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Better Regulations: A Case in Point

Several recent articles have been written concerning governmental regulations that impact directly on the conduct of research. This article will describe the final phase of the regulatory cycle on one such set of regulations—the FDA's Good Laboratory Practices (GLP) regulations—and how input to the Agency by those scientists to be regulated importantly affected the final regulations.

The background on the GLP's has been reported in several recent articles (*1–3*). The GLP's were published initially as a proposal in the *Federal Register*, November 19, 1976. The regulations in their final form were published in the *Federal Register* on December 22, 1978, and will become effective June 20, 1979. These regulations are intended to improve the quality of animal safety data submitted to the Agency in support of a research or marketing permit in the areas of food additives, drugs, and devices.

As proposed initially in 1976, the GLP's were a detailed series of rules that essentially told the scientist how to conduct his research. Left unchanged, these regulations would have impeded the science of toxicology both in terms of scientific growth and in increasing the costs of safety testing. In addition to toxicologists, the GLP's regulate the scientific input from any scientist contributing data to a safety study. One such group is analytical chemists, who analyze the chemical being tested, samples of animal feed or water containing the chemical, and animal body fluids and tissues to determine the fate of the chemical in the biological system.

The GLP's, when proposed, provided a comment period of 120 days to any interested persons to provide input to the Agency. In addition, two public meetings were held by the FDA for the presentation of oral testimony on the proposal. The results were 22 oral presentations and 174 written comments. These comments were submitted by manufacturers of regulated products, trade associations, medical centers, private testing or consulting laboratories, educational institutions, other Government agencies, and private individuals. Also, other substantive comments were made after the formal comment period and provided additional input during the Agency review period. After these comments

Table I. Major Federal Regulatory Agency Proposals Affecting Analytical Chemistry

Title	Scientific area	Primary analytical involvement	Agency	Status[a]
Good Laboratory Practices (GLP)	Toxicological Safety Studies	Test material characterization; animal fluid/tissue analysis	FDA	Final regulation in *Federal Register* 12/22/78, p 59986, effective 6/20/79
Good Clinical Practices (GCP)	Human Efficacy/ Safety Studies	Test material characterization; human fluid/tissue analysis	FDA	Proposed in part in *Federal Register* 9/27/77, p 49612; further proposals expected 1979
Bioequivalence/Bioavailability	Biopharmaceutical Studies	Body fluid/tissue analysis; methods development (Pharmacokinetic)	FDA	Proposal expected 1979
Federal Insecticide, Fungicide & Rodenticide Act (FIFRA)—Registration Guidelines	Environmental/Toxicology Efficacy/ Studies	Test material characterization; residue analysis	EPA (pesticides)	Proposed in part in *Federal Register* 7/10/78, p 29696. Comments deadline 9/8/78. Final regulations in late 1979
Toxic Substances Control Act (TSCA)—Sect. 4, Testing Standards	Human and Environmental Safety	Method development (trace levels)	EPA (chemicals)	Proposal early 1979
Cancer Policy (Various Federal Agencies)	Human and Environmental Safety	Regulation of hazardous chemicals. Affect facility design; exposure to and how, or if, chemicals can be used	OSHA	Proposed final regulations in *Federal Register* 10/4/77, p 54148, possible mid-1979
			CPSC	Proposed in *Federal Register* 6/13/78, p 25658. Federal court injunction
			EPA	Revised policy possible in 1979
IRLG—Report: Guidelines for Identifying Carcinogens	Human and Environmental Safety	Test material characterization; residue analysis	IRLG (reps. from FDA, OSHA, CPSC, EPA)	Report—"Scientific Bases for Identifying Potential Carcinogens and Estimating Their Risks" was released 2/7/79

[a] For information on any regulations proposed in the *Federal Register*, the federal agencies identified may be contacted for copies of proposals.

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were received, the FDA evaluated each comment for its merit and how the specific suggested change would meet the Agency's need for ensuring the best possible data. In the preamble of the final GLP regulations in the December 22, 1978, *Federal Register*, the comments received by the Agency are each discussed with the Commissioner's reason for accepting or rejecting each suggestion. *Many suggestions were accepted.* A critical one from the analytical aspect was that the material being safety tested can be "appropriately characterized" rather than identity, strength, quality, and purity being automatically specified. This critical change permits sound scientific judgment to be exercised in the characterization of the materials being tested.

Because of the Agency, the final GLP's are more manageable, less costly, and still meet the original purpose. Many of the details on exactly *how* the scientific work is to be conducted have been eliminated, and professional judgment can replace detailed rules.

This final GLP still meets the Agency's needs, but does not place an undue burden on the scientists involved in assessing the safety of new chemicals. The final GLP regulations demonstrate the desire on the part of the Agency to work with those regulated to produce meaningful rules. Without this willingness to adopt scientific input, there would have been a manyfold increase in cost of safety testing. More importantly, the number of safety tests and the time required to complete safety work would have decreased the number of new health products made available to the consumer.

The regulatory area continues to change, and there are many similar chances for scientific input to a governmental agency. For example, the Environmental Protection Agency (EPA) will issue in the coming months their version of the GLP's covering safety studies for the materials they regulate. To avoid considerable confusion, it is imperative that the EPA's rules be consistent with final GLP's from the FDA. Those to be regulated should carefully examine the EPA's proposed GLP rules and provide the EPA with written comments on unacceptable aspects. Table I lists regulatory proposals or anticipated proposals that should be of interest to analytical scientists and deserve their input.

References

(1) William Horwitz, *Anal. Chem.*, **50** (6), 521A (1978).
(2) Robert M. Hodges, *ibid.*, p 531A.
(3) R. A. Libby, *ibid.* (10), 575A (Sept. 1978).