I, Sect. 1) recites that "*All legislative powers herein granted shall be vested in a Congress of the United States, which shall consist of a Senate and House of Representatives.*"

By an unbroken line of judicial decisions it has been settled that the intent and effect of this Article is to prevent the Congress from transferring any of its law-making powers to any other body, public or private, or to any administrative officer or other individual. Recent decisions in the code cases have re-affirmed and emphasized this interpretation of the Constitution, and have declared that the Congress cannot confer even upon the President of the United States the power to

designate and define acts which shall be regarded as criminal, and for which citizens may be punished by fine or other penalties.

The inclusion in the Food and Drugs Act of an issue of the U. S. P. in existence at the time the law is enacted would be distinctly an Act of the Congress itself, as much so as if the language of the U. S. P. had been copied in the Bill, and could not, therefore, be regarded as a delegation of legislative power, but how about later editions of the book, creating new standards, and coming into effect after the law has been placed on the statute books?

By the terms of the Act [Sect. 201, paragraph (*m*)], the particular issue of the Pharmacopœia which shall apply in determining the charge of adulteration or misbranding is the one which shall be "*official at the time any drug * * * * * * is introduced into interstate commerce.*"

It may happen, therefore, that a drug which fully complied with the Pharmacopœia official at the time the law was enacted will not comply with the standards of a later edition of that volume. Would the shipment of such a drug be punishable as a crime under the Food and Drugs Act? If so, it would not be a crime created by the direct act of Congress, but by the action of the U. S. P. Revision Committee in changing the standards after the enactment of the law.

This was the particular question considered in "The State of Ohio *vs.* Emery," reported in 54 Ohio State Report, page 365, which may be regarded as the leading case on this subject.

The Ohio statute, enacted in 1890, while the 1880 Revision of the U. S. P. was still in effect, declared a drug to be adulterated "(1) *If sold under or by a name recognized in the United States Pharmacopœia it differs from the standard of strength, quality or purity laid down therein.*" The statute did not contain a clause permitting variations from the standards of the Pharmacopœia if properly labeled so as to show such variation.

Subsequent to the enactment of the statute the 1890 Revision of the Pharmacopœia became official, and by a regulation of the Ohio Food and Dairy Commissioner was adopted as the standard of his Department, and in Oct. 1895 the defendant Emery was arrested for the sale of adulterated cochineal.

On trial of the case it appeared that the cochineal did conform to the standards of the 1880 Pharmacopœia—the issue official at the time the law was enacted—but did not conform to the standards of the 1890 Revision.

Attorneys for the State contended that under his authority to make rules and regulations for the administration of the Act the State Food and Dairy Commissioner had authority to substitute the standards of the new Pharmacopœia in place of the standards of the 1880 Revision.

Counsel for the defendant contended that the legislature could not adopt as part of the penal laws of the State the contents of a book not then in existence, and that it could not confer upon the Food and Dairy Commissioner authority to designate a different standard than that adopted by the legislature, since to do so would be an unconstitutional delegation of the law-making power.

The Supreme Court of the State of Ohio sustained the contention of the defendant's counsel in the following language:

"The reference in the statute to the United States Pharmacopœia, could be to no other than the edition of the book in use and recognized when the statute was enacted and went into ef-

fect, which was the edition known as that of 1880. It is not to be supposed that the legislature intended to adopt, by reference, as part of the penal laws of the State, an edition of the book not then in existence, and of the contents of which the legislature could have no knowledge. The drug, with the sale of which the accused was charged, was recognized in the edition of 1880, by the name under which it was sold, and a standard of strength, quality and purity therein laid down. It is not claimed the drug sold was below that standard; and the sale could not be rendered unlawful because it is below a higher standard laid down in a subsequently revised edition of the book, though that edition was in use at the time of the sale. To hold that the sale could thus be made unlawful, would be equivalent to holding that the revisers of the book could create and define the offense, a power which belongs to the legislative body, and cannot be delegated."

It will be noted that this decision sustains the power of the legislature to adopt an existing Pharmacopœia as part of the law, but denies its power to authorize the substitution of a later issue for the one in force when the law was adopted.

Although rendered in the construction of a state enactment, the rule laid down in the Emery case has been generally regarded as equally applicable to Federal laws, and this decision was really responsible for the insertion of the variation clause in the Federal Food and Drugs Act of June 30, 1906.

The theory upon which it is argued that the insertion of a variation clause will save the statute from the charge of being an unconstitutional delegation of power is that it will permit the manufacturer to freely select the standard which he chooses to follow, provided his labels indicate the facts truthfully and clearly. In plain English it gives the manufacturer the option either of following the standards of the U. S. P. or other standards as he may prefer, provided that if he elects to follow some other standard the label shall plainly indicate the fact. Thus the manufacturer's liability and obligations always remain the same no matter how frequently the standards of the Pharmacopœia are altered.

If the manufacturer is always free to choose the standards with which his preparations shall comply, then no change in the Pharmacopœia can affect his property rights or legal obligations, and consequently there is no exercise of law-making power when the Revision Committee changes the standards of the Pharmacopœia.

TITLES USED IN U. S. P. TAKEN FROM COMMON LANGUAGE.

Another thought to be taken into consideration is that the titles employed to designate U. S. P. chemicals and preparations are, in a majority of cases, taken directly from the English language, and do not represent any invention or discovery on the part of the revisers of that volume.

