CHAIRMAN Resource

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Attached please find two new papers on the history of the linear dose response and the role of the US National Academy of Sciences.

Sincerely,

Ed Calabrese

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LETTER TO THE EDITOR, NEWS AND VIEWS

An abuse of risk assessment: how regulatory agencies improperly adopted LNT for cancer risk assessment

Edward J. Calabrese

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Abstract The Genetics Panel of the National Academy of Sciences' Committee on Biological Effects of Atomic Radiation (BEAR) recommended the adoption of the linear dose–response model in 1956, abandoning the threshold dose–response for genetic risk assessments. This recommendation was quickly generalized to include somatic cells for cancer risk assessment and later was instrumental in the adoption of linearity for carcinogen risk assessment by the Environmental Protection Agency. The Genetics Panel failed to provide any scientific assessment to support this recommendation and refused to do so when later challenged by other leading scientists. Thus, the linearity model used in cancer risk assessment was based on ideology rather than science and originated with the recommendation of the NAS BEAR Committee Genetics Panel. Historical documentation in support of these conclusions is provided in the transcripts of the Panel meetings and in previously unexamined correspondence among Panel members.

Keywords Mutation · Linear non-threshold (LNT) · Risk assessment · Carcinogen · Threshold dose response · Ionizing radiation

Electronic supplementary material The online version of this article (doi:10.1007/s00204-015-1454-4) contains supplementary material, which is available to authorized users.

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The most significant event in the history of environmental risk assessment was the recommendation by the United States National Academy of Sciences (NAS), Biological Effects of Atomic Radiation (BEAR) Committee, Genetics Panel in 1956 to switch from a threshold to a linear dose–response model for the assessment of genomic mutation risk (Anonymous 1956; NAS/NRC 1956). Within a brief period of time, this recommendation became generalized to somatic cells by other governmental advisory committees and was eventually applied to cancer risk assessment. Although this linear dose–response paradigm was originally intended to be used for ionizing radiation, it would later be adopted by the US Environmental Protection Agency and directly applied to chemical carcinogens (Albert 1994; Calabrese 2013a, b), thereby affecting worldwide cancer risk assessment for the past several decades.

Given the significance of this action by the NAS BEAR I Committee, Genetics Panel and the long history of the threshold dose–response model in regulatory practice, I was interested in learning the answers to several key questions: how was this recommendation made, what was the nature of the debate, what were the persuasive and compelling arguments, and what were the roles played by various individuals on the Panel? I therefore obtained transcripts of the BEAR I Committee, Genetics Panel meetings in 1955 and 1956. It was a bit like reading the book after seeing the end of the movie. To my surprise, the BEAR I Committee, Genetics Panel was uniformly confident in their belief that linearity for genomic risk assessment was the correct perspective, while being arrogantly dismissive of both the threshold perspective and those who supported it. So dismissive of the alternative model was the Genetics Panel that it was never viewed as a debatable issue, nor was it ever debated. What a disappointment. I had so looked forward to retrospectively witnessing how the leading thinkers of

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their time confronted this seminal issue on dose–response, how they intellectually sparred with one another, and whose logic and facts helped carry the day for the linearity model. The NAS BEAR I Committee, Genetics Panel made the switch from a threshold to a linear dose–response risk assessment model by "proclamation," with no debate and without providing a detailed (or actually even any) evaluation, such as would be expected of any scientific advisory group—most certainly of one at the level of the National Academy of Sciences on such matters of national and international significance. In retrospect, this should not have been too surprising as I had documented in previous publications (Calabrese 2011a, b, 2012, 2013a, b) the inherent intellectual dishonesty of key leaders of the radiation genetics community, such as Curt Stern and Hermann Muller on the issue of threshold versus linear dose–response and how they successfully distorted the scientific record in order to achieve their goal of a linear dose–response for risk assessment. The linear dose–response recommendation by this Genetics Panel would be broadly extolled by leading media outlets on the day of its release as the most extensive assessment ever undertaken on the topic by a most prestigious group of American scientists. The National Academy of Sciences report was literally a front-page story in the New York Times with the linearity risk assessment framework leading the way.

