accept. At this point, the substance of the bill he will introduce is uncertain, but staffers have been working hard in recent weeks to hammer it out. However, he has expressed relative satisfaction with the Administration's bill and is likely to incorporate many of its features. Speculation is that he will include an amendment to the immigration laws to stem the flow of foreign medical graduates who are currently receiving licenses to practice in this country in about the same numbers as American doctors. The fate of an extremely controversial provision that doctors be relicensed every 6 years is undecided.

For all the uncertainties in the present legislative dance on Capitol Hill, it is certain that, whatever the outcome, medical schools will never be as free to go their own way as they have been in the past. And, if past experience in the manpower business is any indication of future events, one must conclude it is not certain that measures now being contemplated by Congress and the Administration will succeed in achieving the desired end.

Merlin K. DuVal, a former assistant secretary for health who is now a vice president at the University of Arizona, has aptly pointed out that, during the past 16 years, there have been at least eight full-scale reports by major organizations on the manpower problem. "That none of these reports . . . should have sufficed is, itself, testimony to the difficulties that are associated with accurately assessing the health manpower needs of the United States. Furthermore, that so many such efforts were undertaken at all is rather clear evidence that neither the medical profession nor the political leadership in the United States is entitled to any feeling of confidence that it knows what it is talking about in addressing this same problem today."—BARBARA J. CULLITON

Color Additives: Botched Experiment Leads to Banning of Red Dye No. 2

A deft legal maneuver by Food and Drug Commissioner Alexander M. Schmidt has enabled his embattled agency to climb free of the wreckage of a ludicrously botched experiment on the safety of the controversial color additive known as FD & C Red No. 2. After a frantic 10 days of searching for a way out of the Red 2 imbroglio, Schmidt announced on 19 January that he would ban further use of the dye in foods, drugs, and cosmetics.

Just 2 months earlier his own Bureau of Foods and several members of an expert advisory committee had seemingly given the dye a clean bill of health. But in the interim a new statistical analysis of previously considered data suggested that Red 2 might well cause cancer. The results of the new analysis, which surprised most of the experts who were reviewing the status of Red 2, raised questions in some minds as to the adequacy of the testing and analytical procedures traditionally used by the Food and Drug Administration (FDA) to determine the safety of food chemicals.

Red 2 has been the most widely used food color in this country, and it has always been touted as the "most thoroughly tested" of all the food colors. Yet questions were raised in the early 1970's, largely on the basis of tests conducted in the Soviet Union, as to whether the dye might cause cancer or reproductive damage.

In an effort to answer these questions, two major tests were conducted by FDA. One, a collaborative effort involving two FDA laboratories and a commercial laboratory, concluded that Red 2 does not cause reproductive damage. The other, also originally launched as a reproduction study but then adapted to examine the question of carcinogenicity, soon became such a muddle that it is routinely referred to by FDA scientists as the "botched" or "bungled" study. Yet it is this study which formed the basis for the recent regulatory decision on Red 2.

The study involved feeding Red 2 to four different groups of rats, each at a different dosage level, and then comparing the health of these treated groups with the health of a control group. There were 500 rats in all—seemingly enough for a solid evaluation. But the study was left unsupervised for a long period of time after a scientist was transferred, and it developed two serious flaws. To begin with, the animal handlers managed to put some of the rats back in the wrong cages part way through the experiment, so that an undetermined number of rats were shifted among the control group and the four treated groups. Second, the animal handlers were lackadaisical about retrieving dead rats from their cages and rushing them off to the pathologists for examination. As a result, virtually all of the rats that died during the course of the experiment were so badly decomposed as to be of little use for evaluation. Only those rats that survived to the end of the experiment and were killed—some 96 in all—were available for detailed histopathological examination. "It was the lousiest experiment I've seen in my life," commented one scientist who reviewed the data.

Yet the study was not considered a total loss by the FDA, which reasoned that it would be possible to treat the intact animals which had been fed the largest dose of Red 2—3 percent of their diet—as a "high dose" group and all the other intact animals as a "low dose" group. By comparing the two groups, the reasoning went, it might be possible to learn *something* about whether Red 2 is carcinogenic.

