The text-reading software PRETEXT II will be used, allowing left and right truncation, Boolean operators, and Context operators, particularly useful for searching the chemical nomenclature.

The mean annual price will be approximately $200.00 per profile, including coding cost and processing cost.

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LITERATURE CITED

(1) J. E. Dubois, "French National Policy for Chemical Information and the DARC System as a Potential Tool of this Policy", *J. Chem. Doc.*, **13**, 8–13 (1973).
(2) B. G. Prewitt, "Searching the Chemical Abstracts Condensates Data Base via Two On-Line Systems", *J. Chem. Doc.*, **15**, 177–183 (1975).
(3) M. Milne, D. Lefkovitz, H. Hill, and R. Powers, "Search of CA Registry (1.25 Million Compounds) with the TSS", *J. Chem. Doc.*, **12**, 183–189 (1972).
(4) G. W. Adamson, V. A. Clinch, S. E. Creasey, and M. F. Lynch, "Distributions of Fragment Representations in a Chemical Substructure Search Screening System", *J. Chem. Doc.*, **14**, 72–74 (1974).
(5) R. Fugmann, "The IDC System", J. E. Ash and E. Hyde, Ed., Chemical Information Systems, Ellis Horwood Ltd., London, 1975.
(6) H. R. Schenk and F. Wegmüller, "Substructure Search by Means of the Chemical Abstracts Service Chemical Registry II System", *J. Chem. Inf. Comput. Sci.*, **16**, 153–161 (1976).
(7) J. Powell, J. F. B. Rowland, and M. A. Veal, "Correlated Structure-Text Searching for Chemical Information", United Kingdom Chemical Information Service Report, Nottingham, July 1976.
(8) W. Fisanick, L. D. Mitchell, J. A. Scott, and G. G. Vander Stouw, "Substructure Searching of Computer-Readable Chemical Abstracts Service Ninth Collective Index Chemical Nomenclature Files", *J. Chem. Inf. Comput. Sci.*, **15**, 73–84 (1975).
(9) B. M. Vasta, D. F. Walker, and R. Schultheisz, "Conversion of TOXLINE Chemical Dictionary File into CHEMLINE", presented at the 168th National Meeting of the American Chemical Society, Atlantic City, N.J., Sept 11, 1974.
(10) S. A. Tancredi, R. H. Amacher, J. H. Schneider, and B. M. Vasta, "CANCERLINE: a new NLM/NCI Data Base", *J. Chem. Inf. Comput. Sci.*, **16**, 128–130 (1976).
(11) R. S. Heller, G. W. A. Milne, R. J. Feldmann, and S. R. Heller, "An International Mass Spectral Search System (MSSS). V. A Status Report", *J. Chem. Inf. Comput. Sci.*, **16**, 176–178 (1976).
(12) "Chemical Abstracts Service Specifications Manual for Computer-Readable Files in Standard Distribution Format", Chemical Abstracts Service, Columbus, Ohio, Feb 1976.
(13) W. C. Zipperer, M. K. Park, and J. L. Carmon, "The CA Integrated Subject File. II. Evaluation of Alternative Data Base Organizations", *J. Chem. Doc.*, **14**, 15–23 (1974).

Symposium on Information Handling and Processing by the Food and Drug Administration

Introductory Remarks†

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This symposium on information handling and processing by the Food and Drug Administration was organized to help acquaint the scientific community with how FDA receives and utilizes scientific information in its enforcement of the Federal Food, Drug, and Cosmetic Act.

In addition to being the Bicentenial celebration of our Nation's independence and the 100th anniversary of the founding of the American Chemical Society, 1976 marks the 70th anniversary of the first Federal Food and Drug Act. On January 1, 1907, the Bureau of Chemistry of the Department of Agriculture, headed by Dr. Harvey Washington Wiley, began the enforcement of the 1906 law. Dr. Wiley was an early proponent of consumer protection and was the driving force behind the adoption of the Act of 1906. The FDA of today is a continuation of that first group organized by Dr. Wiley, although today it is organizationally located in the Public Health Service in the Department of HEW.

By 1938, it had become apparent that the Act of 1906 needed strengthening. Thus, the Federal Food, Drug, and Cosmetic Act of 1938 was adopted and, with various amendments added through the years, remains today the principal law governing the interstate movement of food, drugs, and cosmetics in the United States.

The Food and Drug Administration, charged with the enforcement of the Act, has therefore involved itself with the evaluation of scientific information in order to make judgments as to the safety and efficacy of the products it regulates. For example, FDA is involved with evaluation of chemical and toxicological data submitted with New Drug Applications (NDAs), New Animal Drug Applications (NADAs), and Food Additive Petitions. It must evaluate data in order to establish standards of purity and identity as well as safety and efficacy.

After these standards are established, they must be enforced through the collection of scientific evidence by use of investigative techniques and analyses by chemists, microbiologists, physicists, entomologists, and engineers.

As scientists we are aware of the fact that there are no absolute truths in science. Facts are collected and evaluated toward the goal of reaching as sound and as rational a decision as possible. Many of the FDA decisions are controversial and are criticized by proponents of one cause or another. FDA must, therefore, take pains to ensure that its decisions are based upon as sound a scientific basis as is possible with the evidence available.

