so-called quantitative cancer risk assessments do not actually quantify true risk

Frank C. Schnell p.10
Does Money Matter?

Hank Campbell, President
American Council on Science and Health

As I was thinking about this issue of our new Priorities magazine, we had just spent the day testifying at the FDA on the issue of opioid abuse. Obviously, the pharmaceutical industry is a big business and drugs do a whole lot of good for people but they are not perfect. ACSH extols the virtues of medicine all of the time but we have no donors that are pharmaceutical companies.

Meanwhile, the CEO of the CrossFit, Inc. exercise company was criticizing us publicly because a few years ago Coca-Cola had given us some unrestricted grants. It didn’t make a difference in our written content, we have always believed you can enjoy a soda in moderation, but it seemed strange to have someone claim if you care about public health, you can’t take money from one specific company. What better thing can any company do than to get science into the hands of the public?

The next morning I was at the Milken Institute Public Health Summit with Dr. Tom Frieden, head of the CDC, Dr. Francis Collins, head of the NIH, and others, and there were corporate logos all over the place as sponsors. The woman who runs the American Heart Association said she was proud of their corporate sponsors. Why do Mother Jones and SourceWatch and other anti-science groups go after some organizations and not others, I wondered?

It’s a size issue, I was told. Mother Jones can’t attack the AHA, it is too powerful and the backlash would be severe. They have to choose smaller targets. Ninety-nine percent of our donors are individuals, but we are proud of our foundation support and we have been honored with long-term corporate support as well, though no one has ever demanded we cover a topic for their company. We’re certainly going to accept donations from groups that want to send them, because it’s better to be like the American Heart Association and be transparent about funding than to be SourceWatch, which accepts dark money laundered through foundations.

If size is the answer, we’re happy to get bigger and more powerful and in this issue of Priorities you can read about the work we are doing to achieve that.

Thanks for all of your support in getting us to our 38th year!
"ACSH in 2006 called on the federal government to implement critical tobacco harm reduction measures: stop misrepresenting the science concerning smoke-free cigarette alternatives; clearly communicate the risk differentials between combustible and non-combustible tobacco products; and replace inaccurate, misleading federal warnings on smokeless tobacco packages (1). Ten years – and four million prematurely deceased smokers – later, the government is still blindly committed to a tobacco-free society. This year, the FDA has the opportunity to do two things right: adopt accurate warning labels for smokeless products, and regulate e-cigarettes and vapor products according to their vastly lower risk profile."

Brad Rodu
Professor of Medicine
Endowed Chair, Tobacco Harm Reduction Research
University of Louisville

"Since this is an election year, current medical costs, especially the obscene costs of most prescription drugs, will undoubtedly be a focus of considerable discussion. I think we will see the beginning of a more serious effort to ensure that prescription drugs developed by the pharmaceutical industry are effective, safe and available at a more reasonable cost to those who need them."

Chris F. Wilkinson, Ph.D., former Professor of Insecticide Chemistry and Toxicology and as Director of the NIEHS Toxicology Training Program at Cornell University.

"Mental health is essential to overall health and well-being. As such, it must be recognized and treated in the older adult population with the same urgency as physical health. The longer life expectancy that we are enjoying has resulted in rapidly rising numbers of mental health disorders in this population. For this reason, mental health must become an increasingly important part of the public health mission. In fact, the mental health of older people has been identified as a priority by the Healthy People 2020 objectives, the 2010 White House Conference on Aging, and the 2000 Surgeon General’s report on mental health. Yet little has been accomplished by government to address this problem which is already resulting in a huge burden for both families and the US health care system.

The goals and traditions of public health and health promotion can be applied just as usefully in the field of mental health as they have been in the prevention of both infectious and chronic diseases. Public health agencies need to increasingly incorporate mental health promotion into chronic disease prevention efforts, conduct surveillance and research to improve the mental health evidence base, and collaborate with partners to develop comprehensive mental health plans and to enhance coordination of care. The challenges for public health are to (1) identify risk factors, (2) increase awareness mental disorders and the effectiveness of treatment for them, (3) eliminate health disparities based on age, and (4) improve access to mental health services, particularly among populations that are disproportionately affected such as older adults.

Lynn Tepper, EdD, PhD
Clinical Professor
Columbia University
Health Science Campus
New York, NY 10032

"In the next year public health will take further steps toward an “open” public health data environment that enables population scientists to build a scientific modeling base that can help understand and predict the spread of infectious diseases. Progress on this is mixed. We have a long way to go before infection transmission data becomes as open and useful as weather data. Ebola stimulated calls and actions that made open sequence data more accessible in ways that allowed scientists with new methods and ideas to contribute to Ebola modeling and control. Some progress was also made on measles, malaria, and influenza data. But polio is an area where progress on this front is urgently needed, but is slow in coming. We could be close to polio eradication. The key truth will be known when the use of oral polio vaccine is stopped. For type 2 polio that cessation is scheduled for April. Types 1 and 3 will be stopped together when the chances of there being no hidden silent circulation of these polioviruses are judged to be small. But the science needed to insure risks of silent circulation are sufficiently small is deficient. It could be that in places like Africa and Pakistan-Afghanistan that slow waning of immunity has created conditions for prolonged silent circulation that never existed in the past in any other place. If polio data and sequences were archived in ways that made them accessible to population scientists on the forefront of developing new methods, it would be possible to make much better assessment of silent circulation risks and what we should do about them."

Jim Koopman MD MPH (734) 763-5629 office
Dept. of Epidemiology (734) 417-9610 Cell (734) 995-2954 home
1415 E. Washington Heights (906) 484-5119 cottage (734) 998-6837 fax
Ann Arbor, MI 48109 e-mail jkoopman@umich.edu
Despite significant progress over the past decade, malaria remains a serious global health problem. Despite a 60 percent reduction in deaths during this interval, the protozoan infection still kills more than 400,000 people every year, the large majority of who are from Africa. It is indisputable that new drugs are needed to combat the infection, and a research group from the University of Texas, El Paso (UTEP) has discovered a potential game-changing drug called DSM625. The drug looks very promising in the early stages in the development process. But, will it work?

If you are looking for a sure win, avoid betting on whether a drug will make it through the torturous path ahead of it, and ending up on the pharmacy shelf. You would be better off putting your money on a three-legged horse at Belmont.

Industry statistics bear this out. Of about 5,000 compounds that are synthesized by chemists during the discovery phase of the process—before any human tests are done—only one will become a drug. As the drug is studied more (provided that it does not drop out), the odds improve, but not by much. After extensive toxicology studies in different animal species, the company or institution that is trying to develop the drug, must apply to the FDA for permission to conduct safety studies in humans. If the FDA is satisfied with the preclinical studies, it will give the go-ahead to permit the drug to enter Phase I clinical trials—the first time any person receives the drug. Phase I trials are designed to determine drug safety in a small group of human volunteers—usually less than 100.

