Alar: The Aftermath

Eliot Marshall's News & Comment article about Alar and its hydrolysis product UDMH (unsymmetrical dimethyl hydrazine) (4 Oct., p. 20) offered a balanced account of the economic fallout 2 years after Alar was taken off the market, but muddied the waters by putting a somewhat bizarre spin on the results of new rodent bioassay of UDMH. A subsequent editorial by Daniel E. Koshland, Jr. (1 Nov., p. 629) reinforced and compounded Marshall's misinterpretation. Even a cursory look at the actual data in the 1991 and 1973 bioassays shows clearly that "the basic toxicology on Alar" has *not* "taken a surprising turn." In fact, given the vitriolic criticism of the earlier study, the new industry-sponsored results are only surprising for how much crow the critics may have to eat. In the 1973 study (*1*), 42 out of 50 male mice given 23.3 milligrams of UDMH per kilogram of body weight per day (mg/kg/day) developed blood-vessel tumors. Eighteen years later, 31 out of 67 male mice (46%) given 7.3 mg/kg/day developed these malignancies, along with 63% of those given 13 mg/kg/day (*2*). How can these new data be viewed as anything other than a confirmation and amplification of the earlier study, at even lower doses than previously analyzed (*3*)?

Marshall's article and a subsequent response by Victor J. Kimm at the Environmental Protection Agency (Letters, 29 Nov., p. 1276) emphasize small changes in the official point estimate of UDMH's potency. At most, such changes represent a tiny "signal" compared with the "noise" inherent in potency estimates (which itself is only a fraction of the total uncertainty in risk) (News & Comment, 9 Mar. 1990, p. 1173). In the case of UDMH, even the factor of 20 Marshall discusses is largely an artifact of different methods EPA has used to adjust for peculiarities in the bioassay data (*4*). Without all the arcana of potency calculation, one can easily show that Alar posed a potentially serious hazard. Using national survey data on apple juice consumption and the manufacturer's own data on UDMH residue levels, one can show that a plausible dose estimate for many young children was about 0.0005 mg/kg/day, or about 1/2000 of the equivalent dose that causes tumors in roughly half of all mice (*5*). Therefore, unless the dose-response function is sharply nonlinear or has a threshold, the excess risk to many children was roughly 1 in 4000, or 250 times the 1 in 1 million standard generally regarded as de minimis.

So, it seems that the risk assessments Koshland disparages as "clearly dubious" were more prophetic than were the dire

predictions of economic hardship and consumer dissatisfaction that Marshall debunks. In light of the new scientific and economic evidence, for *Science* to continue to take the side of the real "alarmists" over those who urged or took prudent action about Alar is sour grapes, plain and simple.

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REFERENCES AND NOTES

1. B. Toth, *J. Natl. Cancer Inst.* **50**, 181 (1973).
2. E. I. Goldenthal, "Two-year oncogenicity study in mice 'with UDMH' " (Report No. IRDC-399-065, International Research and Development Corporation for Uniroyal Chemical Company, Mattawan, MI, 1990).
3. There is some question whether the 13 mg/kg/day dose caused toxic effects that confounded the carcinogenic response, but even Bruce Ames' colleague Lois Gold apparently accepted the validity of the 7 mg/kg/day dose. Thus, the statement in Marshall's article (attributed to Gold) that "there appeared to be some significant tumors" at 7 mg/kg/day leaps off the printed page; such a statement could lead a reader unfamiliar with the study to believe that there were only three or four animals with cancer rather than 31.
4. An explanation of the rationales for, and influence of, two EPA adjustments that, if omitted, would together bring the 1973 and 1991 estimates closer by a factor of 16 is available from the author.
5. For a 20-kilogram child, the 7.3 mg/kg/day dose corresponds to just under 1 mg/kg/day (if you believe interspecies conversion should be based on body surface area) or about 1.5 mg/kg/day (if you use the proposed EPA–Food and Drug Administration compromise approach of scaling based on body weight to the three-fourths power).