Despite the widely acknowledged success of the BEAR I Committee, Genetics Panel in getting their message out to the scientific community, governmental bodies, and the public, the reports of the BEAR I Committee, Genetics Panel were eventually read by members of the scientific community. This resulted in a number of leading biologists challenging the Genetics Panel, demanding to know the scientific basis of the decision in favor of linearity. However, as noted above, the Genetics Panel had not undertaken such an assessment and was not in a position to explain their actions nor to defend a report that lacked a scientific foundation. Showing its disdain for those challenging this report, the Genetics Panel decided not to provide the information to the scientific community. This decision was rendered to the President of the National Academy of Sciences without any evidence of his objection. The adoption of the linear non-threshold (LNT) dose–response model by the National Academy of Sciences therefore was made without a scientific assessment and, of course, a refusal to provide one when challenged.

The recommendation to switch to a linear dose–response by the NAS BEAR I Committee, Genetics Panel, as announced to the world by leading media outlets, reflects an abdication of societal responsibility on a critical and enduring public health issue. This paper provides the first reporting of these actions in the history of the National Academy of Sciences and in governmental risk assessment practices for cancer. It reveals that current cancer risk assessment practices originated from an ideological set of beliefs from leading scientists rather than a scientific assessment. A fully documented assessment of this story is provided in the Supplementary Data section.

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Conflict of interest Author declares no conflict of interest.

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Supplementary Material

LNT'S FAILED HISTORY:
An Abdicated Responsibility - How the US NAS BEAR I Committee Genetics Panel Failed To Assess LNT Prior To Recommending Its Use by US Regulatory Agencies

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Abstract

The U.S. National Academy of Sciences (NAS) Biological Effects of Atomic Radiation (BEAR) I Genetics Panel report recommended a linear dose response to assess the risk of genomic mutation from ionizing radiation. This represented a major change assessing risks which had been based on a threshold dose response model. This recommendation was soon generalized to somatic injury and applied to cancer risk assessment for ionizing radiation and later for chemical carcinogens. An evaluation of the transcriptional records of the Genetics Panel, intra-panel correspondence and work products, reveals that the Panel failed to provide an assessment of which dose response model best characterized the effects of ionizing radiation on the genome. Lacking such an assessment, the recommendation for a linear model was based upon an assumption of the Panel.

The Panel's failure to assess the scientific basis of the dose response for ionizing radiation, while recommending strongly a switch to linearity, represents an abdication of responsibility. It led to a deliberately false public understanding that their risk assessment for ionizing radiation was based on "the most comprehensive effort" ever undertaken in the United States by a committee of outstanding scientists as characterized by a front page New York Times story (Leviero 1956) one day after the release of the Panel report (June 13, 1956) and similarly reported in other scientific and public venues.

Key Words: linearity, threshold, mutation, risk assessment, dose response, cancer

Introduction

The US NAS BEAR I Committee Genetics Panel in 1956 recommended that the risks associated with ionizing radiation to the human genome no longer be evaluated via the use of a threshold dose response model but with a linear at low dose model. This recommendation was quickly adopted by the scientific and regulatory communities and soon generalized to somatic cells for application to cancer risk assessment for ionizing radiation (Taylor 1960, 1963, 1965). Some two decades later the U.S. NAS Safe Drinking Water Committee (NAS 1977) relied upon this linearity at low dose recommendation for assessing risks of chemical carcinogens. In many respects, therefore, the report of the 1956 BEAR I Genetics Panel was the most influential advisory report ever published on risk assessment. The Genetics Panel published two reports, one as part of a general NAS document intended for the media and the general public (NAS/NRC 1956), while the other was a more technical paper published in the journal Science (Anonymous 1956a). The key conceptual conclusion of the Genetics Panel was that ionizing radiation induces genomic mutations which are nearly always harmful and the damage is irreversible, cumulative, and directly proportional to dose, such that there is no safe level of exposure.