Even if drug candidates clear this hurdle, 80 percent of them will subsequently fail, either in Phase II (efficacy, safety), or Phase III (large, multi-center, efficacy plus additional safety) trials. So, it is absolute folly to try to predict the success or failure of a potential drug before it has even entered Phase II trials—when you find out whether it will even do what it is supposed to do. Phase II trials are very often deal breakers.

Yet, for a variety or reasons, I’m betting that DSM625 will make it across the finish line.

The process of drug approval is comprised of a diverse set of often-unpredictable roadblocks—any one of which can stop a program
dead in its tracks. Yet, it is not hopeless—scientists have developed a set of tools that can provide certain predictions of the performance of a drug, even before it is tested in a single person. The information that is derived from these tools can lead to a GO-NO GO decision for a particular drug candidate, or even the entire program.

What follows is an illustration of some of the key issues that apply to most drugs in development—those that are meant to be taken by mouth—and DSM265 in particular. It is not comprehensive, but, rather a summary of some of the most important determinants that will decide the fate of any drug in development.

1. Is the molecular target of the drug known? If so, is it relevant?

The effect of any drug is from its impact upon a biological process, either in the body itself, or a pathogen that inhabits the body. These processes are mediated by receptors, which trigger cellular responses, or enzymes, which enable biochemical reactions to take place. Receptors and enzymes are called molecular targets. Depending on the particular function of the molecular target, a drug may be required to either inhibit, or stimulate the target.

The molecular target of DSM265 is a well-known and crucial enzyme called dihydroorotate dehydrogenase (DHODH). DHODH controls one of critical steps in the series of biosynthetic reactions that leads to the production of DNA, RNA, ATP, and other crucial biomolecules. In the absence of these biomolecules, the bugs that are responsible for malaria infection cannot reproduce. DSM265 efficiently inhibits protozoan DHODH in Petri dishes.

Odds that DSM265 will target an essential process in malarial reproduction: 99+%

2. Is there a corresponding molecular target in humans, and if so, will the drug affect it and lead to side effects?

Yes there is, but it doesn’t matter. Although DHODH is ubiquitous and essential in living organisms, large and small, including humans, the shape of the binding site on the protozoan DHODH is quite different from that on the human enzyme, even though it performs the same function. It is so different that DSM265 binds 14,000-times better to malarial DHODH than to the human version of the enzyme. This magnitude of selectivity makes it highly unlikely that the concentration of the drug needed to kill protozoa will have any effect on the human enzyme.

Odds that DSM265 will have a sufficiently high selectivity for malarial DHODH over the corresponding human enzyme: 95%

3. Is the drug potent and selective enough to do its job at concentrations that are low enough that it will not cause unwanted side effects?

It is always preferable to use the lowest possible dose of any given drug. The 16th century adage—"the dose makes the poison"—holds true centuries later. High selectivity for the specific desired target is also paramount since at a high enough dose, all drugs will be toxic. This is because at sufficiently high concentrations, there will be interactions with human enzymes and receptors—often many of them—that can cause toxic side effects. The cost of manufacturing the drug can sometimes be a factor as well, but this is not typical. In mice, when DSM265 was used at a typical dose, the blood levels, even after one week, are about 100-times the concentration to kill the bug.

Odds that DSM265 will be sufficiently potent to be capable of inhibiting malaria at an acceptable human dose: 90+%

4. Are the animal models predictive of human disease?

The relevance of an animal model to the corresponding human disease state is routinely a showstopper. There is a huge range in the degree of the predictive power of a model, depending on both the disease, and the animals that are used.

But, one area where models are usually predictive of an outcome in humans is infection, especially bacterial infection. It is trivial to determine if the potential antibiotic will kill bacteria in a Petri dish. After this, mice are infected with the same bug. If the antibiotic works, they live. If not they die. Antibiotics that protect mice usually will treat the same infection in humans. The validity of the mouse model in studying protozoan infections (the malaria pathogen) is well established.

Odds that DSM265 will cure malaria in humans if it does so in mice: 95%

5. Will the drug work in pill form?

For a variety of reasons, such as cost and ease of administration, it is almost always preferable to give drugs as pills rather than by injection. But, not all drugs can be...
swallowed and get into the bloodstream. Bioavailability—a measure of how much of oral drug gets into the blood—is an important factor in determining the success or failure of a drug. This issue alone has been responsible for many clinical trial failures in the past, and can be one of the most frustrating aspects of drug discovery.

Drugs with very low bioavailability either:

- Pass through the intestinal tract without being absorbed and are excreted unchanged in the feces.
- Are absorbed efficiently into the blood only to be rapidly degraded when they reach the liver, the primary site of metabolism in humans and animals.

In either case, the result may be that blood levels following oral administration will be insufficient to have an impact on the disease or infection that must be treated.

Human bioavailability of a drug candidate is notoriously difficult to predict. This is because there is great variability in different animal species. Since most bioavailability studies are conducted in rats and dogs, one must be very cautious in interpreting these results. Even within the same species, bioavailability can be affected substantially by whether the drug is given with food, or what other ingredients are present in the pill (formulation).

That said, a bioavailability of less than 20 percent is a red flag, albeit an imperfect one.

The bioavailability of DSM625 ranged from 60-100 percent (excellent) in mice, rats, and monkeys. In dogs, the number was greater than 20 percent (moderate).

Odds that DSM625 will be absorbed in the gut following oral administration, and then enter the bloodstream: 90+%

6. Will DSM625 remain in the blood for enough time to be effective?

The amount of time it takes for half of a drug to disappear from the blood is called the half-life (t1/2). A typical drug has a half-life of a few hours.

Sometimes short is better. Ambien is a popular sleep aid because it has a half-life of two hours. So, in eight hours, only six percent remains. By contrast, Benadryl has a half-life of about eight hours. This is why people who use it as a sleep aid are frequently groggy in the morning.

For antimicrobial drugs, longer is better. The longer the drug remains in the blood, the more effectively it will kill the microbe. The predicted half-life of DSM625 in humans is about one week, which is extremely long. This is why the UTSW scientists state that one pill may be sufficient to cure malaria.

Odds that DSM625 will resist metabolism and excretion, and therefore remain at levels that are high enough to treat the infection in humans: 98%

7. Are there any potential human safety issues that can be identified in advance?

The best that can be said for the determination of human toxicity of a drug based on data from animal models is that it is probably predictive more often than not. While this is hardly a glowing recommendation, if significant toxicity occurs in multiple animal species in quantities that approximate a therapeutic dose, then it is fairly likely that the potential drug will be toxic—perhaps prohibitively so—in people.

