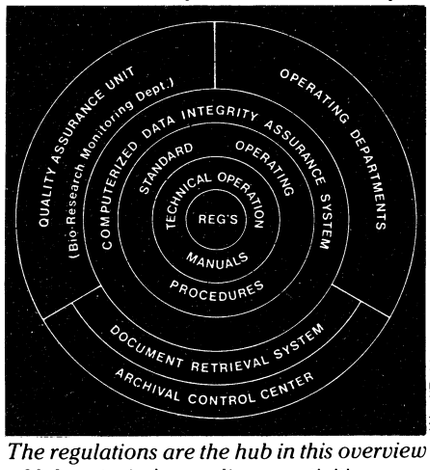
Good laboratory practice rules take effect

Laden with checks and cross-checks and quality assurance units, the Food and Drug Administration's "Good Laboratory Practice" regulations took effect this week. All research intended to establish the safety of FDA-regulated products, such as food additives, drugs and medical devices, must now comply with those standards.

There was little last-minute rush in testing laboratories to begin meeting the regulations. For both the FDA and the laboratories, the major impact has been spread over the last two years. The regulations were first proposed in 1976 when congressional hearings and administration investigations uncovered sloppy and even fraudulent data that had been submitted to the FDA (SN: 11/27/76, p. 343).

A major effect of the regulations, according to Dave McCurdy of ICI Americas Inc. in Wilmington, Del., is that the "product" of a testing program will no longer be just the end report. "Now the final 'product' is your files and your records of which the final report is only one part," McCurdy says. That change involves much more documentation and standardization of procedures, such as writing out detailed operating procedures. Robert J. Van Ryzan, director of preclinical safety assessment with Sandoz Pharmaceuticals in East Hanover, N.J., says "There is more checking and approval and signing and dating, so we can reconstruct the study at a later date."

One important change is that the regulations' final form, which was published in the Dec. 22 FEDERAL REGISTER, does not include references to regulations enacted by different agencies, for example under the Animal Welfare Act. "We also greatly tightened the criteria for disqualification of a laboratory," FDA's Paul Lapore says. In the proposal, a testing facility could be disqualified for one violation of the regulations; in the final rules disqualification would result only when a laboratory failed to comply with one or more rules; the violation adversely affected the validity of more than one study; and lesser regulatory sanctions failed to work. The lesser sanctions include disqualifying the studies involved and rejecting product applications.



Ward/Robins

The regulations are the hub in this overview of laboratories' compliance activities.

Perhaps the most novel section of the regulations is the requirement that testing facilities have a "quality assurance unit." That person, or group, is responsible for overseeing the testing operations. In the proposed regulations, the unit was conceived as being an independent assessment and reporting group. However, in deference to small testing companies, the final rules permit an employee to wear multiple hats. A scientist may be the director of one study and the quality assessor for another.

At least one point is still a source of disagreement. The regulations require laboratories to save for several years a sample of test material from every batch mixed. The Pharmaceutical Manufacturers Association is filing a petition asking the FDA Commissioner to delay implementation of that requirement and to delete it. "One drug can easily produce over 23,000 samples from eight pivotal studies," says John W. Ward, director of biological research at the A. H. Robins Co. in Richmond. "Special storage conditions and accountability problems are mind-boggling."

One reason for the rapid compliance of testing laboratories with the proposed rules is the inspection program the FDA began two years ago. Partly to determine whether the rules were practical and partly to show they meant business, inspectors have already visited most U.S. laboratories that submit safety data and also several European laboratories. The pilot inspections also helped the testing laboratories to determine in detail what changes the FDA expected. The day before the rules took effect, Ward of A. H. Robins Co. was still pondering the exact requirements. "Every time you meet with the FDA you get a better idea," Ward says. "By now I'm sure we're in compliance, but we may be doing a lot of things we don't need to do."

The pilot inspections turned up differences between the different types of laboratories in how well they met the standards. Product sponsors doing their own tests best met the most proposed regulations, and universities did worst. Contract laboratories fell between the other two groups. The universities most frequently lacked quality assurance units and adequate data storage and record retention.

Although the regulations increase the cost of safety testing (most industry estimates fall between a 15 and a 50 percent increase), the FDA and industry agree that the rules promote accurate results. "In my judgment, a higher standard of laboratory practice prevails throughout the industry today as a result of the GLP's," says Donald Nielsen, representing the National Association of Life Science Industries, Inc., a group that includes many toxicology laboratories. Charles Cleveland of the Pharmaceutical Manufacturers Association concurs. "They will probably improve result quality." □

Ozone linked to sun's UV flux

Ozone has been a star attraction in atmospheric studies for several decades. And for good reason. Ozone is the molecule that is created about 35 kilometers above us as oxygen absorbs the sun's ultraviolet radiation, thus protecting life below from harsh UV rays. Therefore, it is not surprising that the amount of ozone in the stratosphere may vary with the sun's output of UV radiation.

NASA Langley Research Center scientists Linwood B. Callis, Murali Natarajan and John E. Nealy set up a model to calculate stratospheric ozone and temperature variations in relation to published data on the sun's changing UV flux between the early 1960s and 1976. The three researchers concluded that observed ozone and temperature trends may be due to a large extent to variability in the solar ultraviolet flux associated with the 11-year solar cycle.

They report in the June 22 SCIENCE that the agreement between their calculations and actual measurements of ozone concentrations in the temperate latitudes during that period was "generally good." As the UV flux sinusoidally increased and decreased during the solar cycle, so did the ozone. Variations in the temperature followed a similar pattern.

Changes in 0_3 come about from both photochemical and thermal processes. As the flux of UV radiation increases, the photochemical production of 0_3 likewise steps up. That increase in ozone concentration is partly offset by rising temperatures, which tend to reduce the amount of 0_3. All these interactions were included in the radiative-convective-photochemical model set up by the three researchers to study the effects of a changing UV flux on the stratosphere.

Although the comparisons were encouraging, the NASA scientists cautioned that more comprehensive data on the variation of 0_3, temperature and the solar UV flux for wavelengths less than 300 nanometers are needed before the question of UV flux and ozone can be definitely resolved.

It was noted that there are other natural phenomena that may induce ozone variations over the course of a year. These include atmospheric absorption of galactic cosmic rays, solar proton events and sudden stratospheric warmings. □