NAS Genetics Panel

Since the toxicology, medical and regulatory communities were still being dominated by the threshold dose response model for all endpoints during this time period, the rejection of threshold dose response and its replacement with the linear model constituted no less than a major scientific and regulatory revolution. As such, one would expect that a principal task of the Panel was to document the strengths and limitations of the threshold and linearity dose response models and thoroughly debate this topic during their sessions prior to recommending the retention of the threshold model for genetic risk assessment, a switch to linearity or some other risk assessment approach. In anticipation of reading such an historic debate, yet knowing in advance that the Genetics Panel recommended the rejection of the threshold model and the immediate transition to linearity, the transcripts of the Genetics Panel meetings were obtained from the US NAS Archives. I was surprised to learn that the Panel did not research, assess, nor debate the dose response question. The issue of dose response risk assessment model selection had been "decided" by the closely knit radiation genetics community prior to the creation of the Panel, based on the leadership of Hermann J. Muller and Curt Stern [Calabrese 2013; Crow 1995). In fact, at the first meeting of the Genetics Panel on November 21, 1955 at Princeton University, the well-known geneticist Alfred Sturtevant from California Technical Institute was dismissive of the issue of dose response as he had "no doubt about the correctness of the linear dose response" model and that any effort to further document support for it would only be for "propaganda value," as means to educate and convince the non-geneticists. This dismissive, and indeed arrogant attitude, was pervasive amongst the geneticists on the Panel concerning their unique professional insights on the issue of mutation. In line with this perspective, the key leaders of the genetics community ascribed to a series of firmly held beliefs about radiation and mutations. In fact, at the second meeting of the Panel (February 5, 1956) Tracy Sonneborn, a member of the Panel and colleague of Muller at the University of Indiana, read into the record what amounted to a detailed series of "beliefs", in essence, a geneticist's creed, about dose response, mutation, ionizing radiation and risk assessment (starting on page 81 of the transcript) (i.e. nearly always harmful, irreversible, cumulative and linear) (NAS 1956). Amongst the Panel of 17 members, of which 13 were prominent geneticists, there was no dissent.

The "Debate"

The only attempt at "dissent" was initiated by Bentley Glass on February 5, 1956 (page 108 of the transcript) (NAS 1956). Glass stated that the only challenge to their geneticist creed as articulated by Sonneborn, to which he was aware, concerned the concept of linearity. Glass stated he wanted to explore the question (i.e., the challenge to linearity) within the Panel, "not because I believe personally in the objection that I am going to raise but to play the role of the devil's advocate here." What follows next is the transcript discussion immediately after the comment of Glass:

"DR. CROW: Which assumptions are these?

DR. GLASS: Well, they were in Dr. Weaver's formation too, but they are the two at the beginning of Sonneborn's genetic considerations.

After having made a talk to the physicists at Rutger's recently on this general topic of "The Geneticist Views the Dangers from Atomic Radiations," I was surprised to find that one of the geneticists who dained to come out to hear the talk challenged this particular assumption which I had put out as one of the assumptions that all geneticists are agreed upon, and his line of reasoning – which, of course, is something that the physicists will very eagerly and quickly seize upon I think because most of them want to believe in a threshold effect as at least a possibility, if not demonstrated beyond all question at the moment – his line of reasoning was as follows: that the view that there is no threshold in the response of mutations to dosage is largely based, apart from the experimental data, on the target theory of the effects of radiation, and that the microbial geneticists (and this man was a microbial geneticist) having shown that there is a chemical and indirect mediation between the production of ionizations and the

occurrence of point mutations makes it altogether probable that somewhere or other there is a threshold, and he felt very uncomfortable about the assumption that there is no threshold if you go down to low enough doses. This is heresy in their midst.
DR. WRIGHT: In energy if not in ionization. Isn't your threshold there in energy? Perhaps one electron volt or two does account for the threshold. But ionization is so far above any possible threshold that it does not seem to me that bears on the ionization argument at all.
DR. STURTEVANT: I have met with this objection. They have usually been willing to agree, however, if I worded it that at the moment the best bet is that there is no threshold and we have to proceed on that.
DR. GLASS: That is all right. But I think we have to take some cognizance of this argument.
DR. CROW: Do you know for certain in any area?
DR. WRIGHT: Isn't the experimental evidence practically conclusive there, to the extent that they have been spaced so that from the physicist's standpoint there is no possibility?
DR. CROW: If you have one ionization per hour or whatever.
DR. GLASS: It is convincing me, too.
DR. RUSSELL: There is both the theoretical and the practical viewpoint they have these several orders of magnitude from all the other kinds of things that we are questioning and recommending research on."

