Consumers Union
Publisher of Consumer Reports

November 6, 1989

Bruce N. Ames, PhD
Department of Biochemistry
University of California
Berkeley, CA 94720

Dear Dr. Ames:

Thank you for your recent letter in response to our article about the pesticide controversy.

After due consideration, we have decided not to print your rebuttal statement. We don't agree that our article contained errors, or that we have distorted your views or those of other activists who have drawn upon your work. We believe the issues we addressed, including the scientific ones, are debatable, and that the public benefits by exposure to more than one point of view. We think the public has been amply exposed to your side of the debate through your appearances on network TV, the ACSH film, your syndicated newspaper Op Ed piece and other vehicles. Through our article, they have been exposed to another side of the debate as well. One article on this topic is sufficient for Consumer Reports; to rehash the debate would be excessive coverage.

Your comments about CU's "new activist mode" reflect some ignorance of our history. Activism on behalf of consumer interests has been an integral part of our work for 53 years. In fact, we published several reports on pesticides in foods in the 1930s. The problem then was lead arsenate, but the debate was very familiar indeed.

We would be quite interested in seeing any documentation you can provide that identifies those "people" you mention who "are talking about millions of cases of cancer due to pesticide residues, or about cancer epidemics that have no scientific justification." We have not seen such claims for many years.

You suggest that we get the best scientists to advise us. We agree that we benefit from consulting with highly qualified outside experts on such topics; we always have consulted with such experts, and we do so now.

Internally, our own Technical Director, Dr. David Pittle, served for nine years as a member of the U.S. Consumer Product Safety Commission. In that capacity, he dealt repeatedly with scientific data and approaches, uncertainties, and policy judgments in the regulation of potential carcinogens. In fact, he

remembers working with you 15 years or so ago when the Tris debate was before the Commission. Our Associate Technical Director for Policy and Public Service, Dr. Edward Groth III, also has outstanding qualifications. He earned his Ph.D. at Stanford in Biological Sciences, specializing in environmental policy. He spent five years as a staff member of the National Research Council of the NAS, where he worked with the nation's top environmental health scientists on some major environmental issues. He is a member of the International Society of Regulatory Toxicology and Pharmacology, and has about twenty years of professional experience in environmental health sciences, risk assessment, risk management policy-making processes, and risk communication.

Between them, Dr. Pittle and Dr. Groth have a wealth of professional experience on the interactions between science and policy in the regulation of chemicals. They also have access to a large number of top-flight scientists, among them highly qualified experts in fields related to cancer risk assessment. CU consults with such advisors repeatedly and effectively in our work, and did so for our most recent article as well.

With such expertise to draw on, Consumer Reports has long been and will continue to be one of the very best sources of information on questions of risk and risk management related to consumer products. You are simply mistaken when you suggest that we lack scientific acumen, or need better scientific advice. We recognize that there are many scientists, including you, Dr. Ames, whose political views and value judgments on matters of risk do not match our own. We think our differences with you involve some important value judgments, as well as legitimate criticisms of your scientific statements.

In lieu of a published continuation of the debate, I have asked Dr. Groth to respond to your rebuttal. We hope such an exchange of scientific perspectives will be mutually useful.

Sincerely,

Rhoda H. Karpatkin
Executive Director

cc: R.D. Pittle
E. Groth III

Consumers Union
Publisher of Consumer Reports

December 7, 1989

Bruce N. Ames, Ph.D.
Professor and Chairman
Department of Biochemistry
University of California
Berkeley, CA 94720

Dear Dr. Ames:

A few weeks ago, Rhoda Karpatkin asked me to reply to the response you sent to our October report, "Too Much Fuss Over Pesticides?" When I began working on this reply, you and I were scheduled to debate each other on the radio show "Head to Head," on December 18. I began drafting this letter with the intent of delineating our areas of agreement and disagreement before we debated, to help focus the discussion. I have now learned from Dr. Shienbaum that you declined to participate if I was part of the show, so we will not debate. Nevertheless, I hope this response will be useful in the same way. I believe you and I agree on many things, though we certainly could have had a lively debate on others. I hope this letter will help us to focus on our real differences.

To help you know me a little better, and to reciprocate the gesture you made, my c.v. is attached.

Before getting into the specifics of your response to our article, some preface is required. I believe you and Consumers Union (and I personally) have several goals in common. We all seek to help consumers make intelligent decisions about risks they face in daily life--risks from consumer products, risks from environmental agents, risks from personal and lifestyle choices. A substantial part of what citizens need to know about risks is scientific information, and CU is as committed as you are to making sound interpretations of current science available to our audience. At the same time, defining a risk and what to do about it involves much more than just scientific data. It includes ethical choices, subjective perceptions of importance, and other value-laden judgments. Let me briefly outline CU's views on these two aspects of risk: the scientific and the nonscientific dimensions.

In our view, the dominant feature of most scientific components of risk assessments is uncertainty. We are all familiar with the uncertainties inherent in using animal data to predict risk to humans, or in extrapolating from high-dose data to low-dose actual exposures, and these are but two among a myriad of

important risk-related issues on which science currently does not have all the answers. Yet, in debates over public policy, we in the scientific community are often under pressure to speak as if we did, indeed, have all the answers. It is not easy to explain to the public how much we don't know.

Uncertainty also means that on scientific issues related to public policy there is generally room for more than one interpretation of a given set of facts, and that scientists will disagree over what the data mean. Such disagreements can't be resolved by some heuristic as simple as the eminence or number of the scientists who hold a view. Science speaks with many voices, and no one holds an exclusive claim to "the truth."

At the same time, science is not static; an ever-enlarging body of knowledge is available to support risk assessment. New discoveries in many areas are improving our models, reducing uncertainties, offering some experimental data to replace the "default" assumptions made when knowledge is insufficient. But new ideas, no matter how powerful and useful, still must run the scientific gauntlet of criticism, challenge, synthesis with existing knowledge, and incremental reinterpretation before we can determine their proper place in the structure of knowledge and their value for making public policy.

Given the inherent uncertainties in the science of risk and the tentative nature of all new knowledge, scientists must make many subjective judgments in stating what they know. What is a fact, and what just an interesting theory? How much weight are we to give to a novel approach to an old task, comparison of relative risks, such as your HERP method? There is no single "scientific" answer to such questions, only a variety of opinions. And opinions on such questions are likely to stem from people's values, social views, political roles, and other factors beyond their scientific training and knowledge.

That brings me around to the non-scientific components of risk issues. Given scientific uncertainties, risk managment decisions often hinge on questions like "What should we do when we do not know for sure?," which is an ethical question, not a scientific one. Many scientists (and other citizens) may think society has gone too far toward "erring on the side of caution" in order to protect public health. But that is an ethical perception, not a scientific fact. I have observed that many of our fellow scientists seem to confuse their own value judgments with their scientific knowledge. It's important to recognize the difference between expressing our opinions as citizens and speaking on matters of science, but this distinction is often buried in the "scientific" debate on policy questions.