But, there are human enzyme, receptor, and whole cell assays that are quite useful in spotting problems ahead. Some of them can be sufficient to discontinue the development of the drug, while others serve as warning flags. When taken together with animal toxicity data, the prediction of unacceptable human toxicity becomes more reliable. Here are some of the more important assays:

- Ames Test: A measure of mutagenicity, and a red flag for carcinogenicity. All potential drugs must be tested for mutagenicity. Another mutagenicity assay called the mouse micronucleus test examines whether or not a chemical causes chromosomal abnormalities — a measure of mutagenicity. Result: DSM265- negative in Ames, and does not cause chromosomal abnormalities.
- Receptor Panel: DSM265 was tested against a panel of more than 120 human receptors that are responsible for a wide variety of functions in the human body. If these receptors are affected by the drug—either activated or blocked—off-target toxicity is more likely, although, the
absence of activity in this panel does not mean that the drug will be safe in real life. Result: There was no significant interaction of DSM625 with any receptor.

- Drug-drug interactions: Sometimes one drug can indirectly affect the blood levels of another. The two do not physically interact, as the name implies, but rather, one drug can inhibit or induce certain enzymes in the liver that are responsible for metabolism of another drug. This can sometimes result in toxic, or even lethal levels a drug, which would normally cause no toxicity. These metabolic enzymes are called “CYPs,” short for cytochrome P450. Result: There was no significant inhibition or induction by DSM625 of any of the CYP enzymes that were tested.

- Disruption of normal heartbeat: Certain drugs can affect what is called the QT interval of the heart, causing arrhythmias (irregular heartbeats) that can be fatal. This effect alone can result in the discontinuation of clinical trials, but it can be measured in a number of tests, both in vitro and in animal models. Result: DSM625 is not expected to affect the QT interval.

- Animal toxicology: DSM625 was administered at multiple doses far above the therapeutic dose to mice, rats, and beagles. Result: Even at these high doses, there were no clinical effects noted, except for vomiting in beagles, which is common. In mice, there were no changes in microscopic examination of various tissues.

Odds that DSM625 will be safe enough in humans to permit the continued development of the drug: 95%

8. How critical is the medical need? 

Very. Although the use of mosquito netting, spraying of insecticides, and improved access to drugs has substantially reduced the worldwide toll of malaria over the past decade, more than 400,000 people still die each year from the infection. Although malaria can be cured by a number of existing drugs or drug combinations, emerging resistance, a long treatment interval, and side effects remain substantial obstacles in the eradication of the infection.

Even though some drugs remain effective against the infection, drug supply and patient compliance in politically and economically unstable areas of the world remains problematic, making the development of a vaccine so crucial, but none exists at this time. A single-dose cure is the next best option after a vaccine.

Odds that DSM625 addresses an unmet medical need in humans: 100%

Prediction

Based on available data, DSM625 has all the properties that are required to become a successful drug, and none of the liabilities that would prevent it. It inhibits a known target that is required for the protozoan to reproduce, but does not inhibit the human version of the same target. Its potency against the target is high, and its bioavailability is excellent, meaning that the drug will eliminate the infection once it enters the bloodstream, where it stays for a very long time, making the possibility of a single pill cure—an enormous advantage—real.

The drug is effective in rodent models of malaria, which are good predictors of human efficacy.

Based on available data, DSM625 has all the properties that are required to become a successful drug, and none of the liabilities that would prevent it.

Its safety profile is excellent, both in vitro (outside the body), and in animal toxicological tests. It is not mutagenic, nor does it significantly affect human liver enzymes or receptors. It is not expected to cause cardiovascular effects in man. The in vivo toxicology profile in three animal species appears to be very clean.

Based on these preclinical data, as well as a tolerable safety profile in Phase I human clinical trials, I believe that has a very good chance of making it to the finish line, despite the lack of any Phase II human efficacy data.

I would estimate that the probability of approval of DSM625 is 80 percent. This is about as good as it gets at this stage. This drug looks extremely promising.
First, some definitions:

Intelligence: The ability to acquire and apply knowledge and skills.

Stupidity: Lacking this ability; the opposite of intelligence.

Wisdom: The ability to use good judgment.

Foolishness: Lacking this ability; the opposite of wisdom.

We have a civilization dependent on science and technology, but in which almost no one understands science and technology. This is a prescription for disaster. (Carl Sagan)

Particularly fatal is the combination of foolishness and intelligence. (Matthijs Van Boxsel)

Most people have intelligence, but few are wise, few have the ability to wisely use their intelligence. And this can have disastrous consequences to humanity, today facing problems that foolishness will not solve. Physical problems include global warming, overpopulation, growing ineffectiveness of antibiotics, diminishing fossil energy resources, pollution of the oceans and threats to ocean life, threats to clean air and fresh water supplies, and many others. Then there are the societal problems stemming from the inability of humans to get along with each other, to live in peace with each other.

Humanity’s social problems today likely stem from the genetic make-up that has enabled our species to survive. Paranoia and self-interest are examples. Paranoia helped primitive man to survive attacks of animals or hostile tribe members. But today the consequences of paranoia are negative, promoting unpleasant and society-damaging causes. Malevolent leaders utilize paranoia to maintain their absolute control and their fortunes, focusing the paranoia of their populace away from themselves and on to scapegoats, often using religion as a tool. Paranoia is also behind many misguided causes backed by the educated but unwise.

Then there is Self-interest, which generates productive incentives. But to enable essential social cooperation extreme self-interest that damages the self-interest of others must be constrained.

Today, science offers the best, perhaps the only method of solving humanity’s problems. But, as our problem-solver, science is ineffectual without wisdom. In our country, as the general level of education rises one would expect a concomitant rise in the wise use of intelligence. But, sadly, sometimes it seems that the opposite is true. In too many cases, the better-educated a person is, the more likely he is to espouse a wrong-headed cause. A step in the right direction would be to mandate the appropriate and wise teaching of proper scientific protocols throughout the country’s educational system.

Here is a small, partial list of typical causes strongly promoted by many of the educated, but completely unsupported, even condemned, by science:

- Alternative “holistic” medicine
- Anti-vaccine
- Anti-mercury in dental fillings
- Precautionary principle (zero tolerance)
- Organic food and farming (“all natural”)
- Anti-GMO’s (Genetically Modified Organisms)

Religion-inspired causes:
- Anti-stem cells
- Anti-abortion
- Anti-birth control
- Murder for God (If you think this is just a new radical Islamic idea, read the bible)

Science opposes all these positions. Unless humanity can, somehow, globally uphold the intelligent and wise use of science, and reduce the disagreeable use of paranoia, and set some limits on self-interest, there may be little hope for our future.
Is Science Falling Short?