Chairman Weaver then refocused the discussion by inviting Panel member Bernard Kaufmann to discuss research of Arnold H. Sparrow from Brookhaven National Laboratory on mutations in plants at low doses. Kaufmann stated that Sparrow and Singleton (Sparrow and Singleton 1953) reported that 0.41 r per day gives a statistically significant mutation effect. Kaufmann failed to note that (on the top of Sparrow & Singleton's page 37) there was actually mutation data for a dose (0.084 r/day) lower than 0.41 r/day and that it had no treatment effect. This finding would have challenged the linearity position if it had not been omitted by Kaufmann. The page 37 statement of Sparrow and Singleton (1953) is as follows:

> "The data in table 2 show that 0.084 r per day caused no significant increase but that 0.41 r per day (or higher) did show a statistically significant effect (table 2). However, the increase was less than twice that of the control. Since 0.41 r per day of radiation is more than one thousand times greater than the naturally occurring intensity these data do not support the theory that the spontaneously occurring micronuclei are produced by naturally occurring ionizing radiation."

After the brief discussion of the Sparrow data and the misrepresentation of his data by Kaufmann all discussion on the issue of linearity vs threshold ended for the BEAR I Genetics Panel.

It is difficult to comprehend that this was the extent to which the Genetics Panel acknowledged the dose-response controversy and discussed the key scientific issues concerning the nature of the dose-response in the low dose zone. This had been a matter of contention for the past two decades with various high level advisory committees in the US and internationally. It was also a critical component of Muller's Nobel Prize lecture (Calabrese 2011a, 2012) and a major component of the health effects research of the Manhattan Project (Calabrese 2012, 2013; Caspari and Stern 1948; Spencer and Stern 1948; Uphoff and Stern 1949) and of the Atomic Energy Commission. In many respects, the principal reason for the creation of the Genetics Panel was to address the issue of how to assess genetic risks at low doses of ionizing radiation. In the end, the Panel provided the scientific community and the public with a statement of beliefs, none of which was researched, documented, assessed, debated and refined as might be expected if a legitimate evaluation process had been followed.

Acknowledgement of the BEAR I Genetics Panel Failure

On November 26, 1956 Bentley Glass wrote to the BEAR II Genetics Panel stating:
"From impressions I have gathered during the course of the past five and a half months since our report [BEAR I Genetics Panel Report] was released to the public [i.e., June 12, 1956], I have come to the

conclusion that there are several matters of some urging for consideration by our Committee." The second of these considerations related to the linearity question as now stated by Glass:

> "II. I have met continuing doubt from well-informed biological scientists in regard to the geneticists' assumption that there is no threshold for mutation. This leads me to believe that there is a need to prepare a statement and exposition of this point that will (A) summarize existing data on the matter, (B) present the physical arguments against the existence of a threshold, and (C) deal with the experimental possibilities of further investigating the question in suitable biological material."

The statement of Glass is significant in light of the report of the Genetics Panel in Science (Anonymous 1956a). It is clear that he received significant push-back to the LNT assumption by some "well informed biologists" such that he now felt it was necessary for the new Genetics Panel (i.e., BEAR II) to provide documentation in support of linearity and against threshold. Now that the Panel's report was challenged, Glass felt the need for an appropriate scientific response. Even in the case of Glass, his written statement indicates bias as he recommends not a search for scientific understanding of the nature of the dose response in the low dose zone for ionizing radiation, but how to make the case for linearity and against threshold. Based on such insights into the actions of NAS BEAR I Genetics Panel, this group was selected based on both high achievement and their unified belief that genetic mutations were considered irreversible, cumulative and linear with respect to dose. So strong was their collective belief that the group failed to provide any scientific justification for their highly influential linear dose response recommendation. Despite this suggestion by Glass now nearly six months after the release of the report, there was no demonstrable attempt to address this most fundamental issue, but rather their first item on the BEAR II Genetics Panel agenda was to propose a funded research program for the genetics community (Memo to Members of the Academy Genetic Committee - i.e., BEAR II) (Beadle 1956a).