One specific criticism I have of your own work, and that of many others who have compared relative risks (Cohen, R. Wilson, and so forth), is that such comparisons generally ignore all dimensions of risk other than the size of the hazard (usually, the expected annual mortality, though Cohen has used loss of life expectancy as an index.) But there is a massive body of solid research in social psychology and other sciences showing that "risk" is really a far more complex phenomenon than just magnitude of hazard. It has many other definable, quantifiable attributes, such as fairness, voluntariness, immediacy, dread nature of the outcome, and so forth. Slovic's article in the 17 April 1987 issue of Science (adjacent to your HERP paper) summarized most of that work. Sandman's paper (see your cc of my letter to Reed Irvine) also states the problem very well.

My perspective is that the public responds not only to the size of various risks, but to how acceptable they are, which is determined by many attributes in addition to size of a hazard. A very large risk, such as cigarette smoking or driving a car, is acceptable to most consumers because these are self-chosen activities, and the benefits accrue immediately and directly to the person at risk. On the other hand, a small risk, such as UDMH in apple juice or radiation from nuclear power plants, is unacceptable to many people, because they have no choice in the matter (which is seen as ethically intolerable) and because the distribution of risks and benefits is perceived as unfair.

For example, consider the recent history of public policy on cigarette smoking. As long as it was perceived that only smokers were at risk, public opinion favored giving freedom of choice greater weight than protecting health. But once smokers were seen as threatening the health of others via "second-hand smoke," smoking in public places, on planes and trains, and in offices has been aggressively restricted, even though the risk to passive smokers is a small fraction of that borne by smokers themselves. I submit that public policy is driven not by how large these two risks from tobacco are, but by how acceptable they are in moral terms. And, I believe that moral acceptability is a very important component of risk, not a trivial or "irrational" subjective perception that risk managers should disregard. In a democracy, the public has a right to pick and choose among risks, to find some morally acceptable and others morally abhorrent, and to ask government to manage risks based on their acceptability, not only on their size.

To return to your work, now, this perspective suggests one major criticism I would make of it. I believe, by your focus only on the relative size of various hazards, you have implied that the size of the risk is all that matters in setting public policy priorities. CU agrees that size matters (i.e., that we

need to know the relative size of risks). But clearly, size is not all that society needs to consider in managing risks. Your analysis, provocative as it is, considers only one dimension of a multi-dimensional phenomenon. By being unduly narrow, it may be quite misleading.

In particular, you say "It makes no sense to apply a double standard to human exposures to natural vs. synthetic chemicals." Toxicologically speaking, the risks can be compared on the same scale, and it makes sense to do so. But in moral terms, these two categories of risks are very different, and a "double standard" indeed does apply. That is, people clearly perceive that a natural risk is morally far more tolerable than one inflicted by a human agent or institution--especially if the human agent was aware of the risk, but imposed it anyway, out of economic self-interest. This de facto "double standard" is sensible and proper in an ethical context: People can be held responsible for the consequences of their actions, while Nature cannot.

So I would therefore respond to your statement as follows: "It makes no sense to ignore the indisputable fact that people <u>do</u> apply very different moral standards to risks of different types." When you treat all risks alike in your analysis, you are making an implicit value judgment that all risks are morally equal--a point of view I think few people would endorse, if it were openly stated. (This is an example of what I meant about value judgments that are "buried" in scientific debates about risk management.)

In practical terms, natural and synthetic hazards for the most part <u>are</u> treated alike. Aflatoxin, urethane, and other known natural carcinogens can't often be banned, but they can usually be regulated, as tightly as economic costs allow. The practical issue is avoidability, not natural vs. synthetic. But moral acceptability is a significant factor in judgments of the relative importance of controlling risks of each type.

Forgive me for this long preface, which has some attributes of a lecture. Having sat through one of yours (on video tape), I feel well informed on your views. I wanted to give you some background on ours, to put our specific disagreements in better context.

Let me now respond to points in your letter. The issues are quite complex, and despite my desire to be brief, this response reflects that complexity. In general, I have followed the outline of topics in your October 16 "rebuttal;" this led to some repetition, which was probably unavoidable, since the topics are highly interconnected.

In your opening statement, you referred to our report as an "attack on [your] scientific work." We do not accept that characterization. The primary target of our article, as I think we clearly stated, is the political argument that pesticides need not be a concern because natural hazards are greater. That is what many people (ACSH and others) are saying your work shows, and you have said as much yourself in your more political published writings and interviews. Criticism of your scientific work is appropriate, and we offered some. But let us separate your scientific work from your value judgments, and from the politically weighted conclusions you have drawn from assessing the work of others. The latter are both more complex and more debatable, and were the chief focus of our report.

We agree that good scientists are committed to rigorously challenging assumptions. And new theories that challenge major current paradigms deserve to be challenged as well, before they can replace the existing theories. Thus, we see both your own work and our response to it as important, legitimate parts of the scientific debate necessary to improve the ways society copes with risks from toxic substances in the environment.

We are, in fact, extensively familiar with your views. I have read many of your published papers on this topic; read your letters to Science and your Op Ed piece in the Los Angeles Times; viewed your videotaped lecture twice in its entirety; watched the ACSH film and your appearances on 60 Minutes and 20/20 several times each, also through the magic of video tape. Your views are clearly and consistently stated in those materials, and I think we understand them quite well. Our response to most of the material in your letter would be, "we already know that." To elaborate on that response, I will highlight both some areas on which we largely agree and points where we disagree with your interpretation of existing data.

(1) Discovering the causes of cancer. I agree that science is learning more about the causes of cancer at a rapid rate, but I believe an accurate accounting of proven causes of human cancer is much farther off than the next decade. We can expect (maybe hope is the better term) that new knowledge will reduce, rather than expand, uncertainties, but I think this will happen at an incremental pace, more than in quantum leaps.

I have been a student of the literature on the epidemiology and toxicology of cancer for more than 20 years, and many of the things you say are true. At the same time, I believe your letter, and some of your papers, oversimplify issues that are far more complex than you have stated them. This is a common problem for all scientists, both when writing for the public

and when trying to be concise in a letter. I will therefore assume that you and I both know the issues are more complicated than you put them in your letter. Nevertheless, much of this response to your letter deals with topics on which I believe your statements are too simplistic and unscientific.

I believe we agree that cancer is a complex process with a number of stages and a multifactorial etiology. I suggest that the way you use the term "carcinogen" is therefore inherently misleading. As we both know, the toxicological community now generally speaks of "initiators" and "promoters," rather than just "carcinogens." These days, when toxicologists do use the word "carcinogen," they generally mean "initiator." There is still a vigorous debate among researchers as to the importance of promotion in human carcinogenesis; not all experts concede that promoters play an important role. (More on this later.) And some authorities, such as John Weisburger, have enumerated several different mechanisms of initiation and promotion, which suggests that the nomenclature will get more complex yet. But to the average consumer, a "carcinogen" is an agent that causes cancer, by itself. Years of public education will be needed to teach the public to draw the distinctions that experts now draw routinely.

In my judgment, calling a substance like salt or ethanol a "carcinogen" is incorrect, given current scientific use of the term, and misleading, given public understanding of the word. Salt is indeed a gastric irritant, and its action may predispose to cancer. And ethanol may well enhance cancers initiated by other agents. But neither of those actions is what the public thinks "carcinogens" do. We should try to teach the consumer to draw distinctions, not perpetutate confusion bred of obsolete terms. Sloppy terminology breeds sloppy thinking.