The need for transparency in decisions that are based on science

The history of guidelines addressing nutrition and diet go back to the early 20th century and eventually the Department of Agriculture provided numerous guidelines dealing with specific needs. For example in early 1940's guidelines were provided that were helpful in feeding the military personnel during the Second World War. In an article where science falls short in the Washington Post (Feb.19, 2015) Charles Lane describes the need for skepticism resulting from the decision of the Dietary Guidelines Advisory Committee (DGAC) to reverse previous decisions on cholesterol in diet. Similar articles have appeared in other media including in the Wall Street Journal (Feb.20, 2015) as well as commentaries in TV. A lengthy article authored by Park and Kluger and published in Time Magazine (February 8, 2016) claimed to identify new rules of the heart, describing the relationship between nutrition and avoidance of certain diseases. The Time story described the old science and how the new science modified the old science. In order to appreciate the roles of the scientific community in providing advice to government including regulatory agencies and the role of the media to report scientific issues we need to recognize the existence of two relevant schools. The Jeffersonian school requires that transparency is mandatory in societal decisions while the anti-Jeffersonian school believes the public is inherently unable to make sound decisions. The first school is traceable to Thomas Jefferson who stated that “If we think [the people] not enlightened enough to exercise their control with a wholesome discretion, the remedy is not to take it away them but to inform their discretion”. The anti-Jeffersonian school goes in the opposite direction. The best example of this school is views expressed by professor Gruber of MIT “voters are stupid” and “lack of transparency is a huge political advantage”.

The disagreements described above are based on the lack of recognition of key foundation issues of regulatory science an emerging scientific discipline. One of the primary tools of regulatory science is Best Available Science (BAS) and Metrics for Evaluation of Scientific Claims (MESC) derived from Principles of BAS. (see www.nars.org/bas and www.nars.org/2-uncategorized/15-what-is-regulatory-science.) A closer look at the scientific foundation of DGAC, Lane, Time Magazine, and others are based on lack of recognition of the level of maturity of underlying science (ranging from scientific laws all the way to speculation), the role of the scientific community on drawing societal conclusions from science, transparency of scientific decisions, and other issues identified in BAS/MESC system.

Let us start by addressing an important issue included in the Time article: It may be recalled that Time made a distinction between old science and news science. According to authors of the article published in Time whereas old science assumed that all saturated fat to be bad, the new science “is complicated but trans fats are the worst for the heart”. Apparently Time is basing its statement on the decision of the Food and Drug Administration (FDA) that trans fats can no longer be considered to be natural food and thus would require safety testing before they can be used in the market. However, there is no reason to believe that trans fats contribute any more to the LDL than any other saturated fact.

Before we address the issues related to the DGAC we must emphasize that do not belittle the efforts of the authors of the GDGAC and assume that they did their best. Nutritional science is evolving and as described in the BAS/MESC system is largely Association-Based implying that an investigator studies two groups that are identical in their habits, living conditions, and every other parameter except for their eating habits. For obvious reasons the conclusions drawn from such a study have significant uncertainties. Clearly the science related to the composition of the diet and numerous related issues addressed in the DGAC are evolving and one should not be surprised that they change as science evolves.

Another key issue is compliance with the Transparency Principle of BAS that implements the Jeffersonian principle and requires that scientific issue of societal concern must be described in a language that the affected community can follow. Ideally, the DGAC should have provided the status of science; identified uncertainties; the assumptions and judgments in their scientific assessment; and if necessary draw scientific conclusions. In contrast the recommendations should have been the task of administrators and regulators. Instead, the anti-Jeffersonian approach is used and the recommendations are based on the judgment or speculation of the DGAC. The articles mentioned above (e.g. Lane and Time Magazine) quote individuals who support a specific process. It is easy to identify an individual including a professor who expresses an opposite view. Instead the authors would have been wise to quote an article published in a reputable scientific journal. If necessary, the author of the article could have been interviewed to clarify the content of the article.

Finally another relevant issue is the role of scientific community in application of science in regulatory and other policy decisions. Although it is common that scientific assessments include policy recommendations, once scientific issues are addressed by the scientific community their application to societal decision can be done by people outside the scientific community. In effect the scientific community and individual scientists are no more qualified to draw conclusions than members of other professions.

In summary, the authors of the publications described above should have described the level of maturity of the underlying science consisting of the inclusion of assumptions, judgments and related issues. In addition, the authors should have stated how the conclusions would have been different if alternative assumptions, judgments, and related issues would have been used to draw conclusion. Contrary to implications that science is not working, is falling short, and numerous similar allegations, the science did not fall short. The scientists, authors, and the process did.

A. Alan Moghissi PhD, President Institute for Regulatory science, Adjunct Professor Georgetown University School of Medicine

Liliana Benitez-Owen, MD
Georgetown University School of Medicine
ACSH has taken on the Public Interest Research Groups (PIRGs) in the past over their junk science on such issues as lead poisoning (1), playground hazards (2), and toy safety (3, 4).

As an ACSH Science Advisor I documented that 58 scientists at the City University of New York cited New York’s PIRG (NYPIRG) for having engaged in scientific research misconduct in five of their studies (involving air pollution, water pollution, recycling, auto safety, and the SAT exam; 4, 5).

Gullible reporters often pass along the PIRGs’ press release “research” in news articles, helping to mislead the public and distort public policy. But recently it was the reporters themselves who were burned by a PIRG deception: they were fooled into reporting plagiarized quotes and bogus authorships for USPIRG’s annual toy safety survey and, thereby, into violating journalistic standards. Here are the details.

U.S. Public Interest Research Group (USPIRG) is the national umbrella for PIRG affiliates in various states. Every year, USPIRG performs an annual report on toy safety, and issues a press release. This year, as is typical, that release includes a quote from a USPIRG representative. (6)

Various state PIRGs then issue similar press releases, but portray the toy safety study as their own. Further those releases attribute the words of the USPIRG representative to their own local representative.

News organizations from eight states were duped into both (1) falsely assigning authorship of the toy study to a state PIRG, and (2) falsely attributing a quote about that study to a local PIRG representative.

This identical quote appears in each article: “Parents and other consumers should be able to trust that the toys we buy are safe. However, until that’s the case, toy buyers need to watch out for common hazards when shopping for toys,” but was attributed to Jennifer Wong in Arizona; Jason Pfeifle in California; Evan Preston in Connecticut; Michelle Surka in Massachusetts; Michael Basmajian, also in Massachusetts; Lauren Hirsch in Missouri; Carli Jensen in New Jersey; Kat Lockwood in Oregon; and Stephanie Monahan in Pennsylvania.

News organizations in two additional states assigned false authorship, but did not use the quote.

(All of the examples are listed, with links, at the end)

Each state PIRG, by falsely representing the toy reports as its own creation, exaggerates the work it does in their state and, thus, enhances their ability to raise funds locally through door-to-door solicitations and via student fee collections at the state’s universities.

Journalists who were fooled into portraying a study performed by a Washington DC lobbying group as the product of its local affiliate, unwittingly misled the public and aided the political agenda of those lobbyists.