This challenge of Glass (1956) would be a continuing one (August 24, Beadle Memo to Genetics Panel) (Beadle 1956b) for the Genetics Panel, even proceeding the letter of Glass (1956) and a finalizing of their internal debate based on a September 11, 1957 letter from the Chairman of BEAR II Genetics Panel (G. Beadle) (Beadle 1957) to Detlev Brock, President of the NAS and copies to Weaver (Chairman of BEAR I Genetics Panel) and the Panel. In this September 11, 1957 letter, Beadle stated that the development of a detailed technical document that would provide the scientific basis for the BEAR I Genetics Panel report was not justified since it would require excessive resources (i.e. one or two geneticists working full time), and there did not appear to be mounting external pressure to do so. Beadle then offered the incomprehensible suggestion that since several published review papers (none were identified) that presumably included some topics addressed in some manner by the Panel, there was no need to consider this issue further. Thus, the request of Glass was finally tabled, and the NAS leadership was fully informed of this decision.

Discussion

So what do these historical insights mean? The switch from threshold to linearity for risk assessment by the US and other governments that followed the NAS report was not based on an assessment of the issue, but rather on a set of pre-conceived beliefs. As demonstrated in a series of previous articles (Calabrese 2011a,b, 2012), these beliefs had been acquired via deliberate misrepresentation of the scientific literature by key leaders of the radiation genetics community, led by the Nobel Prize winner H.J. Muller and Curt Stern (Calabrese 2011b, 2013). It is apparent that the NAS administration, the scientific community and regulatory agencies failed to demand that the Genetics Panel provide a scientifically supported basis for their recommendation of a switch to the linear dose response.

A strong indicator of their public success became evident almost immediately when the New York Times (Leviero 1956) provided a front page story on June 13, 1956 with the title "Scientists Term Radiation A Peril to Future of Man: Even Small Doses Can Prove Harmful to Descendents of Victim". The first paragraph of the article stated that "A committee of outstanding scientists reported today that atomic radiation, no matter how small the dose, harms not only the person receiving it but also all his descendents." The next paragraph would claim that "it was the most comprehensive United States effort to determine how the future of the human race might be affected by the unleashing of nuclear power." Similar reports were also found in the Washington Post (Haseltine 1956), Time Magazine (Anonymous 1956b,c), US News and World Report (Anonymous 1956d), News of Science Section, Science journal (Anonymous 1956e), The Saturday Review (Muller 1956), Challenge Interviews (Weaver 1956), Journal of The Franklin Institute (Weaver 1957a), Bulletin of Atomic Scientists (Weaver 1957b), Public Health Reports (Weaver 1957c), Scientific American (Crow 1959; Beadle 1959), The Lancet (Anonymous 1956f,g) and other leading publications.

As the present paper demonstrates, the Genetics Panel's effort was anything but comprehensive. Rather, it represented an abdication of professional and ethical responsibility, using their outstanding reputations to present a false image of a detailed and objective assessment when it was their ideology that prevailed. While previous articles have captured Muller and Stern's scientific deceptions on the issue of linearity and their impact on the Genetics Panel (Calabrese 2013), and several members of the Panel in serious self-serving comments that undercut the credibility of the Panel (Calabrese 2014), the present paper has captured their silence and illusion as far as an effort to assess the nature of the dose response in the low dose zone.

Policy should be based on facts, not assumptions. In the absence of a factual foundation, the assumptions should be stated, explained, and justified. Not only did the Genetics Panel fail to serve the public, it was permitted to mislead US national policy and cancer risk assessment predictions and that of other countries by a compliant NAS administration, scientific community and press, under the false impression that their recommendation represented an objective and comprehensive assessment. The implications of this deception have been enormous and continue to the present.