Our report was careful to discriminate between the known cancer risk of alcoholic beverage consumption and the question of whether ethanol per se is a carcinogen. I have less problem with your calculation of HERP scores for the nitrosamines and urethane in alcoholic beverages than I do with the HERP scores for ethanol. It can be argued that ethanol is an important co-carcinogen, or promoter. But I don't think it is theoretically sound to treat initiators and promoters as if they were directly comparable. Their mechanisms of action and their dose-response curves might be completely different; we really don't know that they act in like ways. Is it good science to treat them alike?

We also differed with your judgment in accepting the single rat study you relied on as positive evidence that ethanol is a carcinogen, whereas the majority of studies suggest that it is not. I suspect you would agree with the NAS/NRC and the IARC in

their assessment that the evidence is insufficient that ethanol itself causes cancer. I agree that it probably enhances cancer progression, but we disagree over whether HERPs or statements to the public should treat it as a "carcinogen" because of that. If, indeed, there is a threshold in ethanol's effect on cancer growth, as you suggest, isn't a HERP index based on, say, the ethanol content of orange juice, rather misleading?

While you point out in your letter that "HERP comparisons can be refined as we learn more about mechanisms," the large uncertainties in the comparisons you have made so far, and the ways HERPs gloss over distinctions that current, reasonably mainstream scientific theory says should be drawn, are largely being ignored in political references to your work.

(2) Animal Cancer Tests. I have wrestled with the limitations of animal tests since my days on the staff of the NAS/NRC, 15 years ago. There has been much new science over that span, and it is slowly resolving uncertainties, and refining what animal tests are and are not good for. Most experts agree that animal data are relevant and useful for assessing human risks. And at least for now, we must continue to use them as best we can, as the only ethically acceptable option.

Your letter raises two major issues related to animal tests for carcinogenicity: The scope of substances tested (both those that have been tested and those that need to be tested); and the use of animal test results in risk assessment.

(a) Scope of Animal Testing

Here, again, some of your statements are overly simplistic. For instance, you say there are "millions of chemicals, 99.9+ percent of them natural, to which we are exposed in low or moderate doses." Here, I believe you have gone beyond what can be stated as a fact based on current knowledge. There are some 70,000 synthetic chemicals in commercial production, to which we may theoretically be exposed. How many of them do we actually encounter in our daily lives? I don't know, and I submit that no one really does. The sort of inventory of uses and environmental pathways required to answer that (in effect, an environmental mass-balance analysis for 70,000 substances, not counting breakdown products and reaction products) hasn't been done, nor is it really doable. When we look at nature, there probably are millions of different chemicals. But how many of them are we really exposed to? It actually seems quite unlikely that most Americans will ever be exposed to, say, the natural plant substances produced by native vegetation of the Amazon basin, or even those in most wild plants growing in a vacant lot down the

block. Who has done an inventory of such substances, and added up how many we really encounter? Once again, I suggest that it has neither been done nor is it even doable.

Given those assumptions about the state of knowledge (which you are free to challenge), I think your use of numerical shorthand like "99.9+ percent natural" is very misleading. It seems to imply precise knowledge, where you and I both know that it's a back-of-the-envelope number in the face of enormous uncertainties. Such numbers are very useful for propaganda impact, and that is in fact how they are being used. But this is a prime example of what we meant by "stretching science out of shape," in our article. To try to elevate such intuitive estimates to the status of scientifically established facts is untenable.

Your own work certainly calls attention to the need to know more about the toxicity of natural substances. In truth, most food toxicology texts (at least the ones I've read) have more chapters on natural hazards than on synthetic ones, but that does not mean we don't need to test a much wider range of the more prevalent suspected natural initiators and promoters. My view is that we really need to know more about <u>both</u> natural and synthetic hazards, not to switch our attention from one to the other. We don't know enough yet about either category.

Your statement that about half of the tested substances in both natural and synthetic categories are carcinogens seems to be based on a rather selective listing of what has been tested. As Efron's book points out, there are widely differing reports of how many substances have been tested, and some authorities have catalogued as many as 10,000 that have been tested in at least one bioassay for carcinogenicity. Yet the NTP and IARC list only some 200 to 400 substances for which there are enough decent data to call them even <u>suspected</u> carcinogens. Based on those numbers, the ratio of "carcinogens" is closer to 2 to 4 percent. Other authorities have put the number between 10 and 20 percent. I don't believe your estimate of "about half" is anything like a consensus estimate.

One reason there is no consensus is that there are no universally accepted criteria for when a substance should be included in either the numerator or the denominator. I appreciate your stating your criterion that you consider a substance "tested" if it has been subject to a long-term bioassay in both rats and mice. That criterion by itself makes the list a very selective one. It could reasonably be argued that substances that had been tested in one rodent species and showed no evidence of carcinogenicity in those tests would be low-priority candidates for tests in a second rodent species. But does that mean they should be excluded from your denominator? I wouldn't

think so; to do so would clearly bias the ratio toward inflating the proportion of "carcinogens" among "tested" compounds.

I also think there should be some additional criteria for the denominator. Can we ignore the methodological soundness of the bioassays? Not all such studies are of equal reliability. Many older studies tended to be done on smaller scales and with fewer dose levels; some found cancer in 100 percent of a small group of animals, while those reporting negative results might be too limited in design to rely on. How should we "count" the pre-NTP studies? How does quality of the study figure in your denominator?

Concerning the numerator, we need to know what we mean by "carcinogens." As mentioned earlier, your list seems to include quite a few substances that might be termed co-carcinogens, or promoters, but are not initiators. And whether a substance is an initiator is also an issue that requires some discriminating judgments. The IARC, EPA and other agencies use complex classification systems that separate "carcinogens" into four or five classes, from "proven human carcinogen" through several degrees of "probable/possible carcinogen," depending on the quality of the evidence, to "unclassifiable." Those distinctions matter, both scientifically and in the regulatory context. You seem to have lumped into a single category substances that the EPA and IARC now place in four or five quite different categories.

In short, I think there are many unstated assumptions and subjective judgments in your estimate of "about half," and that most of those assumptions and judgments are debatable, and not demonstrably "good science." Here, too, I think your use of a numerical "shorthand" to illustrate this point vastly oversimplifies a scientifically complex problem. To say "about half" of the natural and synthetic substances tested are "carcinogens" may be effective propaganda, but it is not a scientific fact. It does not enhance the quality of public debate on managing carcinogenic risks when partisans treat this highly judgmental and debatable conclusion as if it were a fact.

We are familiar with your HERP database, published in Environmental Health Perspectives in 1984-86. There appear to be over 900 substances listed there. Frankly, I am not so familiar with each of those substances that I can be certain whether it is "natural" or "synthetic." It is also not clear to me which 427 of the 900+ listed substances are the ones you referred to as "tested for carcinogenicity," or which 75 among them are the "natural" ones, of which 47 percent are carcinogens. I would also like to know which 47 substances (25 of them carcinogens) you have classified as "nature's pesticides;" that isn't made clear in the materials I have on hand. It would help to clarify

your point (and save me from having to do the analysis) if you have an updated list with this information. Do you have such a print-out of the 427 substances, with the needed information on it? If so, may I have a copy?

