JOURNAL OF OCCUPATIONAL AND ENVIRONMENTAL HYGIENE
https://doi.org/10.1080/15459624.2024.2311300

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COMMENT

Cancer risk assessment, its wretched history and what it means for public health

Edward J. Calabrese

Department of Environmental Health Sciences, School of Public Health and Health Sciences, University of Massachusetts, Amherst, Massachusetts

Introduction from the editor

This commentary presents a cohesive summary of the development of the linear non-threshold model of cancer risk assessment contained in about 100 papers in the peer reviewed industrial hygiene, toxicology, health physics, and radiation health scientific literature. These publications provide detailed documentation spanning the last 100 years, including references to peer-reviewed publications, personal research journals, and private communications of scientists discussed in this commentary with examples of scientific misrepresentations and misconduct to support the conclusions and perspectives offered. Since it was the goal to provide a comprehensive and easy-to-read commentary, it was agreed that the paper would minimize the use of citations and avoid detailed endnotes. I requested that the author provide a comprehensive list of supporting information for the interested reader. A graphical abstract and supporting references are provided in the supplementary material and key citations are provided in this commentary.

The author has previously published two research manuscripts in this journal that provide additional supporting information: (see (a) and (b) below). For the interested reader, a 22-episode Health Physics Society (HPS) documentary of the historical and scientific foundations of cancer risk assessment and the LNT model provides additional context, including key references, personal letters, and other documents cited in Professor Calabrese's publications (see (c)).

a. "Muller Misled the Pugwash Conference on Radiation Risks" with Paul B. Selby. DOI: 10.1080/15459624.2023.2268664.
b. "Background Radiation and Cancer Risks: A Major Intellectual Confrontation within the Domain of Radiation Genetics with Multiple Converging Biological Disciplines" with Paul B. Selby. DOI: 10.1080/15459624.2023.2252032.
c. "The History of the Linear No-Threshold (LNT) Model Episode Guide" available from HPS.org.

I have read many of Professor Calabrese's publications and watched the HPS documentary. I find his evidence compelling. I have also reviewed publications that offer alternative viewpoints to those of Professor Calabrese. In the spirit that science should always maintain the capacity for self-correction, JOEH invites manuscript submissions offering alternative viewpoints. Thank you for your interest in this important subject.

Michael D. Larrañaga, PhD, CIH, FAIHA
Editor-in-Chief, JOEH

A call to action

The foundations of cancer risk assessment represent a century of significant uncorrected mistakes and scientific misconduct, dominated by powerful self-interests and politicized ideological actions involving the US National Academy of Sciences (NAS), *Science* journal, multiple Nobel Prize winners, and elite leaders of the field of radiation genetics from the 1920s to the 1990s. This scientific debacle by a "who's who" of the genetics community, was advanced by extremely troubling publication decisions by the journal *Science* that promoted such corruption. In its 50 years of operation, the US EPA has done little to understand or correct this problem (Calabrese 2019a, 2022). In fact,

CONTACT Edward J. Calabrese edwardc@umass.edu Department of Environmental Health Sciences, School of Public Health and Health Sciences University of Massachusetts, Amherst, MA 01003, USA.

Supplemental data for this article can be accessed online at https://doi.org/10.1080/15459624.2024.2311300. AIHA and ACGIH members may also access supplementary material at http://oeh.tandfonline.com.

their actions appear to be just the opposite. A recent Freedom of Information Act based article in *Junk Science* (https://junkscience.com/2023/06/emails-reveal-radiation-safety-establishment-tries-to-censor-blockbuster-debunking-of-the-lnt-and-cleanse-the-health-physics-society-of-lnt-critics) has shown that the EPA continues to stonewall debate on the issue and to threaten those in their organization who ask the key challenging questions. What has brought this issue to a head has been a 22-episode documentary on the historical foundations of cancer risk assessment by the Health Physics Society (https://hps.org/hpspublications/historylnt/episodeguide.html), a documentary based on numerous detailed publications (see References and Supplement #1) in the peer-reviewed literature exposing this massive historical corruption. This Commentary is a Call to Action as it points out that the US scientific and regulatory system is broken based on past uncorrected errors and corruption with a continuing self-serving lack of leadership by the journal *Science*, the NAS, and EPA. After five decades of failure, it is quite clear that the EPA cannot self-correct on these critical matters, which were based on falsified data, misconduct, and a history of public deception. It is time that the scientific community, including professional associations such as the American Association for the Advancement of Science, American Industrial Hygiene Association, Health Physics Society, Society of Toxicology, Society for Risk Analysis, Society of Environmental Journalists, as well as the NAS, and others inform their memberships and elected leaders of this history of public deception and work to correct the scientific record. Finally, what is needed is a Congressional oversight investigation into this troubling history of cancer risk assessment that started in the US and now has affected the chemical and radiological risk assessment policies and regulations of most countries around the world.

Introduction

The story about to unfold in this commentary will be disturbing but perhaps not too surprising now in contemporary society. You will be taken on a path of discovery that explores the history of cancer risk assessment for radiation and chemical carcinogens. This commentary is about a history of errors made by scientific leaders that have long remained hidden and uncorrected. The evidence shows that major biases led to deliberate misrepresentations (i.e., blatant dishonesties) of the scientific record by the very people society was supposed to trust, including multiple Nobel Prize winners. Equally troubling have been the dishonest actions of organizations, such as major advisory bodies, including the US NAS and the journal *Science* that have repeatedly succumbed to violations of the public trust. As disappointing and upsetting as such statements are, it is hard to believe that this historical record could get even more corrupt, but it does. It has become known that major US scientists conducting important mutation and cancer studies hid data and deliberately withheld results from the public and scientific community. Why? Because the findings didn't fit their preconceived beliefs and would not enhance opportunities to obtain more funding for themselves and their programs. Yes, the destructive self-interest of the research community, especially governmental and university scientists, in this case, presents a prominent but long-hidden dimension that unfolds in a complex journey of discovery.

Society is faced with questions over who can be trusted in today's world: government, scientists, prestigious advisory groups, like the United States National Academy of Sciences (US NAS), and major journals like *Science*, *Nature*, *The Lancet,* and others. These have historically all been the entities that society has trusted for decades. The historical record presented here, therefore, involves powerful and high-profile individuals and groups that manipulated the public for personal gain and is presented in the following eight-part expose.

Part 1: Fear—A weapon to exaggerate environmental and radiation risks for political gain

Fear is an important human trait that enhances survival. However, like most emotions, it needs to be properly controlled and acted upon. Fear can distort reality and be crippling, leading to irrational decisions that hurt people in many ways, affecting how they think, their health, and their very lives. It can lead to not only very poor and self-destructive personal decisions but also harmful government policies that affect just about everyone. Fear has become a weapon used by elected officials, government regulators, such as the leadership of the United States Environmental Protection Agency (US EPA), and especially many university research scientists to advance their political, professional, and personal self-interests when the data often say just the opposite. This is occurring all over the world with numerous types of chemical phobias, crippling and irrational fears of low-level radiation,

and also some of the dire predictions of climate change that are strikingly wrong.

The story of scientific corruption documented here is not a simple one. It has its beginnings about a century ago, traveling through multiple generations of scientists and scientific and regulatory organizations to people in powerful positions today. While this historical record is complex at times, it is important to follow the details and to see how some very smart people corrupted their science, and our world, and why. The good part of this story, however, is that many lies and deceptions of these organizations and leaders have been discovered in a trail of letters and documents that they have left behind, mostly preserved in libraries around the world. See supplementary material. The trail of letters and documents permits these individuals, who have corrupted society for their own interests, to tell the story in their own words, testifying against each other and ironically themselves. The striking thing about this approach is that the historical pieces, like the jigsaw puzzle, nicely fit together and tell a coherent story. Part 2 of this series begins putting this puzzle of scientific corruption and corrupt science together.

Part 2: Muller lied during his Nobel Prize acceptance speech

A major turning point in the corrupted science that many call cancer risk assessment was the Nobel Prize Lecture on December 12, 1946 (Muller 1946), of U.S. radiation geneticist and University of Indiana professor, Hermann J. Muller, for being the first to produce gene mutations. Muller did so by X-raying tiny creatures called fruit flies, that like to eat very ripe bananas. While Muller has been a major figure in the history of science, especially in radiation genetics, it is now known that Muller never induced gene mutations, probably fooling himself, at least for a while, but definitely fooling most of the scientific community for decades, and even many to the present time. The doubters of Muller's accomplishment would be proven correct with Muller himself eventually admitted this mistake in writing, some 10 years after receiving his Nobel Prize (Calabrese 2017a, 2018, 2020a).