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LETTER TO THE EDITOR, NEWS AND VIEWS

Cancer risk assessment foundation unraveling: New historical evidence reveals that the US National Academy of Sciences (US NAS), Biological Effects of Atomic Radiation (BEAR) Committee Genetics Panel falsified the research record to promote acceptance of the LNT

Edward J. Calabrese

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Abstract The NAS Genetics Panel (1956) recommended a switch from a threshold to a linear dose response for radiation risk assessment. To support this recommendation, geneticists on the panel provided individual estimates of the number of children in subsequent generations (one to ten) that would be adversely affected due to transgenerational reproductive cell mutations. It was hoped that there would be close agreement among the individual risk estimates. However, extremely large ranges of variability and uncertainty characterized the wildly divergent expert estimates. The panel members believed that sharing these estimates with the scientific community and general public would strongly undercut their linearity recommendation, as it would have only highlighted their own substantial uncertainties. Essentially, their technical report in the journal Science omitted and misrepresented key adverse reproductive findings in an effort to ensure support for their linearity recommendation. These omissions and misrepresentations not only belie the notion of an impartial and independent appraisal by the NAS Panel, but also amount to falsification and fabrication of the research record at the highest possible level, leading ultimately to the adoption of LNT by governments worldwide. Based on previously unexamined correspondence among panel members and Genetics Panel meeting transcripts, this paper provides the first documentation of these historical developments.

Keywords Mutation · Cancer · Risk assessment · Linear no-threshold (LNT) · Threshold dose response

In 1956, the US National Academy of Sciences (NAS) published their long-awaited reports addressing national concerns about how ionizing radiation may affect such entities as oceans/fisheries, agriculture/food supply, meteorology/atmosphere, medicine/pathology, genetics and disposal of radioactive wastes. As it turns out, the report that dominated the attention of the scientific community and media was that of the Genetics Panel. It proclaimed there was no safe level of exposure to ionizing radiation and offered dire warnings about severe adverse biological effects occurring in present and future generations. Societies, world governments and medical communities needed to heed the mutational risks that could persist across generations as a result of exposures to even low doses of ionizing radiation. The panel emphasized that the then extant threshold dose–response model was wrong and misled society on the hazards of low doses of ionizing radiation. To better protect the public health and to provide more accurate predictions, the report urged the risk assessment community to adopt a linear dose–response model. This recommendation represented no less than a paradigm shift that would alter the courses of both international environmental policy and cancer risk assessment to the present time. The LNT dose response was soon generalized from assessing the radiation risk of mutation to the radiation risk of cancer and then generalized once again by the US EPA to assessing the chemical risk of cancer. In retrospect, the road to linearity can be directly traced back to the BEAR Committee, Genetics Panel (Calabrese 2009, 2013).

Despite their tidal wave of success in 1956 and in the years following, the radiation genetics community had

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already been seeking a switch from the threshold to the linear dose–response model for nearly 30 years (Calabrese 2013), i.e., starting from a time soon after Muller's famous Nobel Prize winning discovery in 1927 that X-rays can induce mutations in the sperm of male fruit flies. Muller, Curt Stern and other prominent researchers from the radiation genetics community had long challenged the risk assessment methods for ionizing radiation and proposed using the far more conservative linear dose–response model. However, at each turn in the road, another similarly recalcitrant medical committee opposed their challenges and supported the more lenient threshold dose–response model instead. This frustrated Muller and his kindred radiation geneticist colleagues. In all major advisory committees to that point, the cards were "stacked" against them. However, with the creation of the NAS Committee, which was funded by the Rockefeller Foundation, the political tide turned their way. The decision to create an NAS Genetics Panel meant that Muller and his group would no longer be token geneticists on a committee oriented toward and dominated by the medical community; they would now be the dominant force on a BEAR I Committee whose 17 members included 13 notable geneticists. This may have seemed like a dream come true as the panel would now have no opposition to the big issue of the day: that is, finally getting linearity to drive the mutation risk assessment. The panel would soon proclaim that LNT was the new risk assessment "law" of the land, with little, if any, need for discussion, debate or evidence-based examination via scientific assessments. Thus, the panel moved to other challenges. Instead of debating the merits of the threshold vs LNT, the Chair of the Panel requested that all the geneticists on the panel provide their best estimates with upper and lower confidence intervals for the number of adversely affected children born to parents' whose gonads were exposed to a certain dose of radiation.

