1, 2] that bacteria were undoubtedly observed and described by Leeuwenhoek as early as 24 April 1676, and *not* 1681, as stated. Further, De Waard [see A. Schierbeek, *Measuring the Invisible World* (Abelard-Schuman, 1959)] has discovered that Zacharias Janssen was born in 1588, and his son Hans, in 1611, so that neither could have invented the compound microscope in 1590.

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Food Additives

The 27 May 1960 issue of *Science* [**131**, 1581 (1960)] gave editorial approval to the report of the Panel on Food Additives of the President's Science Advisory Committee. The principal recommendation of the panel was to set up an advisory board "to weigh evidence and make recommendations to the Secretary of the Department of Health, Education, and Welfare on the basis of available scientific data on applications for the approval of food additives." In evaluating this recommendation two facts should be considered. First, the panel probably would be under heavy pressure from corporations who would want exemption *now* for additives for which there is *some* evidence of carcinogenic effect in animals. Second, on the basis of present data and techniques, there is no way to make a reliable prediction of the "safe" level of a carcinogenic compound, and—to quote the report—"definitive answers useful in extrapolation to man may not be expected for many years to come."

While the report discusses a number of the major difficulties in the path of scientific decision-making in this area, there is one particular difficulty (which gets bare mention in the report) that we would like to stress here because it is often overlooked. This difficulty arises because (i) the population at risk is of the order of 10^8 persons; (ii) our primary emphasis is on controlling the *number* (rather than the proportion) of cancer cases; and (iii) direct estimates of the risk probabilities would be based on relatively small experiments (10 to 10^3 animals). Since we would be concerned if an agent produced, say, 100 cancer cases, a "safe" level would require risk probabilities of the order of 10^{-6}. Statistical theory indicates that to obtain adequate direct estimates of such small risk probabilities would require a sample of 10^6.

From this standpoint, consider the decision rule: If no cancers develop in 1000 test animals, classify the corresponding level of the agent as "safe."

The probability of obtaining zero cases in a trial sample of size n, when the true incidence is p, is given by the last term of the binomial expansion $[p + (1-p)]^n$, $(1-p)^n$. Thus, if an agent were capable of producing 100,000 cases of cancer in the United States population at risk ($p = .001$), there would be about one chance in three $[(1 - .001)^{1000}]$ that the agent would be classified as "safe." Even if we make the common assumption (which is not always legitimate) that dividing the dose level by 100 would be equivalent to obtaining no cancers in 100,000 test animals, in such a test of an agent which could produce 1000 cases in a population of 100 million ($p = .00001$), there is a one-in-three chance $[(1-.00001)^{100,000}]$ that no experimental tumors would occur.

The present alternative to direct estimation of risk probabilities is extrapolation from dose-response curves. The report states that "dose-response curves for certain potent carcinogens in animals have been worked out from which can be reliably predicted the probability of an individual, in a given size population, developing a tumor from a given dose of carcinogens." This statement requires qualification. While a given technique (such as probit analysis) will often be adequate for ordinary applications (which involve interpolation or very limited extrapolation), the extrapolation required here makes the estimate heavily dependent on the assumption about the underlying distribution (such as the normal distribution). This point is evident when several alternative linearizing transformations (probits, logits, angits, and so on) are used on the same data. While all may provide a fair fit to the observed points and very similar estimates for the LD_{50} (50-percent probability), the *extrapolated* estimates for very small probabilities will not even be of the same order or magnitude. Such predictions are clearly not reliable enough to be used in a decision where human lives are involved.

Until reliable decision-making procedures for the food additive situation are developed—and to develop them is certainly not an easy task—we would question the advisability of vesting an advisory board with power to exempt chemicals that have some experimental carcinogenic effect from the present Food Additive Amendment of the Food, Drug, and Cosmetic Act. An advisory board to review procedure to be considered adequate for testing chemicals for carcinogenic effect in man would, of course, be useful. The creation of such a board probably does not require any amendment to existing legislation.

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Goals of Secondary School Teachers

As a secondary school teacher (in biology), I feel I must reply to Merritt A. Williamson's letter in *Science* [**132**, 1732 (1960)].

In his statement, "college teaching, as contrasted with secondary school teaching, is concerned with the development within the student of the power to think, reason, appreciate, and discriminate . . . ," he implies that these are not the objectives of the secondary school teacher. He is very wrong. These are the objectives I had when I taught sixth-grade and eighth-grade biology and which I now have in teaching tenth-grade biology. That I am not alone is evidenced in the fact that, through the American Institute of Biological Science's Biological Sciences Curriculum Study program, hundreds of secondary school teachers (among others) contributed to the development of three different approaches to the teaching of biology, all of which embodied these same objectives.

There are 118 teachers now using