(b) Use of Animal Data in Risk Assessments

I agree with some of your first paragraph under (c) on page 2 of your letter, but think the term "worst-case assumptions" is overused. While EPA and others in general try to err in the direction of overestimating risk (an ethical choice, based on a desire to overprotect, rather than underprotect, public health), there are several ways in which current risk-assessment models are not especially "conservative." See Adam Finkel's paper in the Columbia Journal of Environmental Law (Volume 14, No. 2), 1989. (Finkel has a Ph.D. from Harvard in Environmental Health and is a specialist in carcinogenic risk assessment, so don't be put off by the fact that he published his analysis in a journal accessible to policymakers.)

An important point made by Finkel in that paper, an echo of one I made earlier in this letter, is that risk assessment is a value-laden process, not merely a scientific exercise. Whether to use the 95-percent upper confidence limit estimate of a risk or the 50th-percentile estimate is a value judgment; neither of these estimates is more or less "scientific" than the other. The choice depends on what we want a risk assessment to accomplish, not on differences in scientific rigor.

Risk assessment is as much an art as a science, and it has been changing over the years, with the advances of underlying knowledge bases. The models and assumptions used by EPA today to assess carcinogenic risks are not the same as they were ten years ago, and they will be different still five or ten years from now. It seems that critics of regulation treat regulatory science as monolithic and unchanging, whereas in fact there is a continuous process of trying to incorporate new and better science into procedures. Research scientists may be impatient with the speed of institutional change, but I perceive that it has picked up lately. We need to move forward at some steady pace, not recklessly throw out good current approaches along with obsolete techniques we would like to replace.

In that context, I recognize what you and your colleagues have tried to do with the HERP approach. But I don't believe you have succeeded yet in producing a viable alternative to the approaches now used by the EPA and others.

(c) Methodological Problems With the HERP Approach

We believe your work with the HERP approach can be evaluated on two different levels. On one level, you have promoted the idea that "nature is not benign," and that we need to pay more attention to naturally occuring sources of cancer risk. That is a sound concept, as long as the importance of moral distinctions between natural and human-made risks is not overlooked in the effort to put hazards of synthetic chemicals in perspective.

But on another level, you are promoting the HERP approach as a method for ranking risks and setting priorities, with the implication, at least, that this task has not been done (or not done properly) up to now. Since you, and a phalanx of political actors who are using your work to argue for changes in national risk-management priorities, are trying very hard to present the HERP method as a scientifically sound, credible tool for making such policy judgments, criticism of HERP methods cannot be dismissed as "nit-picking;" it is at the heart of the matter.

In general, I believe the EPA's Q* approach provides much more useful information on potency than your TD_{50}. The Q* approach was developed over the past decade by some of the best toxicologists and biostatisticians in the nation. It includes many accommodations to the nature of the data, designed to give it as much biological "realism" as possible, given unavoidable uncertainties. It deals with sampling error in bioassays, and represents the slope of the dose-response curve in the low-dose region; TD_{50} values do neither of these. Someone with more expertise in biostatistics than I have could undoubtedly expand on this critique. As Wilson and Crouch (and others) have now shown, when actual human dose-response data for the few carcinogens for which we have such data are compared to the low-dose extrapolated risk estimates from animal data for those substances, the human data fit reasonably well with the projections from the animal data. The human data are scattered on both sides of the animal data curve; there is no evidence of systematic overstatement of risks that you assert occurs.

I also must note a major inconsistency between what you <u>say</u> about extrapolating results from high-dose rodent tests to low-dose human exposures, and what you <u>do</u> when faced with a need to say something about low-dose risks. In your 1987 Science article, you said "It is not scientifically credible to use results from rodent tests done at the MTD to directly estimate human risks at low doses." In your recent letter to CU, you said it is essentially impossible to know the risks at low doses. Some of your other writings have attacked the linear low-dose extrapolations used by regulatory officials as invalid, unscientific

methods that inaccurately estimate risks. Yet you concede that your HERP index is nothing more than a very simplified linear extrapolation from a high dose (the TD_{50}) in rodents, to the low doses humans are exposed to. HERPS assume that potency is constant, and risk changes linearly with dose. Your proposed method of dealing with the "inaccuracy" of such extrapolations is to ignore absolute values, and instead to compare risks. For example, your letter says the public ought to be told that the risk from the UDMH in apple juice is 1/18 that from aflatoxin in peanut butter, 1/50 that of eating a mushroom, 1/1000 of a beer a day, and so forth.

But your approach is no solution at all. In fact, it seems almost certain to compound the inaccuracy inherent in linear extrapolations (or extrapolations by any other models). Ratios are in truth the product of two estimates (actually, of one and the inverse of the other); as such, the uncertainty of a ratio is the product of the uncertainties of the component values. To question the absolute accuracy of a risk estimate extrapolated from high-dose animal tests is scientifically correct, and most practitioners of risk assessment raise the same questions when presenting their estimates for use in regulatory decisions. To substitute ratios of two very uncertain numbers and offer them to the public as "better science," however, makes no scientific sense at all. It seems to me that you have taken this approach because it yields conclusions you want to believe are true, not because it is scientifically sound.

In other ways, the Q* approach seems at least as good as the HERP approach. There are many animal tests for carcinogenicity that don't provide adequate dose-response data to calculate a Q* value. Similarly, there are many animal studies whose data can not support calculation of a TD_{50}. So neither method allows a fully representative comparison of the potency of carcinogens; and before we conclude that one approach is better than another, or use it to extrapolate to untested compounds, we need to know the biases inherent in each. Within those limitations, however, quantitative risk estimates calculated with Q_1*'s can be just as fruitfully compared across risks as HERP indexes can.

On the human exposure side, I belive that EPA methods for estimating exposure are more systematic, more sophisticated, more consistent, and in many cases, more accurate than methods you have used in your published papers. You have not answered the criticisms of your exposure estimates that we published in Consumer Reports, and I still believe such criticism is fully warranted. I'll get into some specifics in an example, below: a look at one of your favorite HERP comparisons, and how it might turn out if attempted with scientifically sound methodology.

An Example: Aflatoxin vs. UDMH

To illustrate the problems inherent in the HERP comparisons you have made, let's examine your statement that the risk from aflatoxin in a daily peanut butter sandwich is 18 times the risk from UDMH in a daily glass of apple juice. (Note: My letter to Reed Irvine referred to two other estimates of this risk ratio attributed to you. In your June 29 letter to Don Hewitt at CBS, you stated the ratio as 10; in the September 1989 issue of FDA Consumer, Commissioner Young puts the ratio at 30, and credits it to you.)

First, a general point I made to Mr. Irvine: There are so many significant scientific uncertainties in both the estimates of potency (especially for humans) and the exposure estimates that it is silly, as I put it, to suggest that the ratio of the two risks can be quantified to two significant figures. (This is even more true when we consider the compound uncertainty of the ratio, discussed above.) Once again, it seems to me that you have lent an undue air of scientific credibility to a very tenuous exercise by putting a precise value like 18 on this risk comparison, and publicizing it widely.