The bottom line: in light of the PIRGs’ deceptive practices, past and present, journalists would do well to treat with more caution information originating from the PIRG network.
An update on the "doomsday chemical" of the 1970s and 1980s

Professor Gordon W. Gribble
Department of Chemistry
Dartmouth College

Dioxin, once proclaimed by the environmental community as the “doomsday chemical” of the 20th Century and the “deadliest substance ever created by chemists,” has faded from the media spotlight. Why? Why did the EPA official who recommended the evacuation of Times Beach, Missouri, recently admit that he made a mistake and that the evacuation of this community following the spraying of dioxin-contaminated oil on roads and a subsequent flood was an unnecessary overreaction? What are the latest facts regarding adverse human health effects from exposure to dioxin?

Although dioxin’s teratogenic (birth) defects in some animals were not discovered until 1970 by Dow Chemical Company scientists, the industrial community was aware of a mysterious skin disease “chloracne” since it was first reported by Herxheimer in Germany in 1899. Chloracne was originally incorrectly attributed to chlorine gas exposure and only in 1957 was it recognized by the German scientists Kimmig and Schultz that dioxin impurities in certain chlorinated phenols were responsible. Unfortunately, this research paper was not widely read by the scientific community and it was not until 1969 that the existence of dioxins and their acnegenic properties were widely publicized. We now know that dioxin (really a family of related chlorinated chemicals, the most toxic of which is 2,3,7,8-tetrachlorodibenzo-p-dioxin
or TCDD) is produced when chlorinated phenols, used to manufacture herbicides (such as 2,4-D), insecticides, and antiseptics (hexachlorophene) are heated to a high temperature. In particular, during the manufacture of the herbicide 2,4,5-T, which, in combination with 2,4-D, comprised Agent Orange, it was necessary to heat the chemical ingredients in a large “pressure-cooker” chemical reactor. As was later discovered, if the temperature of this process is not very carefully controlled, then variable amounts of the byproduct dioxin can form. Some chemical companies were better able to control this temperature than others. In fact, of the seven companies involved in the production of 2,4,5-T for use in Agent Orange, one company consistently produced batches relatively high (>500 parts per billion) in dioxin. Although Dow Chemical Company, the largest producer of 2,4,5-T, was eventually able to produce very “clean”—essentially dioxin-free—2,4,5-T, public pressure forced the discontinuance of the manufacture of this chemical, despite the fact that pure 2,4,5-T has always been a perfectly safe herbicide, like the still used 2,4-D.

Physicians and epidemiologists have been observing the health of those thousands of people (industrial workers, civilians, Vietnam veterans) who were exposed to dioxin over the past forty years. From all these studies, described in detail below—and despite the public perception to the contrary—no human deaths can yet be attributed to dioxin exposure. The only documented health effect from dioxin exposure is chloracne, which, although attributed to dioxin exposure. The only documented health effect to date is chloracne. Of the 193 cases of chloracne ever measured in a human—the only adverse health effect in the Ranch Hand Group. An October 1991 update recently provided by Dr. William Wolfe, the senior physician in charge of this study, reaffirms these conclusions.

Studies of more than 800 occupationally exposure workers in nine industrial plant accidents, including those in the massive Nitro, WV, Monsanto accident in 1949, and chemical mishaps in 2,4,5-trichlorophenol plants in England, Germany, France, Czechoslovakia, The Netherlands, and the U.S. fail to indicate serious long term health effects in these men, some of whom have dioxin concentrations exceeding 1000 ppt 30 years after their initial exposure. Some 465 cases of chloracne were observed in these workers. A study of 2200 Dow Chemical Co. workers who were potentially exposed to dioxin revealed that they had a slightly lower mortality than a control group, and have no total cancer increase.

Dr. P. Bertazzi of the Institute of Occupational Health, University of Milan, last year published a detailed evaluation of the human health effects of the Seveso, Italy, accident, in July of 1976, involving 37,000 people. Although some of the exposed children in “Zone A,” the area of heaviest exposure, had dioxin tissue levels as high as 56,000 ppt immediately following the accident in 1976—the highest dioxin level ever measured in a human—the only adverse health effect to date is chloracne. Of the 193 cases of chloracne, 170 were in children under the age of 15, and the skin lesions in all but one of these cases had disappeared by 1985. Although we need to continue to monitor the health of the people in Seveso, Dr. Bertazzi concludes that there are “no increased birth defects due to dioxin exposure,” as the children born during the period from 1977-1982 failed to demonstrate an increased risk of birth defects. Similarly, the aborted fetuses shows no conclusive abnormalities. The cancer mortality findings after 10 years do not allow firm conclusions to be drawn, although mortality from cancer of the liver, one of the organs targeted by dioxin, is no different from unexposed people.

There is no doubt that the family of chemicals known as “dioxins” and the related dibenzofurans have a unique and unusual toxicity in some animals (e.g., guinea pigs, hors-
es, mice, the Long-Evans rat), but are much less toxic—in some cases a thousand fold—in other animals (e.g., hamsters, dogs, the Han-Wistar rat, and, it would appear, man).

The general presumption by politicians, the media, and environmental groups that dioxin is highly toxic to humans even at very low doses just is not supported by the scientific and medical evidence. The only documented health effects in humans are chloracne and mild, reversible peripheral neuropathy and liver enzyme induction. Simply put, and despite the protestations of environmental apocalypticists, dioxin is not the “doomsday chemical” that they would have us believe.

Although adverse health effects in humans have not been linked definitively to dioxin, despite our fears to the contrary, the past ten years have uncovered much new information about this extraordinary chemical. Not only is dioxin produced when nearly any organic material is burned (lead gasoline, wood, municipal and hospital waste, tobacco), but it is estimated by some scientists that forest and brush fires are the leading source of dioxins in our environment. It is approximated that Canadian forest fires produce annually ten times the amount of dioxin emitted in the Seveso accident! Since most of the world’s annual 200,000 forest fires are lightning caused, it is obvious that much dioxin is naturally produced, and, in fact, has undoubtedly been an “environmental pollutant” since the first forest fire on earth! A soil sample preserved from 1877 was recently found to contain dioxin. Since dioxins are slowly biodegradable, they have not accumulated as much as one might have expected based on this new scientific data.

Even more astounding is the observation that natural enzymatic processes have the ability to produce dioxin from chlorinated phenols! That is, the same chemical reaction which itself is found in an array of natural organisms (insects, marine animals, sponges, seaweed). This extraordinary find, published by one of the world’s leading dioxin researchers, Dr. Rappe of Sweden, opens the door to the extraordinary find, published by one of the world’s leading dioxin researchers, Dr. Rappe of Sweden, opens the door to the possibility that a heretofore unrecognized source of dioxin is naturally produced, and, in fact, has undoubtedly been an “environmental pollutant” since the first forest fire on earth! A soil sample preserved from 1877 was recently found to contain dioxin. Since dioxins are slowly biodegradable, they have not accumulated as much as one might have expected based on this new scientific data.

