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NRDC on Alar

Since its release in February, the report of the Natural Resources Defense Council (NRDC) *Intolerable Risk: Pesticides in our Children's Food* (*1*) has generated substantial discussion, including two articles by Leslie Roberts (News & Comment, 10 Mar., p. 1280; 17 Mar., p. 1430) and an editorial by Daniel E. Koshland, Jr. (7 Apr., p. 9), in *Science*. The report estimated the potential health risks to children ages 1 to 5 from dietary exposures to 23 pesticides resulting from consumption of 27 fruits and vegetables. We would like to respond to the following specific questions that have been raised by the Environmental Protection Agency (EPA) (*2*), by Koshland, and by others and to present new information.

1) *Was the study based on a worst-case estimate of exposure*? Because of the limited data available, the NRDC report actually underestimated total pesticide exposure. NRDC estimated exposures to only 7% (23/300+) of the pesticides currently registered for use on food, including 12% (8/66) of the food use pesticides known or suspected to be carcinogenic (*3*). In addition, NRDC used *average* residue values, derived from government monitoring programs, in its exposure assessments. Tolerances, or legal limits, were not used because pesticide residues in food are generally considerably lower than the tolerance levels.

Because the report identified a high cancer risk resulting from exposure to the daminozide breakdown product UDMH, critics have questioned the exposure estimates used in the calculations. Average daminozide and UDMH residues were derived from a 1985–1986 market basket survey (*4*). Daminozide levels in apples averaged 1 part per million or 1/20 of the existing EPA tolerance for daminozide, while UDMH levels averaged 2 to 23 parts per billion (*5*). NRDC did not factor into its exposure estimates metabolic conversion of daminozide into UDMH, which EPA now estimates to be 1% (*6*). Had a 1% metabolic conversion been included, NRDC's exposure estimates for UDMH would have been increased by 36%.

Consumption data used in the report were derived from the 1985–1986 nationwide survey of daily food intakes of 489 children ages 1 to 5 (*7*). Exposure estimates for UDMH were calculated on the basis of an average consumption of approximately 3 ounces of apple products daily (*8*).

EPA's current estimate for UDMH exposure, based on a larger 1977–1978 U.S. Department of Agriculture dietary survey, differs only slightly from NRDC's. For commodities covered by the NRDC report, EPA currently estimates that the average daily exposure to UDMH for children ages 1 to 6 is 0.066 μg/kg/day (*9*) or 80% of the NRDC estimate for children ages 1 to 5 (*10*). EPA's current estimate of children's (1 to 6) total exposure to UDMH (*9*) is approximately twice NRDC's.

The NRDC's risk assessment has been challenged as overestimating risk because of the belief that daminozide use has decreased since 1986 and that currently "only 5% of apples are treated with Alar." However, 1988–1989 federal, state, and independent surveys found that 22% to 55% of apples tested had been treated with daminozide (E. Groth, III, Letters, 19 May, p. 755), indicating that the 5% figure may significantly underestimate the amount of daminozide used during the last growing season. Although EPA estimated earlier this year that 5% of the apples were treated with daminozide, the agency has recently revised that estimate upward to 5 to 15% (*6*).

2) *Was a valid cancer potency estimate used by the NRDC study for UDMH?* NRDC used a UDMH carcinogenic potency factor (q_1*) calculated by EPA in 1984 and listed in 1987 by the Office of Pesticide Programs (OPP) and the Carcinogen Assessment Group (CAG) (*11*). At the time that NRDC conducted its risk assessment, this was the only available estimate of carcinogenic potency for UDMH.

NRDC has been criticized (*2*) for using this q_1* because the Science Advisory Panel (SAP), an advisory panel to EPA's Office of Pesticide Programs, gave the opinion in 1985 that the existing bioassays on daminozide and UDMH were not adequate as the basis for quantitative risk assessment (*12*). The SAP opinion, however, was not consistent with other scientific analyses by EPA and other expert groups. EPA's CAG concluded that the existing evidence was more than adequate to classify UDMH as a "probable human carcinogen" (*13*) and was sufficient to serve as the basis for calculating a carcinogenic potency factor for this compound (*14*). Two independent EPA audits of the study that served as the basis for the CAG potency estimate agreed that, despite limitations, the bioassay clearly demonstrated that administration of UDMH led to a significantly increased incidence of multiple types of tumors at multiple sites in both sexes of test animals (*15*).

Similarly, 1 month after the SAP review, EPA's Environmental Criteria and Assessment Office concluded that the existing UDMH studies "provide sufficient quantitative evidence that 1,1-dimethylhydrazine represents a potential carcinogen" and that criticisms raised do not "constitute a basis for altering the fundamental conclusions of EPA's risk assessment for UDMH" (*16*). In addition to the EPA reviews, both the International Agency for Research on Cancer (IARC) and the National Toxicological Program (NTP) concluded that there was sufficient evidence of carcinogenicity (*17*).

Just before the release of the NRDC study, EPA published an updated assessment of the carcinogenic risk resulting from daminozide use based on interim (12-month) results of a new UDMH bioassay being conducted by Uniroyal. Two revised cancer potency factors were calculated that were lower than the previous agency q_1* used in the NRDC computations by factors of 10 (based on hemangiosarcomas) and 4 (based on benign lung tumors) (*18*).

Cancer is a disease with a long latency, and interim results may lead to underestimates of potency. EPA attempted to allow for latency by multiplying the cumulative incidence at 1 year by a factor of 8 to obtain an estimate of the cumulative 2-year "lifetime" incidence (*6*). This factor of 8 appears to be inappropriately small, however. The age-specific incidence of hemangiosarcomas in the Uniroyal bioassay (male and female UDMH exposed groups combined) is approximately proportional to the fourth power of time from first exposure (*19*). If this proportionality is maintained in the second year, the cumulative 2-year incidence will be about 30 times the number of cancers present at the end of 1 year (the sum of effects of a t^4 incidence function is proportional to t^5, so doubling the duration of the experiment would increase the cumulative incidence by 2^5, rather than 2^3, as proposed by EPA). Using the multiplier of t^5 would bring the interim q_1* based on hemangiosarcomas in the current experiment to about 4 mg/kg/day^{-1}, four times higher than the revised EPA q_1* discussed above and approximately half the q_1* used in the NRDC computations.

EPA anticipates that the final q_1*s based on the completed Uniroyal bioassay may be considerably higher than the q_1*s based on the interim data (*20*). On the basis of consideration of subsequent findings at lower doses, the agency predicts that hemangiosarcomas, which are currently significantly in-

creased only among animals in the highest dose group in the Uniroyal bioassay, will be detected at the end of the study in the lower dose groups as well, and risk estimates based on subsequent findings could be one or two orders of magnitude greater than the risk estimates based on the interim study results (*19*). In other words, the agency's final revised q_1* may be similar to the agency's previous q_1* used by NRDC.

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2. Environmental Protection Agency, press release, 16 March 1989.
3. ———, *Fed. Reg.* **53**, 41101 (19 October 1988).
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