While it must have been hard for Muller to finally admit this, he acknowledged that he was only knocking big holes in the fruit fly chromosomes due to the high energy of the x-rays and that he did not discover the tiny point mutations he claimed and was so honored for inducing (Calabrese 2017a, 2018, 2020b), While Muller never deserved the Nobel Prize, Muller understood its power and social utility. He then employed its glory, fame, and prestige to deceive the Nobel Prize audience and the world on the effects of radiation at low doses. Muller used his Nobel Lecture to make the case that there was no safe dose of radiation and that the long-standing use of a threshold dose-response model needed to be discarded and replaced with the linear non-threshold (LNT) dose-response model which suggested that even a single ionization from radiation or even a single molecule of a chemical carcinogen could increase the risk of cancer (Muller 1946). It was a striking performance that delivered a powerful dose of environmental and public health anxiety.

About one month before his Nobel Lecture, Muller received the results of a new and powerful study from the University of Rochester by Ernst Caspari (Calabrese 2019b) who was working under the well-known geneticist researcher, Curt Stern, that discredited Muller's LNT idea. Muller was a paid consultant to that study, knew the research team well, provided the fruit flies for the study, and advised the research team of the type of study to be done. Thus, Muller was a true insider. Letters from Muller indicate that he knew the significance of Caspari's new results and that the people doing the work were competent. Muller therefore knew that the findings of Caspari would discredit his LNT model, and this was a serious problem. While Muller was concerned with Caspari's new findings, he was unable to offer any technical criticisms. He wrote quietly to Stern and strongly encouraged him to obtain more funding to confirm or refute the challenging findings of Caspari (Calabrese 2015).

A handful of people at the University of Rochester likely knew that Muller had just seen the results of Caspari's study, which was the largest and best study to date on the chronic effects of radiation on fruit flies. That study had shown that at the "low" chronic radiation dose rate (i.e., yet still about 100,000 times greater than background), no radiation-induced mutation effects were found. The study supported the threshold but not the LNT model. However, Muller ignored these findings, only sharing with the Nobel Prize audience the conclusion of a highly flawed doctoral dissertation that he directed about six or seven years before at the University of Edinburgh, Scotland (Ray-Chaudhuri 1944). A deep look into that dissertation reveals it to have numerous problems and probably never should have been approved. Even though Muller was the student's advisor, he was never present when the research was undertaken. Once the student

was oriented toward the lab, Muller left for the United States (US) for a prolonged vacation, returning to Edinburgh only after the research was completed. At best, Muller was an absentee advisor forcing the student to figure things out on his own. Letters between the student and Muller reflect serious scientific problems and pressures on the student during the study and many poor decisions. Muller proclaimed to the Nobel Prize audience that the student's findings supported his radiation-induced gene mutation hypothesis and the LNT model, down to a single ionization. He hid any insights into the new and far superior University of Rochester findings from the public. Muller also failed to tell the audience in Stockholm that the dose rate of radiation that he exposed his fruit flies to during his Nobel Prize research was some 100 million times greater than background, making the data of essentially no relevance to humans (Calabrese 2019b).

Muller was also playing on the audience's fear as just one year before the world had seen the horrors of the two atomic bombs dropped on Japan. He used these events to convince those in attendance and listening around the world that all doses of radiation are harmful even those that are at very low levels in our food, water, soil, and cosmic rays from outer space, that is, background radiation. Muller and his followers would claim that such low background radiation was the cause of approximately 10 to 20% of all cancers that occur in the human population and a similar proportion of birth defects as well.

While Muller has long been viewed as a brilliant scientist, sometimes the smartest people can make important mistakes because of personal biases that can cloud objectivity. We now know that Muller was wrong about his Nobel Prize research, grossly and intentionally misinterpreting the findings and their significance. It has since been discovered that Muller even got the nature of the dose-response wrong when he was a graduate student at Columbia University in New York City (Calabrese et al. 2022). In the end, this initial mistake would lead him and eventually the world astray in their assessment of radiation cancer risk assessment. So how did Muller make this transformative scientific error during his graduate days?

Muller and others noted that fruit flies very rarely show visual gene mutations like red-eyed parents producing white-eyed offspring. He reported that only 400 visual mutations had been seen out of about 20 to 25 million fruit flies or only about one mutation per 50,000 fruit flies, a very rare occurrence. Yet, Muller was hoping to find the explanation of biological evolution which needed a cause for gene mutation. But if gene mutation was so rare then how could evolution itself work? Muller made a key error that would prove to be a huge mistake, by assuming that spontaneous mutations could not be repaired since these mutations were rare and needed to fuel the progression of biological evolution. He asserted that only the positive/beneficial mutations would be retained (i.e., selected for survival and reproduction) while the harmful mutations would be eliminated (i.e., would die and not reproduce). So, after Muller induced what he claimed were gene mutations with massively high dose rates of X-ray radiation he soon proposed that background radiation is a cause of evolution. But to do this he had to extrapolate the findings by guessing what would happen at very low dose rates based on the experiments that he conducted that were at massively high dose rates.

Muller did not consider the possibility that the very few mutations that he observed, that is, 400 out of the 20 to 25 million fruit flies (Muller 1929; Calabrese et al. 2022), could have resulted from the occurrence of vast numbers of spontaneous mutations but with an equally profound capacity to repair such damaged genetic material. This is now known to be the case. In fact, Muller never considered a second option. He simply concluded that the genome was very stable (which it isn't) and that there were very few mutations. Whatever mutations occurred, those mutations were the "engine" of evolution and natural selection would take over and the beneficial mutations would drive evolution. This was a major assumption because it led Muller to his next major error: that the dose response for ionizing radiation for the hereditary material would have to be linear at a low dose rate and that there would be no repair for radiation-induced genetic damage. Muller developed this idea with colleagues in the mid-1930s and created the LNT single-hit model for cancer risk assessment. This model contains no capacity for the repair of damaged genetic material/DNA. The model also assumed that Muller's research had actually induced gene or tiny point mutations when most of what Muller did was blow big holes in chromosomes. In fact, Muller got the major interpretations of his research wrong, and then 40 years later this flawed model would be given by the NAS BEIR I Committee in 1972 to the newly formed US EPA and other similar organizations around the world to guide radiation and chemical cancer risk assessment regulatory policy for the general public (Albert 1994; Calabrese 2019a). In effect, cancer risk assessment evolved as a type of scientific

horror show in which the experts were wrong and dishonest but greatly trusted by leaders in government and the general public. In the end, this disaster in the making became the cancer risk assessment policy for all nations that followed the incorrect and dishonest leadership of Muller.

Part 3: Saving the LNT single-"hit" model

Muller and his followers knew they were in trouble with the new study from the University of Rochester by Ernst Caspari, under the direction of Professor Curt Stern, a well-known fruit fly geneticist. The Caspari study was a strong one, the best to date, competently done, robust, and very importantly, it supported a threshold dose-response model, not an LNT model. Caspari's study was to become the so-called "fly in the ointment," and it was the problem that would not go away. Yet, Muller and Stern were fully committed to supporting the LNT model, apparently at all costs. But what does "at all costs" mean in a professional scientist's sense? In the case of Caspari, at first, it meant that Stern refused to accept his study data. Like the full professor he was, Stern asserted that Caspari had a problem with his study that invalidated the research. Stern claimed that the control group (i.e., the flies not exposed to the radiation) displayed aberrantly high numbers of mutations that led to a false threshold conclusion. This meant that the study could not be accepted (Calabrese 2015). However, Caspari challenged these assertions by looking into the fruit fly literature. Indeed, he found similar studies with the same control group mutation response as he observed, showing that the Stern accusation was wrong. When Caspari challenged his mentor on this very point, Stern withdrew the complaint and backed down. While it looked like Stern was brave enough to overcome his biases and do the right thing with Caspari, remember, strong biases often die hard. So, what happened next?