But let's suppose we wanted to make the comparison anyhow, for its instructive value. How could it be done better? For potency, my preference would be to use Q_1^* values, derived from the best available dose-response data, and not TD_{50}s.

EPA has published a Q_1^* for UDMH, based on the interim sacrifice data from the Uniroyal study. A better value will be available early next year, when the final results of the study have been reviewed, but the interim Q_1^* is based on the best available data. I have not seen a Q_1^* based on rodent data for aflatoxin; are you aware of any (and if so, could you tell me where to obtain it/them?) However, my understanding is that aflatoxin is a potent carcinogen in rats, but a less potent one in mice, hamsters, and monkeys. Which species is the best model for the risk to humans? Since human data are also available on aflatoxin and liver cancer, a Q_1^* derived from epidemiological evidence may be the best solution to the animal-model problem. At the same time, human data are confounded by the likelihood that hepatitis infection is also a major risk factor for liver cancer among the studied populations. All things considered, I would view human data as the best available. I understand that the California Proposition 65 risk assessment group has recently completed a draft risk assessment for aflatoxin, in which they use a Q_1^* derived from an epidemiological study in China.

Some legitimate questions might be raised about comparing a Q_1^* based on human data and one based on rodent data. Still,

I am inclined to use the EPA's Q_1* for UDMH and the Q_1* from the Chinese study for aflatoxin, as the best available data on each substance. I have not yet obtained the California risk assessment, but I understand that it finds the dose of aflatoxin compatible with a cancer risk of 1×10^{5} to be 7 nanograms per person per day.

Turning to exposure, I would reject the arbitrary examples you have chosen (one daily glass of juice, one daily sandwich) because they are non-comparable. The proper way to estimate exposure is to develop specific intake estimates for different age (and sex, if appropriate) groups, since intake of each food varies among populations. Adults drink very little apple juice; young children drink a great deal. My own 4-year-old daughter, for instance, used to drink about a gallon a week (about three six-ounce glasses a day), and from discussion with other parents I believe that's not extreme. (She now drinks mostly milk, for nutritional reasons, not to avoid UDMH.) Young children eat comparatively little peanut butter, while the 8-to-12 year old cohort eats a great deal, and adults fall in between.

Rather than assume a daily peanut butter sandwich, which is an extreme high intake for a toddler and probably well above the average for people of any age, and a daily glass of apple juice, which is far above average for an adult but much less than many children actually drink, I would use data on actual amounts of these two foods that people consume. The EPA has developed an enormous data base (as part of its Tolerance Assessment System, TAS) giving amounts of myriad food items people of different ages and sexes consume. The database isn't perfect; it's based on USDA food consumption survey data that are more than a decade old, and intake of some foods (such as apple juice) definitely has changed over that period. It doesn't include data on all foods--none on peanut butter, for example (just peanuts <u>in toto</u>). Despite the weaknesses in the TAS database, however, I would use it to provide intake data, since it offers comparable data for different foods, and is probably the best available data.

Using those data, the appropriate approach would then be to calculate lifetime exposure, by integrating the time-weighted intakes for different age groups. And one must compare intakes at comparable percentiles--say, the 50th percentile for apple juice and 50th percentile for peanut butter, or 99th for each--something which your one-sandwich/one-glass example definitely fails to do.

EPA used TAS data and Uniroyal's 1986 market-basket residue data to estimate the lifetime risk from UDMH in the food supply. The estimated lifetime cancer risk for an average American was 45 per million (the detailed calculations can be obtained from

EPA if needed). As CU pointed out in our May report, by early 1989 the average daminozide level in apple juice was about one-fourth the level that Uniroyal measured in 1986; total exposure is dominated by apple products, so total UDMH intake probably declined to about the same degree. Thus, an order-of-magnitude lifetime cancer risk estimate for UDMH exposure from all sources (not just apple juice) as of early 1989 was about 1 per 100,000 (1.1×10^{-5}). Since consumption of apple products has grown substantially since the food surveys on which the TAS data are based were conducted, the estimate may be low. (The risk from UDMH since Alar was taken off the market is close to zero, but your HERP comparison was made last spring, so I will calculate the risks as they existed then.)

Turning to aflatoxin, I do not yet have the details of the Prop 65 risk assessment. I also won't spend the time here to calculate individual risks for all age groups; instead, I will use the simplifying assumption that the average peanut butter intake for the U.S. as a whole represents fairly closely the lifetime average for a typical person. Using the TAS data on intake of peanuts (which includes both peanut butter and other peanut foods, and thus represents a larger risk than peanut butter alone), I can calculate exposure. The TAS data show an average peanut intake for the U.S. Population of 0.0695783 g/kg/day (don't ask me why they express intakes to seven significant figures!). For a 70-kg person (assumed for simplicity to be the average lifetime body weight), daily intake is 4.9 g of peanuts, hardly enough for a daily peanut butter sandwich. I will use your assumed aflatoxin level of 2 ppb; the actual level fluctuates from year to year, but 2 ppb is probably a reasonable average for recent years (though not for historical data). The average daily dose of aflatoxin from peanuts is thus about 10 nanograms. Using the Q_1^* from the California Prop 65 risk assessment, lifetime cancer risk is about 1 in 100,000 (1.4×10^{-5}). The peanut-butter component of this risk is somewhat lower, probably not far from 1.1×10^{-5}.

In short, using the best available Q_1^* data, the best available food consumption data, and comparing average American intake levels for the two foods, my calculations show that the aflatoxin/UDMH risk ratio is about 1, not 18.

Comparing our two approaches, mine is complex, and for uses such as comparing risks from a broad range of substances, would require cumbersome data and calculations. Your approach is much simpler, but it attains that simplicity by using arbitrary, unrealistic, inconsistent food-intake estimates. While what I've done here could certainly be debated, I sought to demonstrate that there are well-conceived, scientifically supportable methods other than the HERP approach for comparing cancer risks. In

contrast to those established methods, your back-of-the-envelope comparison of apple juice and peanut butter is not good science at all. And by widely publicizing the "fact" that the ratio of the two risks is 18, I believe you have made it more difficult to find a consensus on a good scientific answer to that interesting question. People are now saying "Prove that Ames is wrong" rather than seeking the soundest way to derive the answer.

While I have developed this example to illustrate flaws in the HERP approach, in general I think substance-vs.-substance comparisons of this sort are too simplistic to be meaningful and are probably misleading. Neither apple juice nor peanut butter contains only one toxic substance each. Daminozide is (or was) used on peanuts, too; in fact, peanut butter typically contained UDMH residues at roughly the same levels in apple juice. Peanut butter also may occasionally contain other pesticide residues. About one-fourth of the 24 "carcinogenic" pesticides registered for use on apples are widely used. And patulin, a mycotoxin found occasionally on apples (and especially in farmstand cider pressed from partly-decayed ground-fall apples), is a suspected natural carcinogen, although the data on its carcinogenicity are at best equivocal (and deemed "insufficient" by the IARC). In short, the comparative cancer risk from peanut butter and apple juice is vastly more complex than your ratio of 18 (or my ratio of 1) suggests. Efforts to put the risk of UDMH in apple juice "in perspective" by drawing such comparisons probably mislead, more than they inform, public debate.