A key role in making this determination was to be played by the FDA's Toxicology Advisory Committee, a group of government and outside scientists which was formed last year to deal with just such perplexing and controversial issues as the safety of Red 2. The committee held its first meeting in late November and, to judge from the proceedings, it appeared that Red 2 would be exonerated from suspicion as a carcinogen. The pathology division of the Bureau of Foods submitted a report on the "botched" experiment which concluded that Red 2 had "no apparent adverse effect" on the rats. And many members of the advisory committee seemed to agree, offering such comments as, "I have a feeling that this is an innocuous color" and, "There has been no evidence that I have seen which makes me think that this compound is a significant or major carcinogen."

Still, just to be certain, the committee ordered up three further analyses by experts within its membership. One of those studies—a statistical analysis of the results of the "botched" study performed by David W. Gaylor, principal biological statistician at the FDA's National Center for Toxicological Research in Arkansas—revealed that the Bureau of Foods may have been a bit too hasty in drawing its rosy conclusions. Gaylor found that, while it was indeed true that there was no significant difference in the *total* number of tu-

mors, both benign and malignant, in the high-dose and low-dose groups, there was in fact a significant increase in the number of *malignant* tumors found in the female rats fed the high dose. Gaylor's analysis, dated 31 December, became known to the press, a circumstance which led FDA Commissioner Schmidt to announce on 8 January that he would proceed with whatever action was warranted within 10 days. That launched a rushed reappraisal.

A working group of scientists from the Toxicology Advisory Committee, the FDA, and the National Cancer Institute met on 14 January to review Gaylor's analysis. They concluded, in essence, that Gaylor's statistical approach was valid, but that the strength of his conclusions would depend upon confirming the original pathology data "using a slight redefinition of tumor types." The significance of this is that some of the tumors counted as "benign" might conceivably be reclassified as "important" (benign now, but possibly heading for malignancy) or perhaps even "malignant." If a substantial number of the "benign" tumors in the low-dose group were reclassified, that might wipe out the difference between the low- and high-dose groups, perhaps indicating that Red 2 had no pronounced effect after all. Such, at least, is the speculation among those scientists at the Bureau of Foods who still are dubious that Red 2 is harmful.

The working group noted that the "botched" study was of such poor quality that it could never be used to demonstrate the safety of Red 2, but it suggested further evaluations of the data in an effort to determine whether Red 2 is carcinogenic. However, the FDA commissioner, who had recently been given a rough time on Red 2 by various senators and congressmen, the General Accounting Office, and reporters on a nationwide television interview show, was not about to wait for more evaluations. On 19 January, he announced that he would act immediately to terminate the approval for use of Red 2 in foods, drugs, and cosmetics. He did not claim that Red 2 is carcinogenic. Rather, he noted that Red 2 had only a "provisional" approval, a category that is meant to indicate that studies are under way that are expected to demonstrate safety and thus lead to "permanent" approval. Since the latest FDA study could not establish safety, he said, and since no other studies are known to be under way that could resolve the safety questions, the provisional approval had to be rescinded. The burden of proof, he added, lies with those who manufacture or use Red 2 to prove that it is safe and useful. Then, since he had not exactly ruled that Red 2 is unsafe, he explained that there would be no recall of existing products containing Red 2 since there is "no evidence of a public health hazard."

Industry spokesmen were predictably outraged. The top color scientist at one company that makes Red 2 told *Science*: "I think it's a disgrace. It's a case where media pressure and consumer group pressure really took precedence over scientific judgment. The commissioner acted upon emotion and without a final opinion from the full Toxicology Advisory Committee. As far as I'm concerned, Red 2 is still safe." But consumer activists who believe that Red 2 should have been banned long ago on the basis of earlier suspicious test results were enthusiastic.