Stern could have praised Caspari for his groundbreaking research and his challenge to the LNT model. However, this was not the course of action Stern chose. In the next twist of this scientific drama, Stern convinced and/or forced Caspari to write a paper that stated that these findings should not be accepted until it is learned why the data did not support the LNT model (Caspari and Stern 1948). Stern demanded that it was necessary to know why the Caspari data conflicted with an acute study also under the direction of Stern but finished a year earlier by Warren Spencer, a Ph.D. in entomology. In this acute study by Spencer, the dose was given within a few minutes rather than spread out across the entire lifespan of the fruit fly as done by Caspari (Spencer and Stern 1948). However, this was really a disingenuous ploy by Stern since there were at least 25 important differences between the two studies that made it essentially impossible to answer the questions/challenges posed by Stern. Plus, the Caspari study was conducted in a far superior manner, not having the limitations and serious flaws now revealed about the Spencer acute study.

The action taken by Stern was highly unusual as he tried to discredit the Caspari study without actually criticizing it, a very effective and sophisticated manipulation of the scientific community. In a further questionable and bizarre decision, Stern then published both the Spencer and Caspari papers in the journal *Genetics*, where he was the editor-in-chief, without apparent independent peer-review (Calabrese 2015, 2019a, 2022). That is, it is doubtful that many or any other journal would have published the results of a study (i.e., the Caspari paper) in which the researchers told the readership not to trust the data as Stern demanded. It seems, in retrospect, that Stern had Caspari in a type of trap. He was his boss and controlled his professional future, probably forcing Caspari to write such an outrageous assessment in this paper all in a way to "preserve the LNT single-hit model" (Caspari 1947).

Stern did obtain funding to retest the acute and chronic studies with a first-year master's student, Delta Uphoff. The three experiments of Uphoff did not go well. First, the study design was flawed and could not answer the question posed. One would have thought that with the great experience of Muller and Stern, this should not have occurred. However, this problem arose because Uphoff's study included the assessment of two variables at the same time. In experimental science, it is essential to have only one variable to test a hypothesis. What this meant is that it was impossible to tell what actually may have been causing a treatment effect. Right from the start, therefore, the study had an insurmountable problem. In addition to the study design flaw, Uphoff's control group also was 40% below that of previous research, raising concerns about the reliability of the findings. This was troubling to Stern who wrote to Muller about the problem, asking for guidance. Muller told Stern in writing that his large-scale studies with control group mutation rates gave data just like those of Caspari while the Uphoff findings were aberrant, and not to be trusted. Based on this information from

Muller, Stern informed the granting agency [Atomic Energy Commission (AEC)] that Uphoff's research on this initial study was "uninterpretable." Even worse, Stern raised the suggestion to the granting agency that Uphoff may have been biased to show a radiation effect, possibly to please her professor. This action of Stern, to even raise investigator bias as a suggestion to the granting agency, was potentially damaging to Uphoff's career. His action was predominantly self-serving as he was trying to protect his reputation. This suggestion alone indicates how sensitive Stern was to the issue of bias since he was bringing a powerful anti-threshold perspective as one can see with how he handled the Caspari situation. In the end, it could not be determined why Uphoff got aberrantly low control group readings. It could not be determined whether it was due to her inexperience, bias, abnormal control group variability, or some other factor. In the two remaining Uphoff experiments, another control group was aberrantly low, and again this study became "uninterpretable." The other study, one with a normal control group value, had a treatment response that exceeded LNT predictions by about three- to four-fold making this study nearly impossible to interpret. Taken all together, the Uphoff experiments were a disaster, as nothing went according to plan. Nonetheless, Stern once again decided to attempt his version of saving the LNT model by rejecting for the second time the Caspari findings and saying that the "uninterpretable" Uphoff studies along with its flawed design were the ones to be relied upon. He then inexplicably published Uphoff's research as a one-page note in arguably the top research journal in the world, *Science* (Uphoff and Stern 1949), without ever telling the readers how he had rejected these data only about six months earlier (Uphoff and Stern 1947), effectively hiding this from the scientific community. Now he claimed that these findings were satisfactory but without an explanation. He also promised to publish a comprehensive updated paper on this research providing all the necessary methods, materials, and other important features to the research. However, Stern and Uphoff never followed through on this and the promised paper never materialized. A further disturbing note is that the data of the two key chronic studies of Stern/Uphoff have never been found to the present time, now missing for more than 70 years. Yet, the radiation community has cited and relied heavily upon the research of Stern and Uphoff as being critical for the acceptance of the LNT model.

In retrospect, we have a study based on an invalid design, two experiments with aberrant control groups and a very high genetic damage response in a third study, data that have never been located for the two chronic studies and where a promised paper with all the necessary research descriptive information was never produced. Yet, this research became one of the gold standard papers used by the US NAS Genetics Panel to support and save the LNT model.

Making matters worse was that the AEC funded a study at the University of Rochester by Professor Donald Charles involving nearly a half million mice. The study was also a total failure with no relevant findings being published. Thus, the major genetic toxicology research efforts by the US government during the Manhattan Project of World War II yielded nothing of real scientific value except for the Caspari study, which was rejected by Stern and Muller because it supported a threshold, rather than an LNT model.

In 1949, a new problem for LNT arose when a famous health physics professor at Massachusetts Institute of Technology (MIT), Evans (1949), published a paper in the journal *Science* strongly supporting the Caspari paper and its threshold interpretation. Furthermore, Evans contacted about 50 leading geneticists and other scientists bringing forward the significance of the Caspari paper and its threshold implications. These actions greatly alarmed Muller who wrote to Stern strongly requesting that he challenge Evans and get Evans to change his opinions. In addition, Muller likewise on his own made such challenges to Evans. What came from such actions was that Muller sought to reestablish his control over the issue. He then wrote a series of papers directly contradicting his own data and his letters to Stern that the Caspari control group data were valid and Uphoff's were aberrant (Muller 1950a,1950b, 1954). The new Muller papers claimed just the opposite. Muller was clearly being dishonest in these papers which attacked the Caspari study but Stern, Caspari, and Uphoff remained quiet, allowing Muller to not be challenged with the dishonesties reported in his papers. In the case of Muller, he was asserting his control over the radiation genetics field in an attempt to provide his version of saving the LNT model even if at the same time exposing his multiple duplicities.

Part 4: The United States National Academy of Sciences: A legacy of dishonest leadership

In the early 1950s, the US began its above-ground testing of nuclear weapons in the state of Nevada in

the western part of the country. It didn't take long before these activities became controversial, generating much media attention and raising concerns amongst those in the radiation genetics field. The official US position, as given by the AEC, was that any exposures were rather trivial, would be far below any threshold of concern, and that there was no public health risk. This is not how the radiation genetics community viewed the question. In 1954, at a conference of the Association for the Advancement of American Science (AAAS), Professor Alfred Sturtevant of the California Institute of Technology (CalTech) issued a very pointed challenge to the director of the AEC claiming that his assessment was wrong and that the above-ground testing would result in significant increases in birth defects, other genetic anomalies, and would increase the risks of various kinds of cancers including leukemias and other health concerns. The presentation of Sturtevant (1954) was then published in the journal *Science*, receiving considerable attention especially since he was challenging the authority of the U.S. government on these public health matters. Likewise, at the same time, there was considerable international conflict relating to the Cold War and it was not just the U.S. that was conducting above-ground testing and contaminating the global environment. Similar testing was also being undertaken by the Soviet Union and on a lesser scale by the United Kingdom (UK) and France.

In early 1955, the Rockefeller Foundation (RF), a major research arm of the powerful and extraordinarily wealthy Rockefeller family, sent a letter to US President Dwight Eisenhower requesting that the president approve an evaluation of the complexities and societal implications of nuclear-related activities for the US and the world. Such a study would have multiple dimensions including medical and genetic effects, but also its effects on crops, oceans, the atmosphere, waste disposal and remediation, and other matters. The letter to Eisenhower raised the specter of fallout having a significant impact on birth defects, affecting public health over many generations. The RF indicated that it would fund this activity and recommended that it be undertaken by the US NAS.