(3) <u>Pesticides, 99.99% all natural</u>. This part of your argument is quite familiar, and your repeating it does little to change our judgment of the persuasiveness of the argument. We would like to know more about the basis for your estimates of 1500 mg per day of natural pesticides and 0.15 mg/day of synthetics. As I understand them, these are rather crude surrogate estimates in the face of inadequate data to estimate the amounts accurately. Ideally, calculations of intake for "natural pesticides" should be based on concentrations of specific substances in particular food plants, and actual dietary intake of the foods. Is that in fact your basis, or have you instead used a simpler assumption, such as a fixed percent of the dry weight of all foods of plant origin? On the synthetic side, the question of most interest is clearly the daily intake of residues of the roughly 70 specific chemicals on the EPA list of suspected carcinogenic pesticides. It would be useful to have residue data for pesticides that have been inadequately tested to classify them as to likely carcinogenicity, too, but that's a secondary concern. The weaknesses in the FDA residue data are well known: Very limited sampling, analytical methods that miss many widely used suspected carcinogenic pesticides (benomyl, EBDC's), and other problems.

The 1987 NAS report on the "Delaney Paradox" used some arbitrary assumptions, such as that all registered pesticides were used, and that residues were present at tolerance levels. They were criticized for using arbitrary constructs, but their purpose, like yours, was to compare risks and set priorities, not to estimate the absolute size of the risks. Actually, I thought their exercise was quite valuable, within its limits. One could argue that a similar approach, with refined assumptions, would be desirable. But the assumptions you have used to estimate aggregate risk seem arbitrary and simplistic, not more refined than the NAS/NRC Committee's approach. Perhaps you have refined your approach since your 1987 paper; if so, I would welcome seeing a more elaborate description of the data and assumptions you have used to derive your estimate that we are ingesting "10,000 times more natural pesticides" than we are synthetic pesticide residues. Your papers seem essentially to assert this as a fact, without providing many details of how a number of this sort was derived, or discussion of the uncertainties involved in the estimation process.

I also must note that your comparison of the gross amounts of natural and synthetic pesticides we consume ignores one of your most basic tenets, the potency side of the risk. I think it is implicit in your comparison of gross intake (regardless of how accurate that comparison may be) that, on average, 99.99% of the "problem" (which includes potency) is natural. I don't think we have nearly enough systematic data on the potency of either group to make such an assumption.

On the issue of how many of the untested natural compounds are "carcinogens," your rebuttal does not reply to the criticisms we published. You acknowledge, as we said, that you are speculating about what <u>may</u> be found, if we could somehow test all the suspected natural substances. We think what you have done in this case is elevate to "B_2" status thousands of compounds that EPA and IARC would classify as "D," unclassifiable. We think that goes beyond acceptable scientific bounds.

(4) <u>Mechanisms of Carcinogenesis</u>. I have addressed some of your points about mechanisms above, in discussing the impact of scientific progress on the evolving models used for risk assessment by regulatory agencies. I think we agree that progress is good, that more knowledge of mechanisms can only improve the basis for regulation, and that this is already happening. We may disagree on when new knowledge is validated enough to be used to revise regulatory approaches, or on whether change in those approaches is occurring fast enough. But many of your general points are things I would agree with.

However, I do dispute two of your key assertions:

First, I think you have mis-stated the importance of cell proliferation as a mechanism of carcinogenesis. It is clear by now that proliferation plays a role in the induction of cancers of some types, by some groups of substances, in some tissues of some species. But it is also clear that proliferation is not, as you imply, a universal mechanism of carcinogenesis. There are substances that produce proliferation but are not carcinogens, and there are carcinogens that do not produce proliferation. Your argument that cell proliferation is the primary mechanism of carcinogenesis in animal tests, and therefore that carcinogenesis occurs only at high, toxic doses, is simply not correct. Dose-response data for known carcinogenic initiators show cancer responses at doses far below the overtly toxic level.

Your argument seems basically to be yet another rationale for the "threshold" hypothesis; i.e., almost anything can look like a carcinogen at high doses, but nothing is carcinogenic at low doses. But this new version of that old red herring is not founded on good science. Your argument that "half of everything ever tested is carcinogenic" is based on very selected data, and your assumption that there is only one basic mechanism of carcinogenesis, or that substances must act by the same mechanisms at high doses and low doses, was rejected by experts in the field as too simplistic, many years ago.

That said, your argument is partly true: Many substances do indeed induce cell proliferation at toxic doses. And cell proliferation may be an important predisposing or enhancing factor in the process of carcinogenesis. I.e., many of the substances you have called "carcinogens" may in fact be better characterized as promoters, and they may well exert such effects only at comparatively high doses. If we assume that that's so, how should we interpret your work? To me, your finding that there are a great many natural cancer-promoting substances in foods, at enormous concentrations relative to pesticide residues and other synthetic carcinogens, does not suggest that we should not worry about the synthetics. Perhaps, indeed, we should worry more about the presence of carcinogenic initiators in foods.

Let's accept for a moment the concept that both initiators and promoters play a role in carcinogenesis. (This requires setting aside the debate over the importance of promotion; Dietrich Schmähl, for example, asserts that nitrosamines cause cancer without any need for promotion, and that there is no evidence that promotion plays any role in most human cancers.) Let's also assume that the myriad of substances, natural and synthetic, that we ingest daily includes both initiators and promoters of carcinogenesis. If, as your work suggests to me,

promoters are everywhere in the diet and substantial doses of them are impossible to avoid, then it seems more likely, rather than less likely, that small doses of many initiators in foods may pose a genuine risk of cancer.

In short, I interpret your work to indicate that the effort to prevent avoidable cancers should probably focus on reducing exposure to initiators. Which initiators we should worry about most would depend on the comparative risks each posed, among other factors. But it seems most important to me to determine the role a substance plays in the process of carcinogenesis, not to call everything a "carcinogen" and compare gross quantities ingested. The highest research priority probably should be to identify mechanisms that distinguish promoters from initiators, so control efforts could be focused where they can do the most good. This idea seems quite different from the political use you and others have made of your suggestion that high levels of "natural carcinogens" are present in most foods.

The second point I would dispute in your discussion of mechanisms is your statement that natural defenses protect us against all carcinogens. That is over-broad and speculative. Defenses against chronic diseases that occur after the age of reproduction would have comparatively little selective value in human evolution. The defenses evolution has provided against natural toxic hazards (mostly of the acute variety) may or may not also be effective against chronic hazards; how effective they might be in that regard is surely a debatable issue. You appear to have overlooked the significant uncertainties in the scientific evidence on this point in order to promote an interesting but unprovable theory. In your letter, you at least said "may." Others citing this idea rarely acknowledge even that much uncertainty.

(5) Trade-Offs. We had little room to go into this aspect in our report, but I am happy to do so now. We agree on the basic point that it makes the most sense to try to reduce the worst hazards first. We also agree that background and perspective on natural hazards is helpful context for regulatory choices. And I am happy to see your statement that pollution needs to be controlled, too; that point has rarely been acknowledged lately in the effort to trivialize pollutant hazards by comparing them to the supposedly "enormous natural hazards" you have revealed.