One potentially significant revelation to emerge from the confused proceedings is that the FDA's Bureau of Foods does not always perform a sophisticated statistical analysis of the results of its studies. The Bureau's report to the advisory committee last November—the one which found "no adverse effects"—was based on an examination by pathologists but not on a detailed statistical analysis of the pathological findings. Bureau officials have since offered two explanations for this. One is that they were so rushed to get a report together for the November meeting of the advisory committee that they didn't have time to do the statistics—an excuse that some participants find preposterous, since the Bureau was able to perform an analysis lickety-split after Gaylor's memorandum challenged their original conclusions. The other is that no analysis seemed necessary in this case. Thus Herbert Blumenthal, director of the division of toxicology in the Bureau of Foods, told the working group that the tumors observed in the study were typical of the particular colony of rats, and that the pathologists were not concerned about them. According to the minutes of the meeting, he said he "would not have requested a statistical analysis of this study." Blumenthal, whose division was in charge of the "botched" study, and who was obviously dispirited after a hectic week, declined to elaborate in an interview with *Science* on why he felt no statistical analysis was needed.

But one participant in the review process believes the Red 2 flap has uncovered a serious flaw in the FDA's system of evaluating tests. "In the past, they've just had people eyeballing the stuff," he said. "They look at the data and look for things that jump out at them. But in so doing, they could quite easily make a mistake. In this case they did. If this study had not been botched, there would have been no statistical analysis. How many things have they done in the past where they just eyeballed the data and said, 'It looks OK'?"

—PHILIP M. BOFFEY

APPOINTMENTS

Amoz I. Chernoff, director, University of Tennessee Memorial Research Center, to medical and scientific director, Cystic Fibrosis Foundation, Atlanta.... **Edward C. Melby,** dean, New York State College of Veterinary Medicine, to chairman, Institute of Laboratory Animal Resources, National Research Council.... **William H. Knisely,** assistant chancellor for health affairs, University of Texas System, to vice president, academic affairs, and president-elect, Medical University of South Carolina.... **Byron S. Gottfried,** professor of industrial engineering, University of Pittsburgh, to director, School of Engineering's Energy Resources Program at the University.... **Louis Padulo,** associate professor of electrical engineering, Stanford University, to dean, College of Engineering, Boston University.... **Robert H. Walker,** acting dean, College of Natural Sciences and Mathematics, University of Houston, to dean of the college.... **Riley Schaeffer,** professor of chemistry, Indiana University, to dean of arts and sciences, University of Wyoming.... **H. Ray Hoops,** chairman, communicative disorders and sciences department, State University of New York, Buffalo, to dean, Graduate College, University of Northern Iowa.... **Joseph T. Durham**, dean, School of Education, Howard University, to dean, School of Education, Coppin State College.... **Edward I. Isibor**, associate professor of technology, Florida International University, to dean, School of Engineering and Technology, Tennessee State University.

Erratum: In the 9 January issue, page 51, the weight of the Trident I missile was incorrectly stated. The correct weight is 70,000 pounds.

Erratum: In the report "Chemical Fractionation of the Lunar Regolith by Impact Melting" by J. B. Adams, M. P. Charette, and J. M. Rhodes [**190**, 380 (1975)], the following should be added to the legend of Fig. 1: "Trace elements determined by instrumental neutron activation analysis were made by D. P. Blanchard, J. W. Jacobs, J. C. Brannon, and L. A. Haskin of the NASA Johnson Space Center. These results are discussed in more detail in J. M. Rhodes, J. B. Adams, D. P. Blanchard, M. P. Charette, K. V. Rogers, J. W. Jacobs, J. C. Brannon, L. A. Haskin, *Geochim. Cosmochim. Acta* **1** (Suppl. 6), in press."

Erratum: In "High speed scintillation autoradiography" by B. G M. Durie and S. E. Salmon (12 Dec., p. 1093), in the third paragraph, the sentence beginning "The scintillator consists of 35 g . . .," the quantity is incorrectly printed. The sentence should read "The scintillator consists of 5 g of 2,5-diphenyloxazole (PPO) and 100 mg of 1,4-bis-2-(4-methyl-5-phenyloxazolyl)-benzene (dimethyl-POPOP) dissolved in 500 ml of dioxane." In the next-to-last sentence of reference (*6*), the formula for dioxane should read $C_4H_8O_2$.

Erratum: In the report "Transcontinental baselines and the rotation of the earth measured by radio interferometry" by I. I. Shapiro *et al.* [**186**, 920 (1974)], the heading for columns 5 and 6 of Table 1 should read "Atomic time–universal time (A.1–UT.1)" and the second entry of column 1 should be followed by a double dagger (‡).