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PHARMACOPEIAS AND THE ROTATION OF THE PHARMACEUTICAL WORLD

Jack Cooper

School of Pharmacy, University of California at San Francisco

In Drug Development Communications, 1(5), 425-442 (1974-1975), Dr. Papariello draws a most unusual analogy by comparing the problems of control of drug quality with the slushy emotional catharsis portrayed in television soap opera. My inclination is to suspect that his knowledge of that intellectual form of audiovisual entertainment is derived from second-hand sources or, alternatively, that he works the night shift in his analytical and physical chemistry laboratories. Much to my astonishment and/or amusement, he vigorously proclaims that his article, with the dizzying title, "As the Pharmaceutical World Turns (A Scientist's View on USP Affairs)", represents an effort to solve "our (pharmaceutical quality) problems and arrive at our utopia." Thirteen years after the passage of Kefauver-Harris Amendments to the Food, Drug and Cosmetic Act, one would

imagine that utopia, like the infinite attainment of zero defects in pharmaceutical products, is an illusory goal.

The main thrust of the author's argument lies in his view that rapid advances in the pharmaceutical sciences render the concept of a public document prepared by a pharmacopeial or any other official public body to be absolutely inadequate as a means of providing a complete, up to date, specification system for drug manufacturers. In general, pharmacopeias have long suffered from the sacrosanct esteem in which they are held, so that any suggestions for significant changes are invariably accompanied by abject apology or exaggerated praise. More exotically, some U.S. authors dilute their critical comments by waving a nationalistic flag of superiority of their pharmacopeia over the competition from other countries or groups of countries. The official status of the USP in no way alters the fact that ultimate authority over the quality of the drug supply in the U.S.A. lies with the Food and Drug Administration and, beyond that agency, with the appointed Secretary of Health, Education and Welfare. Consequently, structural changes leading to improvement must take into consideration the interaction between the USP, the FDA, and the pharmaceutical industry. Without naming the actual power center, the National Formuary (NF XIV, Page xxxii, 1975) calls this a tripartite drug quality scheme through which

the quality built into a product at every stage of manufacture can be controlled.

In his discussion of certain weaknesses of the USP, Dr. Papariello expresses partial disagreement with a few of the eleven conclusions reached by the OTA Panel. Although he accurately quotes the single sentence of Conclusion No. 10, the 3-page analysis in the text of the report which led to that particular conclusion is far more revealing of the flexible thinking of the Panel's members. Among several options suggested by the Panel, the following was included: "The possibility that the USP and NF could merge and make sufficient changes in their structures and functions to fulfill the criteria for an effective standard-setting organization is not precluded, but the changes necessary would be extensive." Ten days before the submission of the Panel's report to the Congress of the U.S.A. on July 15, 1975, the merger of the USP and NF was effected, thereby providing an excellent opportunity for critical review of the role of the modern pharmacopeia in the establishment of quality standards for drug preparations without regard for traditional concepts and procedures.

Some of the suggestions for USP improvement come close to those delineated by the OTA Panel. However, doubling the number of members of the USP Revision Committee in the ab-

sence of a change in the method of selection (election!) or the composite of specialized skills represented on the Committee could be interpreted as a relatively minor reform. As to the problem of bioavailability which was the primary reason for the establishment of the Panel by the Office of Technology Assessment, the Revision Committee of the USP and the NF Committee on Specifications has without doubt been numerically short of experts in the relationship between dosage form design and biopharmaceutics.

Collaboration in the development of test methods and specifications between the pharmaceutical industry through the Quality Control Section of the Pharmaceutical Manufacturers Association and the U.S. compendia has a long and partially successful history. Had this collaboration been more closely integrated with advances in the design of quality rather than limited to the goal of conformance to specifications, the "weaknesses" in the USP pointed out by Dr. Papariello might have been eliminated long ago.

From the point of view of a regulatory agency legally acting in the public interest, the participation of scientists employed by the regulated industry is and will remain a sensitive issue. The OTA Panel cautions against inappropriate industrial or political influence and at the same time, urges the encourage-

ment of scientific input from industry. Political pressure from various professional or consumer organizations and from government officials in the legislative or executive branches concerning drug standards can be potent, but without the participation and contributions of pharmaceutical scientists from industry the formulation of a sound basis for the "dynamic" standards on Dr. Papariello's shopping list would be impossible.

The publication of the OTA Panel report has excised a good deal of the sentimentality associated with criticism of compendial standards and may even have brought into being such articles as the one by Dr. Papariello. Up to the present time, the major influence and participation in pharmacopeial revision has come from the discipline of analytical chemistry. Broadening the scientific base to increase the contributions of active workers in pharmaceutics, pharmaceutical technology, materials science, and biopharmaceutics will provide the dynamism which Dr. Papariello so strongly emphasizes in his critique.