Soon after this request, Eisenhower made arrangements to accept the offer of the RF to pay for the NAS study. The NAS president, Detlev Bronk, was closely connected to the RF. In addition to being president of the US NAS, Bronk was also president of the Rockefeller Institute for Medical Sciences, soon to be renamed the Rockefeller University. Bronk was also a long-standing member of the RF. Thus, the RF had one of its key people as the president of the NAS, organizing the study that they were proposing to fund (Calabrese 2015). This type of conflict of interest is striking and unprecedented. Yet, the Eisenhower administration permitted this arrangement and even more surprisingly, the scientific community and the media never challenged this arrangement with the conflicts of interest being quite evident.

Right from the start, one could see that there were some anomalies in the organization of this NAS project of the six expert panels. Of the six panels, five had chairs that were recognized as strong experts in their fields as would be expected. However, the sixth panel was a new one, never before having been so organized. It was called the Genetics Panel, and this affected the course of cancer risk assessment. Before this RF-funded NAS study, public health and clinically related issues were addressed by a Medical Panel. The Medical Panel would be comprised of a diverse grouping of experts including several geneticists as part of the overall team. Different than the other five panels, Bronk did not appoint a geneticist to be the chair of this Genetics Panel. He selected as chair of the Panel long-time director of research at the RF, Warren Weaver. Although Weaver was not a geneticist, Weaver knew all the major academic geneticists because the RF had been funding them over the past 30 years in his role as research director. Weaver knew the viewpoints and perspectives of these leading geneticists concerning the issue of the nature of the dose-response in the low-dose zone and whether they supported a threshold or an LNT perspective. Of critical strategic importance is that Weaver selected only those geneticists with a strong record of support for the LNT perspective. Weaver stacked the deck with radiation geneticists who held only a single view. This arrangement ensured that the recommendations coming forth from this Genetics Panel would be strongly supportive of the LNT model and reject the threshold dose-response model. In fact, very early in its deliberations one of the Panel members, Tracy Sonneborne, read into the transcript records a common set of beliefs held by those NAS Genetics Panel members on the issue of radiation and dose-response (Calabrese 2015). He claimed that all radiation-induced damage was cumulative, non-repairable, and irreversible, and as a result, would lead to an LNT dose response down to a single ionization. That is, there was no escape from there being a harmful effect at any level of exposure, regardless of how low. When Sonneborne read this radiation genetics belief mantra into the record, there was no debate, and it was uniformly

accepted. Yet, the issue of dose response at the time was very controversial and should have been debated. However, as the Panel was composed of only those with a single viewpoint, there was no debate. This was a very significant feature of this NAS Panel. It showed profound bias toward a particular outcome, failing in the Panel's public responsibility for honest and objective evaluation.

Even before Sonneborne read his radiation genetics mantra into the record, at the very first meeting in November of 1955, a Panel member, James V. Neel, provided a report to the Panel concerning a 10-year study that he directed on the effects of the atomic bombs in Japan on the occurrence of birth defects in the offspring of adults that were exposed to radiation (Neel and Schull 1956). The research of Neel was quite massive under the direction of the US NAS with the cooperation of both the US and Japanese scientists. This 10-year study followed 75,000 offspring, testing for all sorts of genetic anomalies. What emerged in the data was no evidence of radiation-related genetic effects. Neel offered the newly completed study to the Panel. Even though there was strong support voiced by James Crow and Tracey Sonneborne for the use of human data, Hermann Muller stood up and strongly challenged the use of the atomic bomb data of Neel, claiming that the negative findings that they showed were illusionary (Calabrese 2020b). This study, asserted Muller, should not have any scientific standing, and therefore should not be reviewed. So powerful was the position and personality of Muller that the Genetics Panel, which was created to evaluate potential risks in humans, decided not to evaluate the 10-year human genetics study from Japan. Instead, the Panel derived its views from the discredited Delta Uphoff fruit fly studies.

It is hard to believe that the NAS would base their recommendations on improperly designed and flawed fruit fly studies rather than upon the major human epidemiologic investigations led by Neel, yet this is what happened. Now this story gets even more bizarre. Since the Panel had quickly determined that the dose response was linear, there was very little for it to do. Yet, they had enough money in their budget for five or six meetings. Thus, Weaver felt that he needed to give some "make work" projects to the Panel to fill in the time and have their meetings. He challenged the 12 Panel geneticists to estimate the number of birth defects that would occur in the US population from radiation under various exposure scenarios and to provide detailed written reports within one month (Calabrese 2015, 2019a). Of the 12 geneticists on the Panel, three refused the exercise due to too much uncertainty. However, nine provided detailed written reports. When these evaluations were turned in, it became clear to Professor James Crow, who was organizing this information, that there was very little agreement amongst the geneticists and a massive uncertainty for most of them. He realized that if the Panel could not agree amongst themselves in terms of what might be the extent of potential radiation risks at various doses, then how could the public ever take seriously any recommendations that the Panel might offer? He informed Weaver that this assignment was a poor idea and created serious problems. So, on his own, Crow removed the three most divergent estimates. The actions of Crow resulted in reducing the variability from many thousands-fold down to 750 (Calabrese 2015, 2019a). This was still considered far too great to have any credibility with the general public and a decision was made to lower it further to 100 without any documentation, a simple fiat (Calabrese 2015, 2019a).

Making the situation worse is that when the Panel published their findings in the journal *Science,* it was stated that of the 12 geneticists on the Panel, six took up the challenge to estimate what risks might occur within the population with a certain level of radiation exposure (NAS/NRC 1956). However, the record shows that nine geneticists made detailed written estimates (Calabrese 2015, 2019a). This means that the write-up in the *Science* journal (as well as in the Panel's Report to the Public) reflected a deliberate misrepresentation of the research record by the removal of these three divergent estimates and hiding those estimates. This is an example of scientific misconduct because one cannot alter the research record. This was hidden from the scientific community and never exposed until very recently (Calabrese 2019a). Thus, the NAS Genetics Panel not only refused to evaluate this vast atomic bomb study of Neel, basing their evaluations on the flawed fruit fly studies, but they then misrepresented the research record concerning the degree of variability and uncertainty amongst the Panel members when it came to estimating risks from radiation exposure.

It has also been recently revealed that the NAS Report to the Public by the Panel was never written, reviewed, or approved by the Panel and contained serious errors (Calabrese and Giordano 2022). Yet, the NAS asserted that this report was in fact representative of the Panel views and approved by panel members.

We therefore see a wide range of mistakes, errors, misinformation and lies, and other forms of deception by the US NAS Genetics Panel. Yet, this Report was viewed as being done by a "dream team" of radiation genetics and that society could rely upon their judgments. The entire process was deceptive and yet the recommendations came to have a profound impact on radiation and chemical risk assessment in the U.S. and worldwide. The recommendations became the basis for the emission standards from U.S. nuclear power plants that became operational in 1961. The recommendation to switch from a threshold to a linear dose-response by the U.S. government was based upon the recommendation of this Panel (Calabrese 2023; Calabrese and Selby 2023), The fact that this Panel challenged the moral leadership of the AEC led Eisenhower to remove radiation risk assessment from the AEC and to place it into a newly created federal organization called the Federal Radiation Council (FRC). The FRC became ideologically supportive of the LNT model and eventually became incorporated within the US EPA. The newly created FRC carried forth their LNT biases that were created in the 1950s under the leadership of Bronk. This created a scientific revolution within U.S. regulatory agencies that spread throughout the world based upon stacking the deck of the NAS Genetics Panel membership that led to the adoption of the LNT dose-response model for cancer risk assessment.

