LETTERS

IARC Benzene Report

Following the article "Risk estimate vanishes from benzene report" by Marjorie Sun (News and Comment, 3 Sept., p. 914), I should like to clarify the following points.

1) In the heat of the argument concerning benzene, it seems to have gone unnoticed that volume 29 of the *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans* (*1*) published by the International Agency for Research on Cancer (IARC) contains 18 monographs on individual chemicals, one of which is benzene. The monograph on benzene (*1*, pp. 93–148) contains a critical review of all available information on this chemical and ends with an evaluation which reads: "there is sufficient evidence that benzene is carcinogenic to man."

2) The annex to volume 29, with the title "Some aspects of quantitative cancer risk estimation" (*1*, pp. 391–398), is the first attempt the IARC has made to explore the possibility of making quantitative cancer risk estimations. While such quantitative estimates may eventually become incorporated into the *IARC Monographs*, the present annex is in no way an integral part of the *Monographs*. The Working Group which met in October 1981 "recommended to IARC that a special monograph be prepared on quantitative risk estimation" (*1*, p. 391).

3) During the October 1981 meeting that prepared volume 29, there was no detailed or in-depth discussion about methodologies for extrapolation of cancer risks. As is stated in the summary remarks of the annex (*1*, p. 396), "the Working Group restricted their analyses to data available in published form and kept extrapolations to a minimum." With this in mind, the annex was later revised with the aim of making it a solid scientific document that did not attempt to provide risk estimates beyond what the data permit and would represent a sound initial step on which a program to explore the feasibility of making quantitative risk estimations could be built. The text as it now stands reflects the quantitative data derived from published epidemiological studies.

On pages 395 and 396, there is a complete and objective summary of the available evidence of risks derived from exposure to benzene. It is clearly indicated that, at 100 parts per million, the estimated relative risk for leukemia is increased more than 20-fold. Risks of this magnitude should attract attention to the possibility of significant risks at much lower levels. The IARC felt, however, that the data were insufficient to quantify precisely risks at lower levels. It is possible that many people have not read the annex in its entirety.

4) Several officials of the National Cancer Institute have expressed their concern about the issue of quantitative risk assessment. It is clear that, at least in part, this concern is related to the considerable adverse reaction caused within the scientific community by a document on quantitative risk estimates from occupational exposures prepared some time ago by scientists at a number of federal agencies, including the National Cancer Institute (*2*). The opinions of national institutes have been, and always will be, taken into consideration, but this in no way implies that IARC has been or will be ready to accept any interference in its activities and decisions.

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References

1. *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans.* vol. 29, *Some Industrial Chemicals and Dyestuffs* (International Agency for Research on Cancer, Lyon, France, 1982).
2. R. Peto and M. Schneiderman, Eds., *Quantification of Occupational Cancer* (Banbury Report 9, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., 1981).

American Participation in IIASA

We welcome the editorial by Jurgen Schmandt (10 Sept., p. 987) on the International Institute for Applied Systems Analysis (IIASA). We are glad to take this opportunity to let the American scientific community know that American participation will not cease with the end of this calendar year, when the National Academy of Sciences withdraws as the National Member Organization. The American Academy of Arts and Sciences in Boston will take up the role as National Member Organization for the United States as of 1 January 1983 and is seeking to raise from foundations and corporate sources enough money to cover the dues and related administrative expenses for the next several years.

We cannot agree with Schmandt's view that the lesson to be drawn from the Administration's decision to withdraw from IIASA is that the "design was too complex and the goals too ambitious." We think the lesson is a simpler one: short-term and ideological considerations were given too large a weight in the government's decision to stop funding. We expect to demonstrate by continued participation of able American scientists that IIASA's work is of substantial intellectual value and that it can continue to make an indispensible contribution to the understanding and resolution of problems that go beyond the ideological divisions and barriers in the world today.

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NIH 3T3 Cell Line

The current excitement concerning the discovery of similar "oncogenes" in several tumor viruses and several human tumors (Research News, 14 May, p. 724) brings us back to the fundamental question of when a cancer begins. The biological assay system used in most of the recent oncogene work has been the NIH 3T3 line of mouse fibroblasts (*1*), a highly contact-inhibited, anchorage-dependent cell culture in which a less contact-inhibited, less attachment-dependent cell and its descendants can easily be identified. But like the original 3T3 line (*2*) and the Balb/3T3 line (*3*), as well as other "established" mouse lines (*4*), the NIH 3T3 line originated as rapidly growing cells that appeared in a primary culture of diploid cells undergoing the senescent "crisis" inevitable for all diploid cultures. Like the others, it is already heteroploid in chromosome constitution (*5*). Balb/3T3 cells can be shown to be tumorigenic under certain circumstances (*6*), and it seems likely that NIH 3T3 cells would do so as well.

Thus, NIH 3T3 cells already have some of the properties of "transformed" cells and are potentially tumorigenic. They can be made into less contact-inhibited, less anchorage-dependent cells—features that are subsequently acquired stepwise in the evolution or "progression" of all tumors. Factors that accelerate this evolution are not really oncogenes but "progressogenes." Understanding them is of much interest and clinical relevance, but it is not the same as understanding the initial event, usual-