Finally, an irony is that the 1,3,6,8-tetrachlorodibenzo-p-dioxin analogue of TCDD has anticancer properties against human breast cancer, as reported last year in a chemical patent from Texas A & M University, and, thus, dioxin derivatives may ultimately prove useful in saving lives.

References:

Gordon W. Gribble, Ph.D., is The Dartmouth Professor of Chemistry at Dartmouth College, Hanover, New Hampshire.
Risk Estimation: It would come as a surprise to most people to learn that so-called quantitative cancer risk assessments do not actually quantify true risk. The actuarial risk calculated by insurance companies (e.g., the risk of dying in an auto accident), is based on actual data on the incidence of disease-, disaster- or accident-related mortality. However, actuarial data on disease incidence or mortality in humans resulting from very low exposures to chemicals in the environment simply do not exist. Instead, data from occupational studies of more heavily exposed humans are used, where available. However, epidemiological studies seldom have the quantitative exposure data needed for a quantitative risk assessment. To create a surrogate for this missing low-dose data, animals are exposed to very high doses of substances to guarantee that statistically reliable results are obtained. These animal results (or, much less often, the results from occupationally-exposed humans) are then extrapolated, using mathematical models incorporating numerous default assumptions, to humans exposed to very low environmental levels of the same substance. The resulting cancer risk calculated by regulatory agencies is, of necessity, entirely theoretical and will vary greatly depending on the assumptions made and the models used in the assessment. The limitations of quantitative risk assessment were clearly acknowledged in EPA’s 1986 Guidelines for carcinogen risk assessment, as follows:

“The risk model used by EPA [i.e., the linearized multistage model] leads to a plausible upper limit to risk that is consistent with some proposed mechanisms of carcinogenesis. Such an estimate, however, does not necessarily give a realistic prediction of the risk. The true value of the risk is unknown, and may be as low as zero.” (U.S. E.P.A., 1986) (emphasis added.)

Thus, EPA’s cancer risk assessments, which were originally developed in the 1970’s to facilitate and document regulatory decisions regarding cleanup standards and remedial actions at contaminated sites, were never intended to be used for the “realistic prediction” of actual health consequences.

That animal models are imperfect surrogates for human beings is not a matter of debate in the scientific community, nor should the results of carcinogen classification by EPA, IARC, or NTP be interpreted to suggest otherwise. Of approximately 600 chemicals evaluated by IARC, 34% were clearly carcinogenic in animals, but only about 10% of those were also considered by IARC to be human carcinogens based on “sufficient” evidence (Meijers et al., 1992). This low correspondence was partially due to the fact that no adequate human data existed for almost 61% of the animal carcinogens. However, of the 36 known human carcinogens, 15 (41.7%) did not show sufficient evidence of carcinogenicity in animals (Meijers et al., 1992). In many, if not most, cases, the high rate of positive results (30-50%) in cancer bioassays has less to do with the intrinsic carcinogenicity of the chemicals being tested than it does with the magnitude of the doses used, typically in the range of 1/4, 1/2, and one times the Maximum Tolerated Dose (MTD). About 40% of all animal carcinogens tested may cause cancer by promotion mechanisms which can be
expected to exhibit relatively high thresholds.

The Zero-Threshold Concept: Most regulatory agencies use models of chemical carcinogenesis that incorporate the zero threshold policy, i.e. the assumption that there is no dose so small (other than zero) that it could not cause cancer in someone, somewhere. (The Linear Multi-Stage or LMS Model is the best known example.) Contrary to popular belief, this zero-threshold policy for carcinogens is just that, a policy, and not an established scientific principle. In fact, it runs contrary to the most fundamental principle of the science of toxicology, which, in abbreviated form, may be stated as "THE DOSE IS THE POISON." (Physicians and microbiologists, respectively, implicitly recognize the same pharmacological/biological principle in the form of the "therapeutic index" and the concept of virulence, respectively.) In the late 1970s, the largest chronic bioassay ever undertaken (the so-called "megamouse" or ED01 Study) provided compelling experimental evidence of a threshold for chemically-induced bladder cancer in mice; even mouse liver carcinogenesis (which has an unusually high spontaneous rate in laboratory rodents and typically exhibits an apparently linear dose-response when the LMS model is used) exhibited a threshold when the data were re-evaluated by the Society of Toxicology using best-fit models that incorporated time-to-tumor data (SOT, 1981) instead of the Linear Multi-Stage Model used by FDA and EPA (Staffa and Mehlan, 1979). Since that time, it has become increasingly apparent, on the basis of mechanistic considerations alone, that many, if not all, animal carcinogens must exhibit thresholds, especially the so-called "promoters" and weak "initiators" with promoting activity (Williams & Weisberger, 1991, pg. 154). These thresholds will typically exceed, by substantial margins, human exposure levels encountered outside of occupational settings.

The zero-threshold concept is based on (1) the historical observation that radiation-induced genotoxicity (i.e., DNA damage) exhibited no apparent threshold over the observed dose range and (2) the assumption that even a single DNA adduct or mutation has some finite chance of ultimately resulting in the formation of a full-blown malignancy. The second assumption derives from the fact that sub-lethal genetic damage is hereditary and may be passed on to future generations of cells. Thus, unlike cells suffering epigenetic or somatic damage, a single cancer cell has the potential of becoming a whole population of cancer cells. Using the same logic, one might conclude that exposure to a single pathogenic bacterium may suffice to cause disease, since it can, in theory, divide until it becomes a large population of pathogenic bacteria. However, just as the principle of threshold toxicity is fundamental to the science of toxicology, so is the principle of threshold pathogenicity (or virulence) fundamental to the sciences of bacteriology, virology, and immunology. It takes a larger number of less "virulent" organisms to cause disease than it does for a more virulent organism.... just as it takes more molecules (i.e., a higher dose) of a less toxic chemical to elicit a response than it does for a more toxic one. Logically, then, there is no reason to expect cancer to behave any more "magically" than, say, diphtheria or the common cold.