Part 5: Cancer cover-up/flawed studies: More corruption in US government science/academic

The Russell story

In 1956, William L Russell, a radiation geneticist researcher at the Oak Ridge National Laboratory (ORNL), a United States Department of Energy (US DOE) facility, initiated a large study on the effects of radiation on lifespan and cancer incidence in mice. The study evaluated the effects of a large dose of x-rays on the offspring of male mice that were acutely exposed. There was a high expectation that the radiation would decrease lifespan and increase cancer and leukemia incidence; to the shock of the research team, there were no treatment effects seen for these endpoints. This was a major finding and sure to impact the debate over the nature of the dose response in the low-dose zone and cancer risk assessment. However, an unusual thing happened, that is, Russell suppressed the findings. He kept the results quiet, not publishing the findings nor informing his colleagues on the various NAS and other committees (e.g., Federal Radiation Council (FRC)) on which he served. One of those individuals who knew about this study was Arthur Upton, a famous radiation cancer researcher who would become director of the US National Cancer Institute (NCI) and chairman of two NAS radiation committees (Biological Effects of Ionizing Radiation (BEIR) III and V). Upton was also the head of pathology at the ORNL during the time that the Russell study was undertaken and was responsible for the pathological evaluations. Even though this study was completed toward the end of 1959, some 34 years later, a court case occurred in the UK concerning the effects of radiation on the offspring of nuclear power plant worker parents. The nuclear industry was being sued by the parents of affected children and they hired Upton, then a professor at New York University, to consult on this case as a testifying expert. During this process, Upton recognized the similarities between the research done under Russell's direction from 1956 to 1959 and the points of dispute in the UK case. He called Russell and explained that he wanted Russell to make the long-hidden data now available and to meet with the British defense team, including the lawyers and the technical people as soon as possible. Russell agreed and a team from the UK and Upton traveled to ORNL to meet with Russell. An arrangement was made to have a member of the Russell staff (i.e., Paul Selby) become a testifying expert at the court case along with Upton. Russell would publish the now 34-year-old data and submit it to a very prestigious journal in time for the Upton testimony. The paper was submitted for publication to the journal *Mutation Research*, on the very day that Upton would start his testimony in the UK court case (Cosgrove et al. 1993; Calabrese and Selby 2022). This paper was subsequently accepted and published. This paper and the related testimony had a significant impact on the court case that was ultimately decided in favor of the defense.

This episode escaped detection within the scientific and regulatory communities despite its controversial nature and significance. However, about two years ago in conversations with Paul Selby, I learned of the William Russell cover-up story. Of particular importance to the LNT story is that the Russell findings passed peer review 34 years after the study was completed. That is quite a tribute to the quality of the research. That no effect on longevity and any type of cancer was seen was surely a very significant observation and needed to be shared with the scientific community. Yet, why didn't Russell attempt to publish these findings soon after the research had been

completed? Russell addressed this issue in comments at the time the paper was published. He indicated that their findings were substantial, but he believed the public could not properly process such scientific information. He felt these findings would provide the public with a type of false sense of security (Calabrese and Selby 2022). Therefore, he decided not to publish these findings even though he worked for a U.S. federal agency, using tax dollars to fund his research. This story has substantial ethical as well as risk assessment implications. The actions of Russell would likely have had a strong impact on the NAS Genetics Panel as well as on the FRC for which Russell was also an advisor.

The Edward B. Lewis story

At approximately the same time as the Russell cancer study was ongoing, a paper was published in *Science* by Lewis (1957), a *Drosophila* geneticist at the California Institute of Technology (CalTech). His biology department chair, George Beadle, a member of the NAS Genetics Panel and future Nobel Prize winner himself, attempted to inspire his faculty to explore the health implications of above-ground atmospheric nuclear tests in Nevada (Calabrese 2021). Lewis took up this challenge and developed a detailed assessment of the public health impacts even though he was not trained in biostatistics, epidemiology, cancer research, leukemia, radiation dosimetry, and other relevant areas. Nonetheless, Lewis (1957) would claim that exposure to ionizing radiation could induce leukemia in multiple populations including (1) those physicians who are radiologists, (2) patients with an extreme arthritic condition called ankylosing spondylitis where there were heavy exposures to the spine from radiation, (3) children with enlarged thymus conditions who were treated with x-rays to shrink the thymus, and (4) amongst the survivors of the atomic bomb explosions in Japan. Lewis integrated the information from these four different groups and applied it within a dose-response cancer risk assessment framework. He concluded that the risk followed a linear dose-response relationship and that there was no safe level of exposure. He asserted that a LNT rather than a threshold model should be used to estimate cancer risk assessment.

Beadle got Lewis to share his manuscript with the members of the NAS Genetics Panel, including Muller, Neel, and others. After receiving their comments, he published the manuscript in the journal *Science* (Lewis 1957). Of particular note was that one of the members of the NAS Genetics Panel, Bentley Glass, was one of only six senior editors of the journal *Science* at that time and most likely played a significant role in overseeing the evaluation, management, and acceptance of the Lewis paper. When Lewis's paper was published, the editor-in-chief wrote a glowing editorial, pointing out its significant public health and policy implications (DuShane 1957). Since the editor-in-chief had no expertise in this area, it is quite possible that the editorial was ghostwritten by Glass. So significant was the publication of Lewis that within a week it was publicly debated in the major national television program in the U.S. called *Meet the Press*. One week after that, Lewis was called to testify to the U.S. Congress and only a week after testifying, *Life Magazine* had a special issue on radiation, highlighting the work of Lewis and including photographs of him. The Lewis paper would come to have a significant impact on public policy in the U.S., expanding greatly the debate to focus on cancer and leukemia in addition to birth defects. Lewis was appointed to a variety of major committees and influenced the National Committee for Radiation Protection (NCRP) to recommend the LNT model for cancer risk assessment in 1958, the first time this had ever been done.

Even though the paper of Lewis was highly impactful, within the past several years it has come under considerable scrutiny, something that should have occurred during the peer-review process, if there was one at *Science*. What the new evaluation of the Lewis paper shows is that in each of the four cases that he studied, he made critical errors that discredit his conclusions (Calabrese 2021). For example, in the case of ankylosing spondylitis, the experts publishing the research that Lewis cited emphatically stated that their work should not be used for low-dose cancer risk assessment since the doses to the bone marrow were simply far too high. Yet, this is exactly what Lewis did. Lewis never shared with the readership of the journal *Science* that in fact, this was the position of the authors themselves. When it comes to the enlarged thymus, the studies he cited showed no increased risk of leukemia, yet he would use that study to support his low-dose risk assessment application. In the case of the radiologists, Lewis made further errors of judgment when he used very old data from the 1910–1920s with career exposures as high as 2100R. This would be considered a massively high dose with no realistic chance to extrapolate down to lower levels. Subsequent studies by leading epidemiologists studying radiologists showed that the risks were far less and supported a threshold model. Concerning

the Japanese atomic bomb leukemia data, one might think that Lewis' LNT perspective would be finally supported, but this was not the case either. It is now known that Lewis camouflaged the data, inappropriately lumping low and higher doses together to mask apparent protective effects from exposure to radiation in the lower dose zones. This is a common sleight-of-hand trick that has been commonly employed to generate risks where they don't exist, in fact, just the opposite.

In any case, this modern reevaluation of the Lewis data indicates that for each of the areas that he used to build his case, his analysis was inappropriate and led to a flawed study. This assessment of Lewis' paper indicates that his work is discredited and should not have been used. If the journal *Science* had actually conducted an appropriate peer-review of the Lewis paper, it most likely never would have been published.

The findings as reported here concerning the actions of Russell and Lewis at this critical time of risk assessment history indicate powerful biases as well as Lewis' lack of competence. When combining these converging stories, what we find is that these actions came to have a significant impact on the field and inappropriately contributed to the adoption of LNT and current risk assessment policies.

Part 6: A second cover-up from William Russell changes the course of cancer risk assessment

Radiation genetics and its application to risk assessment were dominated by research with the fruit fly as led by Hermann Muller and his colleagues. However, it becomes obvious that when extrapolating results from animal studies to humans, one does not feel very comfortable relying upon data from an insect. Most want a mammalian model for human risk assessment. This was recognized by leaders in the field and there was a decision to add a mammalian model to the radiation risk assessment mix. The person leading this research direction was William L. Russell, a mouse geneticist, who was hired in 1947 by the AEC at ORNL. Russell had an idea for how to make the mouse provide highly relevant data for human risk assessment, but it was complex and was going to require a major investment and many millions of mice. The Russell approach was conceptually clear but difficult to carry out. The Russell approach was to study induced changes in recessive genes that could be detected in the next generation of animals. The Russell research team included Liane Russell, wife of William Russell, and they had figured out an ingenious approach that would require a large number of mice and take perhaps a decade or longer to establish clear answers concerning the effects of low doses of radiation and chemical carcinogens in the mouse model. By 1951, the Russells reported their first major findings of clearly detected radiation-induced mutations with their recessive genes in the next generation. Equally important, their mouse model was approximately 15 times more sensitive than Muller's fruit fly. These findings suggested that the future of low-dose research was now shifting from the earlier work with the fruit fly into the new mammalian age with Russell and ORNL taking the lead.