Alar is now gone from the food supply, and public health is better protected. Despite dire industry predictions, neither the quality nor the quantity of apples has diminished in the absence of Alar. The 4 October News & Comment story and the subsequent 1 November editorial on Alar contained several serious errors, creating the impression that Alar posed little health risk. However, the latest studies submitted to the Environmental Protection Agency (EPA) once again demonstrate that Alar's metabolite UDMH (unsymmetrical dimethyl hydrazine) is carcinogenic and that Alar's dietary risk is 26 times EPA's standard of acceptable lifetime cancer risk of 1×10^{-6}. Even with the revised estimate of UDMH's carcinogenic potency derived from the new bioassays, the dietary hazards of Alar exceed EPA's standard of acceptable cancer risk. This conclusion was affirmed in a letter to *Science* (29 Nov., p. 1276) from Victor Kimm, Deputy Assistant Administrator, Office of Pesticide Programs and Toxic Substances at EPA. The most recent cancer studies confirm the results of the earlier bioassays relied upon in the Natural Resources Defense Council's report *Intolerable Risk: Pesticides in Our Children's Food*—that Alar's metabolite UDMH is carcinogenic; there is *no* dispute that UDMH is a probable human carcinogen.

Science has missed the most important lesson of the Alar episode. As long as cancer remains one of the leading causes of disease and death in our society, the prudent course is to reduce and avoid exposure to carcinogens, particularly those that are unnecessary. The removal of Alar without impacts on apple production was an important step toward the goal of decreasing unnecessary and avoidable exposure to carcinogens in the food chain.

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Response: I believe my editorial and Eliot Marshall's article provide a more balanced approach to the facts than do the two letters above.—DANIEL E. KOSHLAND, JR.

Supermelons?

We folks here in Kentucky are well aware that California produces a lot of fruits and vegetables and we are glad of it, especially in the winter when a hard pink tomato is a real treat. However I garden a bit when I'm not doing biochemistry or reading *Science*, and I was startled to read in the article by Elizabeth Culotta about the "Superbug" (News & Comment, 6 Dec., p. 1445) that Nick Toscano of the University of California, Riverside, found a California field that grows 750,000 melons per acre. I learned as a farm boy that an acre covers 43,560 square feet, so this remarkable field produces about 17 melons per square foot. If these are cantaloupes, with each fruit covering about 1 square foot, I guess they must grow in a stack 17 deep. That sure would be handy for pitching on the truck when picking, but I imagine it makes a tough row to hoe or to spray for those nasty whiteflies. If these unspecified melons are big watermelons the problems must be even worse. Could the weight of these stacks of melons in the Imperial Valley be the cause of California's excessive seismic activity? If so, then the whiteflies may be the only means of preventing the Big One. In spite of these potential problems and Kentucky's proximity to the New Madrid fault, I have just one request: please send me some seeds!

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Response: If Dr. Hoffman gets his melon seeds, he doesn't have to worry about setting off the New Madrid fault. Nick Toscano misinterpreted the growers' figures. That 1-acre field will produce about 500 cartons of cantaloupes—or up to a maximum of about 11,000 melons, depending on how big they are. The 750,000 figure is the total number of melon cartons produced by about 1500 acres in the Imperial Valley. Of course, in the fields with the worst whitefly infestations, the melon yields are zero any way you count them.

—EDS.

The Arginine Fork: Correction

In the paper by B. J. Calnan *et al.* about the interaction of HIV (human immunodeficiency virus) Tat peptides with TAR RNA (Reports, 24 May 1991, p. 1167) (*1*), it was reported that a single arginine in Tat is involved in sequence-specific RNA recognition and that modification of two phosphates at a three-nucleotide bulge in TAR interferes with binding. These phosphates were said to be located between nucleotides A22 and U23 and U23 and C24. However, we have subsequently found that one of the assignments was incorrect and that the two phosphates are actually located one position lower, between nucleotides G21 and A22 and A22 and U23. Both pairs of phosphates, at the junction of the stem and bulge, are consistent with the modeling described in the paper, and the main conclusions are unchanged. We regret any inconvenience this error may have caused.

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REFERENCES

1. B. J. Calnan, B. Tidor, S. Biancalana, D. Hudson, A. D. Frankel, *Science* **252**, 1167 (1991).