However, even if the zero-threshold model of carcinogenicity were data-based and biologically plausible (and it is neither), almost half of the chemicals to which it is applied do not meet that concept’s first and foremost criterion, i.e., that of genotoxicity (or, more specifically, mutagenicity). Non-genotoxic carcinogens, which make up 40% or more of all chemical carcinogens identified to date, do not cause DNA damage, and commonly exhibit demonstrable thresholds (often quite high ones) with regard to cancer. (Exceptions are potent promoters like dioxin and TPA that have an affinity for specific receptors.) Examples of such epigenetic carcinogens include: arsenic, asbestos, benzene, 2,3,7,8-TCDD ("dioxin"), saccharin, phenobarbital, DDT, PCBs, certain food additives (e.g., BHA and BHT), various chlorinated solvents (including TCE, PCE, and chloroform), various hormones (e.g., estrogens and androgens), certain chemotherapeutic agents (e.g., Tamoxifen), iodine (i.e., deficiency), some ulcer medications (e.g., omeprazole and, probably, cimetidine), thioureas and other goitrogens (as may be found in cabbage), common drinking alcohol (ethanol), and even table salt (or, rather, the sodium ion) (Williams and Weisburger, 1991). For genotoxic carcinogens, simple, reversible DNA damage (measured as the number of DNA adducts) may well exhibit no measurable threshold, but mounting evidence suggests that the more complex processes of mutagenesis and, especially, carcinogenesis will (Williams & Weisberger, 1991, pg. 154; Cunningham et al., 1994; Pitot and Dradan, 1996). The thresholds of very strong genotoxic carcinogens may be too low to be determined in ordinary bioassays, but they too almost surely exist because, although complete carcinogens may be able to initiate cells (i.e., cause mutations) at very low doses, they will not be able to sustain the remainder of the multi-stage process of carcinogenesis (Pitot and Dragan, 1996). (Promotion is typically a relatively high-dose, non-genotoxic phenomenon that often involves cytotoxicity, cellular proliferation and inhibition of apoptosis or "programmed cell death." Since cells in the promotion stage are dependent on continual exposure to the promoting agent, promotion, unlike initiation, is reversible with the removal of exposure.)

Even if one were to accept the proposition that there is a finite probability that a single molecule of a carcinogenic chemical could cause cancer, practical thresholds would still
have to exist. At low enough concentrations, for example, the time required for cancer to develop (the so-called latency period), which is inversely related to dose, would exceed a human lifetime, i.e., the person would die of something else before the chemically-induced cancer could ever develop. Another practical "threshold" is based on the limits imposed by population size. At sufficiently low doses, the theoretical probability of effect would be so small (e.g., one in 10 billion) that the entire human population would (statistically speaking) be too small to express even one causally-related case of cancer in a human lifetime. Such population-based practical thresholds will be the rule, rather than the exception, at most contaminated sites where the potentially-exposed populations number only a few thousand and the estimated (i.e., theoretical) "risks" are generally in the range of 1 in 10,000 to 1 in a million or less. In either case, the limiting concentration (i.e., the practical threshold), if it could be determined experimentally, would be indistinguishable from a "true" biological threshold.

If the foregoing logical arguments are not convincing enough, then one need only consider that the existence of personal thresholds is a self-evident, empirical fact. (Everyone who smokes does not necessarily get lung cancer, just as everyone who is exposed to influenza virus does not automatically catch the flu.) The virtual inevitability of "true" effect thresholds for carcinogens derives from the fact that the human body has multi-layered defense mechanisms against cancer formation, including: metabolic detoxification and excretion; sequestration of toxicants in depot tissues; "suicide" reaction with scavenger molecules (instead of DNA); repair of damaged DNA; apoptosis or programmed cell death; and immunologic surveillance. These defenses are much more effective in humans than they are in rodents and other shorter-lived animals (a fact that is generally ignored by zero-threshold models). The effect of these multiple tiers of defense mechanisms is to reduce the chances that a) DNA will be damaged, in the first place, and b) that DNA damage, if it occurs, will be translated into a mutation, and c) that mutations, if they occur, will yield a living abnormal cell, and d) that a cancer cell, if it occurs, will multiply and establish itself as a neoplasm. Only if all of these obstacles are overcome before the individual dies of something else is it possible for carcinogen exposure to actually result in cancer.

In other shorter-lived animals (a fact that is generally ignored by zero-threshold models). The effect of these multiple tiers of defense mechanisms is to reduce the chances that a) DNA will be damaged, in the first place, and b) that DNA damage, if it occurs, will be translated into a mutation, and c) that mutations, if they occur, will yield a living abnormal cell, and d) that a cancer cell, if it occurs, will multiply and establish itself as a neoplasm. Only if all of these obstacles are overcome before the individual dies of something else is it possible for carcinogen exposure to actually result in cancer.

In other words, the same argument that explains the inevitability of effect thresholds for carcinogen exposure to actually result in cancer. Obviously, a force of one would be too weak to overcome even the first line of defenses. And even if the marine did, by some miracle, succeed in causing some damage, the defenders could easily repair or replace any damaged material in time to greet the next day's suicidal assault. Similarly, at sufficiently low doses, a carcinogen will be unable to cause any clinically significant damage, because either a) it is neutralized before it can do any damage at all or b) the little damage that it does do is quickly and easily repaired.

A Threshold model for Chemical Carcinogenesis: Interpreted within the context of the zero-threshold assumption, the term "latency" usually implies that, given enough time, a cumulative effect will be produced by a series of individually sub-threshold doses, i.e., that each and every individual daily dose, no matter how small, effectively contributes to the cumulative dose which, it is assumed, actually causes the observed effect. However, in order to have a genuine cumulative effect, it is only logical that something must, in fact, accumulate. Either the individual sub-threshold doses must accumulate in a tissue until threshold levels of the toxicant are reached and surpassed, or else sub-clinical effects must accumulate until clinical significance is attained (e.g., cirrhosis of the liver in alcoholics). The first case requires bio-accumulation of the toxicant. However, fat soluble substances like dioxin and PCBs are the ones that most often bioaccumulate, and sequestration in a storage depot like fat actually reduces risk by keeping the potential toxicant away from its target cells. The second implies that the individual doses exceeded the thresholds for the sub-clinical effects. But what if the carcinogen (e.g., ethylene oxide or benzo[a]pyrene) does not bioaccumulate and the individual doses are at or below no-effect levels? By what magic, then, would cumulative effects be produced under these most common of circumstances, i.e., in the absence of anything to accumulate? Therefore, notwithstanding EPA's 1986 policy statement to the contrary, the risk model used by EPA does not lead to a "plausible" upper limit to risk, because proposed mechanisms of carcinogenesis i.e., the assumptions) that underlie the model are not plausible, either.

Adherents to the zero-threshold model usually make no effort to address this question. And, when faced with experimental data that appear to demonstrate the existence of thresholds for tumor formation, they typically respond by claiming that an increased frequency of cancer would, in fact, have been detected, if only a large enough population of animals could have been exposed. This argument was even made when the ED01 study, which employed over 24,000 mice, demonstrated a relatively high apparent threshold for
As an organism’s defense mechanisms become less effective with age, chronic exposures that were previously innocuous will become more effective with age.