Another major development with William Russell took place toward the end of the 1950s. This time Russell proved to be on the cutting edge of discovery. Up until then, the field of radiation genetics was of the firm belief that there was no such thing as a capacity to repair damaged DNA. What the geneticists believed was that all damage was harmful, none of the damage could be repaired, that damage was irreversible, and any exposure no matter how small led to a linear dose-response. However, as a result of changes in some experimental protocols, Russell made the unexpected discovery that the mouse spermatogonia and oocytes could repair damaged DNA at low radiation dose rates. What this meant is that if you gave a very large dose rate of radiation, the amount might be so high that it would overwhelm the capacity to repair any induced damage. However, if you took the same total dose and spread it out over a longer period (i.e., lower dose rate) such that you didn't overwhelm the repair capacity of the cell then the damage could be repaired. That would suggest the existence of a threshold rather than a LNT model. These findings of Russell were striking but also threatening to geneticists, such as Muller, as Russell, who had turned the field upside down. Russell reported his major findings in *Science* in December of 1958 (Russell et al. 1958). The data showed that the female mouse oocytes exhibited a threshold response. In the case of the male, there was substantial repair taking place, but Russell had yet to establish a threshold.

The work of Russell would become dominant in the field and as he expected it took millions and millions of mice to establish the reliability of these findings. In fact, by 1970 Russell had utilized over 5 million mice in his research at the ORNL. These findings were so influential that the NAS Panel in 1960 acknowledged that they had been wrong for an entire generation in proclaiming that there was no such thing as repair and that the dose rate was highly

important. In fact, Russell was nominated several times for the Nobel Prize for their discoveries. Russell was challenging the field as he showed that radiation damage did not have to accumulate, could be repaired, was reversible, and, in fact, a threshold model was a realistic expectation.

The question that emerged was how would Russell's data affect the risk assessment process. In 1970, the Department of Health, Education, and Welfare (HEW) of the US government got the NAS to reformulate another committee to evaluate the health effects of ionizing radiation. This was based upon much controversy related to assessments by two scientists at the DOE Lawrence Livermore Laboratory in California by the names of John Goffman and Arthur Tamplin who were claiming that low doses of radiation that were associated with emissions from nuclear power plants could be ultimately responsible for up to 10% of human cancers and leukemias in the US.

In the course of the HEW evaluation, the Russell data, which had been strengthened during the 1960s, came to take center stage. What was decided was that DNA repair was extremely important and that the observed threshold in the female mouse became better documented. However, Russell had still not established a threshold in the male. This led the Biological Effects of Ionizing Radiation (BEIR) I Genetics Committee to reaffirm the 1956 recommendation of the earlier NAS Genetics Panel to support the LNT dose-response model for risk assessment. This recommendation was offered in 1972 to the newly formed US EPA. Several years later, the EPA acknowledged the recommendation of this Committee, adopted the LNT model and applied it to chemical carcinogens as well. The Russell findings were crucial because the limits of epidemiology did not allow confident extrapolation into the low-dose region (and still don't). However, with massive research Russell along with its being mechanistically oriented, provided the capacity to test whether the linear or threshold model might be superior. The BEIR I Genetics Committee concluded, at least tentatively, to stay with the LNT model based on a Precautionary Principle guiding philosophy which in simple terms means that it is better to be safe than sorry.

These developments showed that the investment of the US government in the ideas of William Russell proved to be highly successful. However, something significant happened some 25 years later that involved the discovery of an error in the Russell control group data by a long-time researcher with the Russells, Paul Selby. Selby had been asked by the Russells in 1994 to computerize their data so that none would be lost and could be easily retrievable and evaluated. As Selby set forth to organize the Russells' data, he inadvertently came across a large 1955 study in which there was a series of gene cluster mutations that the Russells never reported. In addition to that, Selby was aware of a similar sort of incident in 1986 with another study in which cluster mutations were also not reported. Selby was aware of two papers that Liane Russell had written on the topic, one in 1964 and another in 1979. These episodes merged and troubled Selby. Selby went to authorities within the US DOE and explained these anomalies. They encouraged him to continue to evaluate the Russell data looking for such other gene cluster anomalies. He followed their instructions and found multiple other examples. In fact, in the very first study of Russell in 1951, Selby found 90 gene cluster mutations, none of which were reported by the Russells. This and other such examples of not reported gene mutations were very concerning to the superiors within the DOE. It led to follow-up hearings in which an independent expert panel evaluated the claims of Selby and questioned the Russells. The bottom line in this evaluation is that the external panel concluded that Selby was right, that the Russells needed to officially correct the research record in the peer-reviewed literature. The Russells published their corrections in two papers, one in 1996 and the other in 1997 (Russell and Russell 1996; Selby and Calabrese 2023). The paper in 1996 indicated that their control group was an error by 120% (Russell and Russell 1996; Selby and Calabrese 2023). Selby suggested that the error was even larger based on his modeling activities. Despite this acknowledgment of such a massive error, there is no evidence that either the NAS or the EPA has reevaluated what this meant for their risk assessment predictions. However, in 2016, I evaluated the Russell-Selby dispute and its risk assessment conclusions and applied the findings back to what it would have meant to the NAS BEIR I Committee of 1972. If the correction had been given to the 1972 Committee, it would have yielded a threshold dose response for both the males and females (Calabrese 2017b, 2017c). It would not have supported the LNT model that was adopted by EPA. The discovery of Selby therefore proved to be a seminal event in the history of risk assessment since the Russell research had become so central and influential.

Upon further reflection and evaluation, if the Russells had not hidden their cluster mutation data starting in 1951, the 15-fold enhanced susceptibility of

the mice compared to the fruit fly would not have occurred. By hiding the data, as the Russells did, the Russells received much acclaim and profoundly greater resources and funding from the US federal government—all very self-serving. The failure of the Russells to report their gene cluster mutation data over their career is tremendously troubling as it led to profound impacts and overestimations of risk in hereditary and cancer risk assessments, serving to inject great fear into the population, markedly affecting technology developments, medical treatments, costs of clean-up activities, and lifestyle decisions that were ultimately largely driven by their self-interest and career ambitions.

Part 7: US NAS and *Science* Journal: How they promoted a fraudulent LNT model

US NAS

The US NAS has considerable stature and serves as a vehicle to bring together various experts to advise the country on a very wide range of issues of national importance. In fact, I have had the honor of serving on multiple NAS committees, including the Air Cabin Safety Committee that voted to ban smoking on airplane flights in the late 1980s. Nonetheless, the NAS has a history of some important embarrassments and failures. One of these is its role in getting the LNT adopted by US regulatory agencies such as the EPA and then indirectly in many other countries.

The most glaring failures were the actions of the NAS Biological Effects of Atomic Radiation (BEAR) I Genetics Panel in 1956, starting with a bizarre and improper relationship between the RF and NAS. That is, the NAS president Detlev Bronk also was president at that time of the Rockefeller Institute for Medical Sciences, soon to become the Rockefeller University. Bronk was also a longstanding member of the powerful RF. Thus, the Rockefeller organization and the NAS were so tightly connected that they were biologically inseparable, kind of like Siamese twins. Being highly inseparable administratively and politically, the RF and NAS nurtured each other's interests, possibly at the expense of the country it was supposed to be serving.

Bronk started the corruption by creating a Genetics Panel and then appointing the non-geneticist Warren Weaver, director of research of the RF, to chair it. Bronk knew that by freeing the geneticists from the constraints of the Medical Panel and giving them their own independent Genetics Panel for the first time he could create a risk assessment revolution that would lead to the acceptance of LNT. The appointment of Weaver removed any possible independence of the Panel, allowing Bronk to determine its eventual outcome in a hidden but powerful manner. These actions were highly manipulative, and unethical, and also challenged the ethics of Weaver, who should have turned down the assignment but failed to do so, as it placed him in an impossible and compromised position. Brock and Weaver then teamed up to make sure that the LNT would be adopted by stacking the Panel with highly biased LNT supporters. These combined actions were inappropriate and reflected irresponsible public leadership. There were no administrative controls over the actions of Bronk as he did what he pleased, assuring a predetermined outcome, lacking ethical principles in these decisions.