You have also injected a relevant issue into the debate by suggesting that plants bred for insect resistance may be more intrinsically toxic than current varieties. But this issue is far more complicated and subtle than you make it appear. So is the question of trade-offs in general.

First, I dispute the assumption (perhaps not one you make, but one Dr. Whelan and others have stated) that by pursuing an "unreasonable" degree of safety from pesticides and other chemical risks, we are somehow doing less than we should about more severe hazards, such as alcohol and tobacco abuse. It's unfair to criticize the EPA for doing its job, which is protecting us from those pollutant hazards that meet some test for "significance." Other agencies of government, as well as many private organizations, spend billions of dollars a year on education, counselling, medical care, law enforcement, legislative efforts and research to reduce the tolls from tobacco and alcohol. And it's fair to say that a lot has been accomplished in the past two decades, especially on curbing smoking. That's not to say that enough has been done; more could always be done about such health risks. But the political obstacles to policies that can effectively change behavior are formidable. In part, the political difficulties arise from the moral character of the risks from tobacco and alcohol, which as I said earlier is very different from that of the risks posed by pesticides. Preserving individual freedom of choice is a dominant concern of public policy on matters involving voluntarily-assumed personal risks.

When the social acceptability of classes of risks is quite different, strategies for managing the risks must also differ. It does not make sense to compare disparate risks on a single scale, then suggest that "priorities" should follow numerical rankings. Priorities need to be set in contexts appropriate to the particular set of risk-managment problems. It seems obvious that tobacco hazards and dietary carcinogens are non-comparable; I note, for instance, that even you and ACSH seem to spend much more energy defending pesticides than lobbying to repeal tobacco subsidies, which would not be very logical if all risks could be measured on the same scale. I would argue as well that natural and human-caused cancer risks in the diet should probably not be compared on the same scale. We should identify the biggest risk factors in each category, and work to eliminate both sets, not force a choice between one set and the other. The two sets are simply too different in their social acceptability to be traded off against each other that way.

On the matter of pest-resistant foods, let's look at the broader picture. Many of the cultivars of major crops now in wide use have been bred in the past 30 or 40 years. They are specifically designed to be high-yielding, rather than pest-resistant, because they were bred for use with high-intensity chemical farming techniques. In that process, many of the more toxic "natural pesticides" have been bred out. While breeding for pest resistance in the future might reverse that process in some particulars, plant geneticists could also very well find ways to enhance resistance to many pests (say, fungal diseases)

without increasing the toxicity of the edible plant parts, and without sacrificing yields. Resistance to pest attack depends on many factors, not just nature's chemical weapons. Improved ability to withstand drought stress, for instance, would reduce vulnerability to a number of important pest problems. Your assumption that the price of resistance would likely be a more inherently toxic food supply (even if it were no more toxic than the foods of 30 or 40 years ago) is quite simplistic and unduly apocalyptic, to coin a phrase.

The trade-offs involved in reducing pesticide use also involve a much broader set of issues than just the toxicologic concerns you have raised. Pesticides have adverse ecological effects, and have undermined the stability of crop ecosystems, often with large subsequent costs. Reducing health hazards from residues in the diet may be the least important benefit society could gain from relying less on chemical pest control.

The argument that pesticides have markedly lowered the cost of food and increased the abundance of food supplies is widely made, but again unduly narrow. If the environmental costs of pesticide use (what economists call "externalities) are included, as I think they should be, the benefit/cost ratio is far less favorable. Consider these facts: In the 1940s, American farmers used some 50 million pounds of insecticides, and lost an estimated 7 percent of their harvest to insect pests. By the 1970s, insecticide use had grown to 600 million pounds, and crop loss to insects had nearly doubled, to 12 percent. (Bob Metcalf has updated the estimate to 13 percent in the 1980s; see Science of 10 Nov 1989, p. 754.) Reasons for the latter trend include breeding crop plants that are less naturally resistant to insect attack, but also include several consequences of pesticide use: the development of insecticide-resistant pest populations; the resurgence of pest populations after natural enemies are killed by pesticides; the emergence of "secondary" pest problems; i.e., insects whose populations were naturally kept to low densities by predators, parasites and diseases, which became serious pests when pesticides wiped out the natural checks on their population growth. A survey found that of the 25 most serious insect crop pests in California (each of which caused more than a million dollars of crop losses annually), 17 were resistant to insecticides, and 24 of the 25 were secondary pests. There is now a broad consensus among pest-management specialists that chemical control of insect pests simply has not worked very well, either in an agricultural context or in a public health context (e.g., pesticide-based programs have failed to control malaria in the tropics, and it still kills more than a million people a year.)

In another vein, communities in agricultural areas, faced with pesticide contamination of their drinking-water supplies,

have increasingly begun to seek alternative, uncontaminated supplies, generally an expensive proposition. While you might argue that the public should not worry about the level of risk posed by pesticides in their drinking water, the level of risk is really not the issue; such risks are not morally acceptable to the public, and the costs of replacing contaminated supplies (or cleaning them up) are real ones that communities probably will choose, politically, to bear.

Such examples only begin to indicate the real costs of pesticide-intensive farming, some of which are much harder to quantify in economic terms. On the benefit side, a surprisingly large fraction of total agricultural pesticide use is applied not to enhance yield, but rather to protect cosmetic quality. Consumers had to learn to expect perfect-looking fruits and vegetables. Right now, they may be willing to "unlearn" that lesson, in return for reduced risk to their health and to the environment.

I think the recent NAS report on "Alternative Agriculture" represents the direction mainstream science and agriculture may soon be flowing. It seems to me that participants in the debate over pesticides often try harder to defend (or attack) chemicals than to look at the trade-offs in the broadest sense. Paying explicit attention to the issue of trade-offs is an excellent thing to do. But you seem to have focused only on those trade-offs that make pesticides look more desirable. The NAS/NRC and other scientific institutions that have examined these issues generally have done so from a broader perspective than yours.

Your final remarks concerned specific statements in our article with which you took issue. I will briefly respond.

Allyl isothicyanate. Our judgment is that the evidence is too sparse to call it a carcinogen. EPA would have to classify this compound as a "D" (unclassifiable), given the data that exist. For the reasons you give, you are willing to treat it as a presumptive carcinogen. We are generally reluctant to call something a carcinogen unless it meets EPA's criteria for B_2 classification, at least. (In print, we try to refer to EPA "C's" as "suspected" carcinogens, at minimum.) We seem to have different criteria than you do for how much evidence is needed to put the label "carcinogen" on a substance, possibly because as a major publisher of consumer information on such topics, we have wrestled with that problem for many years. Perhaps, when you seek examples to illustrate your general points, you could choose substances where there is less debate over the quality of the evidence.

Mushroom hydrazines. We know about the Toth studies, and

like his studies on UDMH and Alar (which were rejected by the EPA's Science Advisory Panel), they are subject to considerable methodological criticism. We'd be more comfortable if there were additional confirming studies. Another study, on agaritine, using an acceptable design, was negative. The one study often cited as evidence that agaritine is a carcinogen substituted mushrooms for the animals' regular feed, which is not a valid test method. (Parenthetically, I note that Toth's studies are widely and uncritically cited in food toxicology tests as evidence that the hydrazines are carcinogens, but the EPA is more critical of the evidence and far more rigorous in reaching a judgment that a substance is a carcinogen. EPA can be sued if it acts too precipitously on a proprietary chemical. But Nature does not sue authors who brand her substances "carcinogens.")