Thus, while regulatory risk assessors have historically considered that the observation of the cancer latency with low chronic doses of chemical carcinogens was compatible with the notion of zero-threshold, it is far more likely that it reflects just the opposite, i.e., the existence of personal thresholds that decrease with advancing age. Childhood cancers are often explainable in terms of genetic predispositions that either reduce the number of steps needed for the formation of tumors (e.g., retinoblastoma) and/or reduce the normal age-dependent efficiency of the body’s defense mechanisms (e.g., xeroderma pigmentosum and defective DNA repair).

The major advantages of this threshold model of carcinogenesis over the zero-threshold model of carcinogenesis are that 1) it relies solely on established principles of pharmacology and toxicology without the need for counterintuitive assumptions, and 2) it is more readily testable by experiment.

The Causes of Cancer: Almost everyone has heard, at one time or another, and in one form or another, a statement to the effect that “approximately 80% of all cancers are caused by environmental factors.” This statement, or
something very much like it, was originally made by Dr. John Higginson at a 1968 International Cancer Conference in Israel. In its original context, the adjective "environmental" was properly understood by Dr. Higginson’s scientific audience to mean all factors excluding those related to heredity (Gots, 1993). However, sometime in the late sixties and early seventies, the phrase "environmental factors" became translated in the media and in the public mind as "environmental chemicals." This widespread misconception grossly distorts popular estimates of cancer risk for people in industrialized societies.

Several investigators have attempted to identify in a semi-quantitative fashion the causes of cancer in humans (Higginson and Muir, 1979; Wynder and Gori, 1977; Higginson, 1968). The classic treatment of this subject is "The Causes of Cancer" by Doll & Peto (1981). The findings of Doll and Peto, two of the world’s leading epidemiologists, have been widely quoted in the scientific literature and still represent the best estimates available in the U.S. According to Doll and Peto, approximately 30% of all cancer deaths are attributable to tobacco, 35% to diet, 7% to reproductive & sexual behavior, 4% to occupation, 3% to alcohol, 3% to "geophysical factors (e.g., ionizing radiations and UV light), 2% to pollution, 1% to medicines and medical procedures, <1% each to food additives and industrial products (e.g., detergents, hair dyes, plastics, paints, polishes, solvents, etc.), and perhaps as much as 10% to infection. Thus, perhaps 75% of all cancer is attributable to the "lifestyle" factors of smoking, drinking (alcohol), diet, and sexual behavior, and very little may be attributable to environmental pollution, as the public understands that term. Even these modest estimates of pollution-related cancer (2%) are highly speculative, being based as they are on high-to-low dose extrapolation from occupational studies.

The Cancer "Epidemic": Another popular misconception relates to the perception of a booming cancer "epidemic" that began with the industrial revolution and continues to grow today. In fact, according to an update from the National Cancer Institute (1988), "the age-adjusted mortality rate for all cancers combined except lung cancer has been declining since 1950 for all individual age groups except 85 and above." (The latter group saw a mere 0.1% increase.) Decreases in cancer mortality during this period have been due primarily to decreases in stomach cancer (by 75%), cervical cancer (by 73%), uterine cancer (by 60%), and rectal cancer (by 65%). Increases have been primarily from lung cancer (due mostly to smoking rather than to modern industrialization) and non-Hodgkin’s lymphoma (by 100%). The increased incidence of some cancers may be due primarily to smoking and natural dietary factors such as fat. However, some apparent increases may actually reflect increases in registration of cases and/or improvements in diagnosis.

Since cancer is primarily a disease of old age and our population is getting older (i.e., people are living longer), it is inevitable that the incidence of cancer, in absolute terms, will increase. However, when age-adjusted rates are used instead of raw numbers, most of the apparent increases disappear, leaving no persuasive evidence that environmental pollution has contributed significantly to human cancer rates. Any theoretical increase in cancer "risk" that might be associated with life in modern society must be balanced against very real health benefits, including reduction of exposure to natural carcinogens in damaged crops and spoiled food, which are much more abundant in the environment than are "unnatural" ones. More immediately apparent, however, is the much greater reduction in death due to causes other than cancer. Given such substantial benefits, few people would suggest, for example, that all medicines and medical procedures should be banned because of speculation that they may be responsible for 1% of all cancers. After all, without modern medicine, many of us would not live long enough to get cancer.

In a very real sense, cancer is as big a killer as it is today in the U.S. precisely because so many Americans do not die of something else first. Mortality due to cardiovascular disease...
and cancer are also substantial in the developing world, but are surpassed by deaths from infectious and parasitic diseases and lower respiratory infections, respectively (WDR, 1993). Many of the developing world’s major health problems, including diarrheal diseases, pneumonia, tuberculosis, measles, malaria, and malnutrition have been largely eliminated or controlled in the U.S. by chlorination of public drinking water, the use of common medicines and vaccines, and the use of agrochemicals to guarantee a safe, adequate food supply. And yet, none of these invaluable contributions to public health is 100% safe. (Nothing in this world is.) But the benefits are real and substantial, while the proposed cancer “risks” are largely theoretical and relatively insignificant by comparison. Because cancer is primarily a disease of old age, eliminating all cancer as a cause of death, while desirable, would actually not extend the average human lifespan by much more than a year or so. The elimination of childhood cancers, however, could add many decades of life to individual children, and should be a national priority.

Criteria for Causation in Epidemiological Studies: According to the Centers for Disease Control, 23.9% of all deaths in 1992 were due to these malignant neoplasms (MVSR, 1995). Thus, cancer was the second leading cause of death, after heart disease which accounted for 33% of all deaths. Against such high background rates, locally elevated rates of mortality due to cancer cannot be causally attributed to low-level environmental chemical exposures with any confidence at all, unless several conditions (called Hill’s Criteria for Causation) are met. At the very least, (1) the exposure must have preceded the onset of the disease, (2) the rates must be high enough to mitigate against chance as the source of the observed variation and, (3) all other known causes or contributors to the effect (“confounding factors”) must be ruled out or adjusted for. The case for causation is further strengthened if (4) the proposed connection between exposure and disease is a biologically plausible one, (5) the health effect is observed to increase with increasing exposure (i.e., exhibits a “dose-response relationship”), and (6) the observations are consistent with those made by other independent investigators under similar conditions (i.e., they are reproducible). Considering the time and expense required to resolve all of these issues in a real world setting, it is not surprising that epidemiological studies rarely satisfy all or even most of these criteria. Causation is much easier to establish in the laboratory where variables are more easily controlled. Hence, the practical necessity of risk assessors’ inordinate reliance on experimentally-derived animal data. Of course, one is then faced with the problem of extrapolating from observed effects in animals to potential effects in humans.

Which brings us full circle.

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Unprompted, almost no one is worried about GMOs and wants to see them on a label. But a vast majority want to know about pesticides. Who objects strongly to pesticide use being listed on food labels? Organic farmers and trade groups. We discuss why.

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"Cautioning 'Prediabetes' is a Bogus Diagnosis" by Mary Gillis

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