On the very first day that the NAS Genetics Panel convened in November 1955, the panel refused to review a just completed 10-year massive study on the effects of the atomic bombings in Japan on the occurrence of birth defects in 75,000 offspring. Hermann Muller, who was the intellectual and emotional leader of the Panel, would insult the study and its director, Neel, also a Panel member, calling these findings illusionary. Thus, literally from day one, the NAS Genetics Panel was determined to go linear. The Panel then defaulted to the use of the Stern/Uphoff fruit fly research to guide their human risk assessment recommendations. As it is now well known the Stern/Uphoff research was fundamentally flawed, could not address the question it was supposed to answer, and had numerous other discrediting features.

There were also other serious problems with the actions of the Genetics Panel. The entire Panel acknowledged the belief system of the radiation geneticist mantra that all radiation exposure was harmful damage, could not be repaired, was irreversible, and led to a linear dose-response, having no discussion or debate on this critical issue. The Panel then participated in a process that resulted in altering the scientific record to mask their striking risk assessment disagreements. Why? They knew that if the public could see both their profound lack of fundamental understanding of risk assessment and their massive disagreements any Panel recommendations would never be accepted. So, they decided to alter their research record, publishing their falsified findings in the journal *Science* (NAS/NRC 1956). Furthermore, the NAS Genetics Panel never read, reviewed, or approved their own NAS "Report to the Public" which also contained falsified data as well as important errors (Calabrese and Giordano 2022).

Bronk indicated that the Report to the Public reflected the views and opinions of the Panel, another of his public deceptions. The Panel itself was also lacking in the courage to correct this outrageous process for fear of offending their research grant supporter, the RF. Despite these unethical activities, the NAS Genetics Panel changed the world, eventually making LNT national policy a corrupt process. Once the above story was finally clarified in recent years, it was then shared with the editor of the journal *Science*, Marcia McNutt, requesting that she retract the fraudulent 1956 NAS Genetics Panel article in *Science*. She refused to do so, claiming that all panel members were dead and could not defend themselves, thereby sustaining and, in effect, rewarding scientific misconduct. During the time McNutt would make this decision on the *Science* paper retraction request, she was a finalist for the position of the president of the NAS with her name posted on the NAS website. She somehow did not have the presence of mind to recuse herself from this decision, a very troubling sign for one in public leadership. Later, as president of the NAS, she was asked to retract the fraudulent NAS "Report to the Public." Again, she refused to do so saying in writing that "she had no dog in this fight." If not her, then who? McNutt, as editor-in-chief at *Science* and later as president of the NAS, had two opportunities to correct major historical errors and refused to do so, failing terribly in her public leadership, yet with no accountability and answerable only to herself.

Science journal

Science journal, like the US NAS, has a long history of service to the scientific community. It wields considerable power due to the size of the Association for the Advancement of American Science (AAAS) society that it serves and the significance of its leadership. However, as was the case with the US NAS, *Science* has played a manipulative and highly biased role in promoting LNT, as seen by its publication of non-peer-reviewed papers, publication of falsified data, and use of inappropriate editorial endorsement to promote now discredited research supporting LNT. Four examples will be briefly summarized.

Example # 1: Muller's Nobel Prize paper

On 1927 July 22 *Science* published Muller's Nobel Prize paper claiming that X-rays produced gene mutations. This groundbreaking paper contained no data, being only a discussion of two experiments, with his third experiment not yet underway. The paper also failed to acknowledge any other published research on the topic, especially a six-month earlier paper that provided the first experimental evidence of radiation-induced gene mutation. The actions of *Science* permitted Muller to avoid peer-review of his research methods and related materials and data to gain worldwide acclaim, due to this journal's reputation. The next year, Muller would publish his findings in a non-peer-reviewed conference proceeding that again lacked methods and materials and cited no references. Furthermore, it has now been learned that Muller in October 1927, had a type of "quid pro quo" arrangement with the owner/editor of the journal *Science*, James McKean Cattell, to identify excellent papers from the 5th Genetics Congress (September 1927), contact these authors, encourage them to submit their manuscript to another journal Cattell owned/edited, the *American Naturalist*, and Muller would oversee the reviewing and make the editorial decisions on acceptance. This is a massive amount of work, yet Muller agreed to do it. Why? One obvious thought is that it was a type of "payback" for Cattell granting him publication in *Science* without peer review, giving him primacy in this most important topic, and allowing him to out-compete the competition that was only a few months behind. In the case of Muller, *Science* showed unfair favoritism, and in so doing, corrupted the scientific process.

Muller's gene mutation conclusion was challenged since he had no evidence supporting that he had induced gene mutation, his major claim. As would later be shown, Muller had not induced gene mutation, confused an observation with a mechanism, and mostly induced deletions or holes in the fruit fly chromosomes. In fact, in 1956, Muller acknowledged these very facts but only ten years after receiving the Nobel Prize that he did not deserve. Such conclusions have been affirmed with modern DNA nucleotide evaluations and acknowledged by his closest supporters. These actions by *Science* gave Muller and LNT major visibility, credibility, and undeserved massive momentum, doing a great disservice to science and society.

Example # 2: The failure of the Stern and Uphoff studies

As previously noted, there were major weaknesses in the Curt Stern and Delta Uphoff studies of the Manhattan Project at the University of Rochester. Despite these discrediting limitations, *Science* journal published their paper without peer review, with no inclusion of methods, materials, and other necessary data. It was a one-page summary of the Manhattan

Project's five fruit fly experiments. As with the Muller *Science* paper, the Stern and Uphoff report had an important and undeserved influence due to its publication within *Science*. The numerous limitations of this paper were clearly implied by the final statement of the authors in which they pledged to publish a detailed paper for the scientific community with proper methods, materials, and other related information. Stern and Uphoff never followed through with this promise. However, the significance of having this non-peer-reviewed, one-page note, published in *Science* made all the difference as it was promoted by the radiation genetics community and became the key paper for advancing support for the LNT hypothesis.

Example # 3: The BEAR Genetics Panel: Science publication with data falsification

Science published a non-peer review paper of the 1956 NAS BEAR I Genetics Panel which contained falsified data that provided support for the LNT model. As noted earlier, the failure of the editor of *Science*, Marcia McNutt, to retract a paper that included falsified data, permits *Science* to have a paper under its name to remain in the open literature that misrepresents the research record and misleads the readership. These actions represent an abuse of authority, and poor judgment by then editor-in-chief McNutt, suggesting that the journal displays an ideological rather than scientific leadership. The paper of the Genetics Panel has been highly significant since it provided the major transition from the threshold to the LNT model, the scientific basis for the emission standards from nuclear power plants, and the foundation for the acceptance of LNT by regulatory agencies worldwide.

Example # 4: The Edward B. Lewis radiation and leukemia paper

In 1957, Edward Lewis published what would be considered the most significant paper on cancer risk assessment. The Lewis paper was particularly important because it made the transition from hereditary to cancer risk and this would change the direction of the field to the present time. The Lewis paper gained prominence not just because it was published in *Science* but because it received an overwhelmingly positive endorsement by the editor-in-chief of *Science*. Such endorsements are rare, and when they are received, make a big difference. The journal *Science* abdicated its professional responsibilities with the publication of the Lewis paper since it has now been shown to have profound deficiencies and biases that strongly undercut its scientific value. The Lewis paper should have been denied editorial endorsement and never been published in the *Science* journal due to its significant deficiencies. However, *Science* was strongly influenced by one of its six senior editors and former student of Muller, Bentley Glass, and it is believed that Glass guided the Lewis paper through the publication process, obtaining the editorial endorsement, which resulted in great exposure for Lewis and the paper. In addition, Glass (1957) would soon publish his paper in *Science* on a similar topic, reinforcing the ideological conclusions of the Lewis paper. The actions of the *Science* editorial board were irresponsible, but due to its power and influence promoted significantly the agenda of Lewis and changed the risk assessment debate.