Perera and Boffetta. I would like to see your detailed response to their critique, if you would send it. We did not rely heavily on their paper. We made an independent assessment of your published papers, and essentially developed our own critique. We quoted their general conclusions because we tend to agree with them. But I have personally pointed out to Dr. Perera a couple of minor errors in their paper.

I accept your criticism that we missed your point about squid. However, the aggregate risk from foods cooked in gas ovens strikes me as essentially unquantifiable at present. Had we focused on your actual point, we would have questioned your use of squid as a "representative" food to stand in for this broad category of risk.

Selection of pesticide examples. The issue of aggregate risk estimates is discussed above. Our criticism was aimed at the substance-versus-substance comparisons inherent in your HERP tables. In that context, your choice of examples definitely is critical, and the two you selected give a biased picture. While we commented that both EDB and DDT had been banned, we stressed that this "particularly" affected the exposure estimate for DDT. We chose that wording to acknowledge that the estimate for EDB might be less distorted, for the reasons you state.

Anticarcinogens. Yes, we know of your work on this topic, and we put that sentence in the report to remind you and us that cancer is a complex, multifactorial process. Our point was that asking whether substance X poses a bigger risk than substances A, B, C...Z is probably looking at the issue through too narrow a lens. We noted that broccoli may contain both natural (and maybe synthetic) carcinogens and anticarcinogens, and that it makes more sense biologically to try to understand the risks and benefits it poses as an integral food, not to define it in terms

of one substance it contains that concerns us at present. What I see the public learning from your work is that broccoli is a "carcinogen." Clearly that is not what either of us would like to teach them.

To summarize a long read, my two most salient messages in response to your letter are:

(1) Comparing risks is important, but what is the best scientific method for doing so?

We agree with you that society needs to use the best available science in making risk-management decisions, including the important task of setting priorities. We do not agree that the HERP approach you have developed is "good science." It is both simple and simplistic. It is laden with arbitrary constructs that are not demonstrably any more scientifically sound than the (often also arbitrary) approaches to the same tasks being used now by risk-managing agencies.

As does any scientific approach, your HERP method must go through a long process of criticism, assessment, and revision before the expert community can determine its ultimate value for its stated purposes. I believe you (and others) have made that process of assessment much more difficult in two ways: First, the use of your HERP approach in passionate political pleadings for changes in regulatory approaches has made HERP intensely, politically controversial, before its scientific merits could be properly evaluated. Second, in your public statements you have put too much emphasis on catchy phrases like "99.99 percent all natural," which are not scientific facts, but rather your own intuitive assumptions, opinions, or crude calculations.

When scientists engage in strong political advocacy, most thoughtful people may suspect that they are selecting facts and interpreting inconclusive data to support their pre-existing political postures, not looking at the data in a balanced, objectively scientific way. Your role as a propagandist in the debate over pesticides poses a large risk that the scientific community may rightly question the objectivity and scientific rigor of your HERP approach. Based on my own research on other controversies, polarization of political debate over a body of research, especially when the research is new, often prevents the work from being accepted as scientifically valid for many years, regardless of its quality. (For example, the very fine work of Clair Patterson on natural background levels of lead was not widely accepted for more than 15 years after he published an incisive analysis on the topic, largely, in my view, because of his crusading advocacy against lead pollution.) The same could very well happen with your HERP research; indeed, it may already

be happening. Do you want to take that risk, in return for the political impact you may have by speaking out strongly?

(2) Setting priorities is more than a scientific exercise.

Good scientific data on the nature and size of risks is only one part of priority-setting; ethical and moral aspects, and other value-laden judgments, are also vital elements in the process. Even where scientific consensus exists about the facts of risks (rare enough), deep divisions exist in society over which risks are most important. Consensus on priorities is unlikely, given people's widely different moral assessments of risks. When scientists ignore the existence of moral dimensions, it is hard to find consensus even among experts. And experts cannot expect to teach the public to see risks from our perspective unless we are willing to see risks from theirs.

Because there is no consensus at present on moral priority among risks, risk-management policies are inherently controversial, and political judgments will always be required. In the debate over those political choices, the rhetorical stance you have adopted (which seems to treat those who disagree with you as misinformed or as incompetent to criticize your views) just fosters polarization. Agreement seems possible only if we all acknowledge the importance of each other's concerns. Let's decide which is more important: ideological warfare, or sound science and social consensus.

It seems reasonable that scientists will disagree over both the interpretation of facts and the values that should receive the most weight in applying those facts to public policy decisions. If you and CU should need to pursue our disagreements in future debates, I suggest we make a priority choice of our own among the goals above, and try to let that guide our behavior.

Sincerely,

Edward Groth III, PhD
Associate Technical Director

Curriculum Vitae

Edward Groth III

Office: Consumers Union of U.S., Inc.
256 Washington Street
Mount Vernon, NY 10553 USA

Home: 150 Burkewood Road, Mount Vernon, NY 10552

Phone: (O) 914-667-9400; (FAX) 914-667-2701; (H) 914-667-8694

Education

Princeton University, A.B., Biology, 1966

Stanford University, Ph.D., Biological Sciences, 1973

Specialization: Biology and Public Policy

Dissertation: "Two Issues of Science and Public Policy: Air Pollution Control in the San Francisco Bay Area and Fluoridation of Community Water Supplies."

Employment History

Current: Associate Technical Director for Policy and Public Service, Consumers Union, 1983-

Supervise research and testing program on health, product safety, environmental and other aspects of selected consumer products. Work closely with editorial department to translate technical test reports into articles for Consumer Reports, a general-audience publication. Collaborate with legal staff in Washington office to submit technical information pertinent to federal regulatory and legislative issues. Assorted management and policy responsibilities in department of 105 people.

Previous:

- Director, Public Service Projects, Consumers Union, 1979-83.

Directed and conducted research and advocacy-support activity on assorted health, product safety, and environmental issues that affect consumers.

- Senior Staff Officer, Environmental Studies Board, National Research Council, Washington, DC, 1976-79

--Directed study on "Lead in the Human Environment"
--Directed study on "Scientific and Technical Assessments of Environmental Pollutants"

Employment History, Continued

- Staff Officer, Environmental Studies Board, National Research Council, Washington, DC, 1975-76

--Directed two panel studies in a project on "Research Needs of the U.S. Environmental Protection Agency"
--Directed study on "Scientific and Technical Assessment of Nitrates in the Environment"

- Research Fellow, Caltech Population Program, California Institute of Technology, Pasadena, CA, 1973-74

Conducted post-doctoral research on environmental impacts of world population growth.

Professional Interests

--Health effects of environmental trace substances
--Health and public policy aspects of exposure to lead and fluoride
--Food safety; environmental contaminants in foods
--Pesticide safety, especially vis a vis consumer products
--Decision-making on environmental issues
--Respective roles of science, ethics, and values in risk management
--Risk communication

Professional Memberships

--AAAS
--Society for Environmental Geochemistry and Health
--International Society of Regulatory Toxicology and Pharmacology
--International Society for Fluoride Research