In order, therefore, to present to you an overall view of the handling of scientific evidence in FDA, I have organized this symposium, loosely, into three parts: (1) setting of standards and tolerances; (2) development of sound investigative methodology; and (3) use of these standards, tolerances, and methods in the day-to-day enforcement of the act.

The first section, on the establishment of tolerances and standards, is covered by Dr. Banes, who, although not presently an FDA employee, is nonetheless intimately responsible for the setting of standards of identity, purity, and strength for the majority of drugs used today. These standards are developed partially with FDA data and are used by FDA in

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ensuring the excellence of our drug supply.

The second portion of the symposium consists of a presentation by Dr. William Horwitz, Deputy Associate Director for Science in the Bureau of Foods. Dr. Horwitz is also the Executive Director of the Association of Official Analytical Chemists and is on the Editorial Committee, along with Dr. Banes, for the *Journal of the Association of Official Analytical Chemists*. This association is one of the prime sources of standardized analytical methodology used in the enforcement of standards and tolerances in the FDA.

The final portion is covered by Mr. Hyman P. Eiduson, of the office of FDAs Executive Director of Regional Operations. Mr. Eiduson is responsible for the coordination and overall management of the activities of FDAs 20 field analytical laboratories. These laboratories are the "Front-Lines" in defending the consumer against adulterated and misbranded foods, drugs, and cosmetics. The final paper by Dr. Thomas Cairns and Mr. Robert Jacobson of the FDA Los Angeles District Laboratory is concerned with new approaches to FDAs analytical problems.

USP and the Development of Drug Standards†

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The history of the *United States Pharmacopeia* (USP), its role in maintaining the integrity of drugs, its relationship with the Food and Drug Administration, and the effect of advances in analytical methods on its standards are reviewed.

The *United States Pharmacopeia* (USP) enjoys a unique distinction among the world's official drug compendia. USP standards for the strength, purity, and quality of drugs are recognized by law as mandatory requirements enforceable by regulatory agencies of the United States and of the 50 states. If a product defined in a USP monograph fails to comply with any of the applicable pharmacopeial requirements, it is violative and subject to legal penalties. Yet the United States Pharmacopeial Convention is not an agency of the Government; it is a self-supporting, nonprofit, quasi-public institution. No other independent pharmacopeia exerts such a crucial influence on drug regulation. The flourishing condition of USP and its continuing leadership among pharmacopeial enterprises attest to its usefulness and effectiveness as an open forum where scientists from the academic, industrial, and governmental sectors can cooperate freely in evolving standards and methods of analysis for characterizing important drugs.

USP has played a major role in maintaining the integrity of drugs in the United States ever since the inception of the compendium more than one and a half centuries ago. The first national Pharmacopeia of the United States was conceived and brought forth by a convention of eminent physicians in 1820. They resolved to standardize those drugs "the utility of which is most fully established and best understood". Standards in the monographs assembled for the first American national compendium were intended to define articles of the highest quality and purity attainable through processes that assured the widespread availability of the drugs as medicinal agents. Thus, the standards reflected the composition of the better specimens of the products then distributed in the channels of commerce. Because scientific and technologic advances continually develop novel entities and improve the quality of drug articles already on the market, new monographs and more exacting standards are continually generated. Consequently, the first Pharmacopeial Convention foresightedly provided a mechanism for the periodic updating of the pharmacopeia through the ministrations of a scientific Committee of Revision. USP has lived in accordance with these precepts of the founding fathers ever since.

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USP standards were widely accepted as authoritative criteria for the quality of drugs throughout the 19th century. In 1906, when Congress passed the Pure Food and Drug Act, it formally accorded legal recognition to the monographs in the then current revision of USP, and most of the 50 states have since done likewise. The Federal Food, Drug, and Cosmetic Act of 1938 superseded the Pure Food and Drug Act, and Congress reconfirmed the precedent recognition of USP standards, tests, and methods as official requirements. However, the federal law now reserves a definitive veto power to the regulatory agency. The law states that if FDA finds a USP test or method inadequate for drug regulation, the Secretary of Health, Education and Welfare, "shall bring such fact to the attention of the appropriate body charged with the revision of such compendium, and if such body fails within a reasonable time to prescribe tests or methods of assay which, in the judgment of the Secretary, are sufficient for purposes of this paragraph, then the Secretary shall promulgate regulations prescribing appropriate tests or methods of assay in accordance with which such determination as to strength, quality, or purity shall be made". It is noteworthy that the Government has never found it necessary to exercise this veto or to set aside methods of analysis adopted by USP.

The actual process of evolving USP standards and test methods is a joint responsibility of a small headquarters staff and the pharmaceutical scientists in the USP Committee of Revision. The latter comprises a group of 50 volunteer scientists—biochemists, pharmacologists, microbiologists, pharmacists, chemists—elected by the United States Pharmacopeial Convention for a 5-year term. The drugs requiring monographs in the forthcoming revision of USP are designated by an expert group of volunteer physicians, constituted as a Committee on Scope, who select the most essential therapeutic agents currently in use and the best dosage forms for administering them. As a point of departure, tests and specifications are first solicited from the manufacturers of these products, and searches of the scientific literature are instituted. Tentative standards are suggested for assurance of excellence, and the originally proposed analytical methods are empirically tested for reliability and adequacy, or are supplemented or supplanted by methods deemed superior on the basis of findings in more recent investigations. In many instances, the