A close look at the impact of the US NAS and *Science* on the adoption of LNT therefore reveals that these organizations that are supposed to be fair-minded vehicles in the search for truth and application of the scientific method often descend into the world of ideological science and fail in their important public responsibilities. When these organizations are challenged to correct the record, they display unbridled arrogance as reflected in an unwillingness to acknowledge errors, limitations, willful manipulations, and gross mistakes. As demonstrated in this paper, these ideological biases and misuses of authority have led to major changes in public policy that continue to affect society with vast implications. What emerges from this evaluation is that the editors of *Science* and presidents of the NAS need to be held accountable for their actions and decisions, something that has long been absent.

Part 8: What is the future of cancer risk assessment?

The LNT model is one that originated with the assumption by Muller that the genome is very stable and that whatever mutations are produced by background radiation and other possible causes are not repaired. Muller believed that humans, and, all living creatures, were victims, of a complex gene mutation-based evolutionary process. Science today tells us that he was wrong, grossly wrong, and so were his predictions of harm using the LNT model.

Contrary to what Muller assumed, science has learned that humans have genomes very susceptible to mutational damage but that we have evolved an amazingly robust, redundant, and high capacity to repair that damage. When the LNT single-hit model was created, those who designed it failed to include a capacity

to repair genetic damage. Why? Because they were following the assumptions and uncompromisingly rigid beliefs of Muller. This model was wrong from the start. Unfortunately, this incorrect model was passed on to regulatory agencies such as the EPA some four decades later without corrections or updates and used to base their governmental environmental and occupational health standards.

Society became victimized by a Muller-led fear-driven process, that claimed all doses of ionizing radiation were harmful and that even a single ionization induced by radiation could cause harm. This idea was applied to chemical carcinogens, with similar assumptions, that a single chemical or fiber could cause cancer, creating widespread chemophobias that have induced crippling fear at all levels of society, from parents to presidents. It was from such distortions of biological reality and evolutionary history that the Precautionary Principle was borne, a principle based on fear, rather than on biology and evolutionary science.

We have learned that Muller was first interested in learning about the mechanisms of evolution, which was thought to be via gene mutation. Soon after his groundbreaking paper in 1927, Muller concluded that background radiation was one of the causes of evolution. However, Muller would be proven wrong again as the most dominating cause of evolution is our metabolism which induces millions of mutations per day in each cell, with 99.99999% being repaired each day. If our repair systems were not so exceptionally good, life would not exist. Our metabolism produces about 200 million times more genetic damage events per cell per day than that induced by background radiation. There is no contest between the two. What this means is that our body is our biggest enemy; it also means that it is also our best friend. The body's great repair mechanisms evolved not to prevent and repair damage from background radiation but to fix the damage that our metabolism induces each day. Thus, the body's repair systems are designed by nature to protect our bodies against ourselves, with background radiation being a very tiny and insignificant factor.

We therefore have learned that the experts got the radiation and chemical mutation idea wrong from the start but they convinced many that they were correct and created debilitating fear in the population at the same time. We also learned that one of the reasons that these great scientists created such fears was to advance their careers and to get a constant flow of government grant monies. This is clear in the letter exchanges of the members of the US NAS Genetics Panel. Some explicitly stated that it was acceptable to stretch the truth (i.e., frighten people) to ensure continued and larger funding. These thoughts were exchanged by leaders in the 1950s and it has not changed in the last 70 years. We also know that politicians act the same way. It is easy to scare people when one talks about birth defects and cancer as these are easy and emotional targets.

It has been very troubling that regulatory agencies worldwide have accepted the fraudulent story of cancer risk assessment as started by Muller and pushed forward from one generation of scientists to the next. Regulatory agencies are supposed to base their decisions on scientific evidence and science should be self-correcting. However, the EPA and other regulatory agencies worldwide have shown that their science is often not self-correcting; their actions are more about creating fear and getting money flowing in their direction. In its more than 50 years of existence, the US EPA has never attempted to discover and report the errors, lies, deceptions, and distortions that its regulations have been based on. What does that tell us about this agency? … First of all, they are not truth seekers, but first and foremost, a bureaucracy uninterested in correcting the scientific record within the US. The worst part is that these actions merged with practices seen with the US NAS and the journal *Science* editorial leadership, where they have often failed in their jobs to honestly serve the welfare of society, rather than their own self-interest or ideology.

What is the road forward? The first step is to recognize biological reality, that is, humans are not victims, but evolutionary survivors. Humans are tough and resilient and when damaged, repair that damage automatically, as these protective processes are built into cells by evolutionary processes. Humans are not the victims that regulatory agencies would like us to believe. While there are innumerable threats that society faces, the biggest daily personal enemy is ourselves, literally our bodies, which generate trillions of adverse genetic events each day that must be repaired. It is this continuous oxidative damage challenge that we face from our bodies each second, each day that makes us age, get wrinkly skin, and otherwise get old. While people cannot live forever, humans can make far better efforts to extend the health span of our lives. This is not accomplished by avoiding stress but by exposing oneself to a wide range of low-level stresses each day to activate the plethora of adaptive mechanisms that we have been endowed by nature to protect ourselves and optimize health.

Environmental regulation is important but it must be science-based, not fear-driven. Society is currently being victimized by a public health-based Precautionary Principle that is fear rather than science-based. This public health Precautionary Principle needs to be replaced with an Evolutionary Based Precautionary Principle (EBPP) that sees humans as endowed with the capacity to protect, repair, adapt, and even improve their health when modestly stressed. One can see how the US EPA has lost its way: the EPA states that "the purpose of a risk assessment is to identify risk (harm, adverse effect, etc.), effects that appear to be adaptive, non-adverse, or beneficial may not be mentioned" (EPA 2004; Calabrese 2006). The wiser and more inclusive goal would be to focus on health assessment and its optimization and to ensure that adaptive and beneficial responses become a central feature of the mission to protect and advance human health.

The continued reliance on LNT for cancer risk assessment hurts society for many reasons. It provides grossly distorted cancer risk estimates that are given to those involved with making risk management decisions. This will almost certainly result in poor policy and resource decisions. This results in illusionary public health protection, a profound waste of limited public resources for no benefit, resulting in "stealing" resources from where they could be properly used to counterproductive areas. The LNT policy has a long history of adversely affecting technical innovations in areas critical to society. It also affects medical practices that can adversely affect patient options and success, the lifestyle decisions of adults, how they raise their children, and what they are taught in schools. The corruption of LNT and its underlying Precautionary Principle philosophy is deep-seated and transforms many aspects of personal and societal life. Even though EPA "science" is not self-correcting, it is hoped that society will convince their elected officials to motivate these self-serving regulatory agencies to revert to first thinking like scientists. This will not be easy since many elected officials, like their regulatory agency counterparts, also are experts in manipulating society with their fear-based strategies and tactics. Nonetheless, successful countries will be those that adopt an evolutionary science-based precautionary principle rather than the fear-driven public health precautionary principle that is damaging society and countless personal lives.

Conclusion

The historical foundations of cancer risk assessment were based on fundamental scientific errors that were never corrected, all within the framework of an extraordinary appeal to the authority of the radiation genetics community, led by Hermann J. Muller. Even though these individuals were greatly talented and accomplished, they were driven by ideological and self-serving professional biases that would lead to both falsifications of the research record and suppression of key scientific findings, all to establish the LNT model for hereditary and cancer risk assessment, replacing the threshold dose-response model. This troubling history has now been revealed in a long series of peer-reviewed publications by the author and summarized in a broad conversational manner in this Commentary. This troubling history remained hidden from regulatory agencies around the globe since its inception. These groups simply and uncritically accepted a flawed and corrupt history, assuming that it was accurate and reliable. Yet this path of historical ignorance led the US EPA, and other national regulatory agencies, to accept a dishonest foundation upon which to base and frame cancer risk assessment, terribly failing in their public service mission. This untenable situation has placed a continuing stranglehold on the actions of all regulatory agencies worldwide, improperly guiding its philosophies, policies, and practices to the present time.

Acknowledgments

EJC acknowledges longtime support from the US Air Force (AFOSR FA9550-19-1-0413) and ExxonMobil Foundation (S18200000000256).

Disclosure statement

Disclaimer

The views and conclusions contained herein are those of the author and should not be interpreted as necessarily representing policies or endorsement, either expressed or implied. Sponsors had no involvement in study design, collection, analysis, interpretation, writing, and decision to and where to submit for publication consideration.

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