If one were to seek a copyright upon such titles as Tincture of Aconite or Hydrochloric Acid the application would be refused upon the ground that these are common words of the English language, the use of which is free to all, and that they may not be monopolized so as to represent exclusively the product of a single individual. If these titles cannot be monopolized to distinguish the products of a particular manufacturer, upon what ground can it be argued that their incorporation in the U. S. P. confers upon them such special qualities that they can no longer be used in their ordinary English sense, especially when coupled with other qualifying words which plainly indicate that the products to which they are attached do not profess to comply with U. S. P. requirements.

To hold that when common nouns and adjectives are once incorporated in the U. S. P. they can—in the absence of deception—no longer be employed in their

original and ordinary senses, would be to establish a rule of law never before recognized in this or any other country.

PRIMARY PURPOSE OF FOOD AND DRUGS ACT TO PREVENT FRAUD AND DECEPTION.

The primary and fundamental purpose of a food and drugs act is not to compel the use of certain products in preference to others, but to prevent fraud and deception in the sale of such substances—to prevent the sale of adulterated or harmful foods as pure and wholesome, or the delivery of adulterated or sophisticated drugs in place of those which are pure and genuine, or as in the case of cosmetics or package medicines, to insure that they shall not contain harmful or dangerous ingredients. It seeks to accomplish these results by requiring that labels and advertising shall state necessary and material facts, and shall not bear false and misleading statements, that inferiority shall not be concealed by the use of color or other artifice, or that the form of package shall not be such as to mislead the purchaser as to the quantity of its contents. In short, it aims to provide the means whereby the purchaser, from an inspection of the package, the label or the advertising, can determine whether the product possesses the qualities he seeks, and to insure that he shall receive what he expects and pays for. If the package, the label and the advertising clearly and truthfully set forth the character of the product, the primary purpose of the law is accomplished.

SUMMARY.

In the preceding pages it has been sought to justify the following conclusions:

1. That a Federal Food and Drugs Act as represented by the Copeland Bill, applies exclusively to foods and drugs while they are within the domain of interstate commerce. By the use of no language can the Federal law be made to apply to commerce after it has lost its interstate character. After once mingling with the goods of a particular state, only the laws of such state can fix the qualities which drugs must possess in order to permit their lawful distribution therein.

2. That the definitions for drugs, and for adulterated and misbranded drugs as found in the Copeland Bill are such that without the addition of a proper variation clause, only such drugs as complied with U. S. P. standards of strength, quality and purity could be lawfully transported in interstate commerce, a condition which if it prevailed would prevent the shipment of hundreds of thousands of tons of drugs and chemicals commonly used in the arts and industries.

3. That each new revision of the U. S. P. presents numerous changes in the standards of strength, quality and purity of the drugs described in its monographs, and also introduces new drugs and preparations which were not commonly used or even known when the preceding volume was issued. If the law-making body confers upon the revisers of the Pharmacopœia blanket authority to change the legal obligations of the citizen so as to render him liable to fine and imprisonment for acts which would have been innocent in law if the Pharmacopœia had not been revised, it would seem fairly evident that there has been an attempted delegation of law-making power.

On the other hand, if the law permits the use of U. S. P. titles which are parts of common English speech, upon articles not of U. S. P. standards, upon condition merely that the label states the fact of such variation, then no new obligation is

forced upon the producer when a new Pharmacopœia becomes official. Under any revision of the Pharmacopœia his legal liability remains the same; he will always have the option either of observing U. S. P. standards or of stating upon the labels wherein his product differs from such standards.

4. That it is the common understanding among physicians and pharmacists and taught in all colleges of pharmacy, that the use of a U. S. P. title without the addition of qualifying adjectives or other explanatory words, implies that the product to which it is attached complies with U. S. P. standards of strength, quality and purity. Unless this be the rule, the primary purpose of the Pharmacopœia—to enforce uniformity in properties and potency—would be defeated.

5. That a proper variation clause is one which would require that when a U. S. P. title is attached to a drug of other than U. S. P. standards the qualifying words shall indicate clearly that the drug does not profess to comply with such official standards. The wording of the label should not be obscure or ambiguous, but such as to enable the reader to form an intelligent opinion as to the character of the product.

6. And finally, that the deletion of the variation clause from the Federal Food and Drugs Act would not close interstate commerce to the shipment of medicinal preparations of official drugs which did not comply with U. S. P. standards. The producer would need only to give his product some attractive coined name and ship it as a proprietary specialty, thus setting his own standards, without let or hinderance from any authority.

A BRIEF HISTORY OF THE DRUG CODE.*

BY E. F. KELLY.

Following the enactment of the National Industrial Recovery Act, the National Association of Retail Druggists appointed a Committee on the Retail Drug Code.

Later, a meeting of representatives of the state pharmaceutical associations was held in St. Louis, Mo., at the invitation of Drug Center, at which a Committee was named to coöperate with the N. A. R. D. Committee in preparing a code for the retail drug trade.

These Committees met jointly in Washington, D. C., and drew up a code which was sponsored by the N. A. R. D. with the approval of the AMERICAN PHARMACEUTICAL ASSOCIATION. Representatives of the Drug Institute of America, Inc., also coöperated in writing the Code. It was estimated that at least 60% of the retail drug trade of the Country sponsored the code.

The original hearing on the Code of Fair Competition for the Retail Drug Trade was held in the auditorium of the Chamber of Commerce of the U. S. A., Washington, D. C., on August 25, 26 and 27, 1933, before A. D. Whiteside as Deputy Administrator, and Donald Richberg as Legal Advisor. It became evident at the first session of the hearing that the Code as submitted would have to be amended and the remainder of the sessions were devoted to an effort to bring about

* Section on Historical Pharmacy, Portland meeting, 1935.