Despite the fact that there was a wide range of geneticists (e.g., human, fruit fly, bacterial, etc.) comprising the panel, it was hoped that there would be a high degree of agreement/consensus on what the specific population risks might be. If the panel members could independently come to a convergent agreement on risks, it would strongly support their risk assessment judgment and the linearity dose–response paradigm that they wanted society to adopt.

It is here where the story gets interesting. Through a variety of unexpected discoveries, it was possible to determine that the panel of geneticist experts wildly differed among themselves on the estimates of population risks, and, in fact, felt very uncertain about their own estimates of mutation frequency in future generations. The emergence of such uncertainties rattled the leaders of the panel and eventually led the Genetics Panel to omit key data from the research record, all in an effort to disguise the vast uncertainty that existed for the projected human risks. These factors and issues were known by the panel and are evident in the numerous letters that were exchanged between them and the Panel Chair; the panel even voted to hide the uncertainty from the scientific community by omitting key data and misrepresenting the predicted risks. In effect, the NAS BEAR Committee, Genetics Panel committed scientific misconduct in their publication in the journal Science in June, 1956 (Anonymous 1956). By omitting and misrepresenting the actual data, the panel hoped to convince the scientific community and the public to adopt their linear dose–response model in the assessment of risks associated with exposures to ionizing radiation, especially at low doses. These falsifications and fabrications are detailed and presented for the first time in the supplemental data section; they expose the fraudulent actions of the Genetics Panel and call attention to the vast impact they have had on cancer risk assessment.

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Supplementary Material

SCIENTIFIC MISCONDUCT BY THE U.S. NATIONAL ACADEMY OF SCIENCES IN RECOMMENDING LNT FOR RISK ASSESSMENT

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ABSTRACT

The National Academy of Sciences Biological Effects of Atomic Radiation I (NAS BEAR I) Committee Genetics Panel (1956) recommended that regulatory agencies switch from a threshold to a linear model for radiation risk assessment of genomic endpoints. This recommendation was generalized to somatic cells for cancer risk assessment and later applied to chemical carcinogens. At the heart of the recommendation were independent estimates by panel geneticists of adverse reproductive effects in humans exposed to a given radiation dose. This paper reveals both an enormous variance and uncertainty in the independent estimates of genetic damage in reports submitted by six geneticists. These estimates were far greater than reported in Science, substantially misrepresenting expert disagreement. While the Science paper indicated that only six (of the 12) geneticists provided estimates, nine did. The three excluded estimates indicated markedly lower damage than did the six. The censoring of the three estimates and the mischaracterization of the uncertainty of the remaining six geneticists deliberately and substantially overstated the degree of confidence and agreement in the estimates of genetic harm. Based on internal correspondence, these actions were designed to ensure that linearity at low dose would be adopted for risk assessment. The omission and misrepresentation of data intended to represent the independent appraisal of panel experts is consistent with definitions of falsification and fabrication of the research record. The principal scientific document therefore supporting the adoption of the LNT was the product of scientific misconduct and that its adoption by regulatory agencies worldwide was based on a process involving falsification and fabrication.

Key Words: linearity, dose response, risk assessment, threshold, mutation, cancer

Introduction

Cancer risk assessment policy in the United States (US) originated from the US National Academy of Sciences (NAS) Biological Effects of Atomic Radiation (BEAR) I Committee, Genetics Panel, in 1956 when they recommended a shift from a threshold to a linear dose response model for the effects of ionizing radiation on genomic mutations. This linearity recommendation was soon generalized to somatic cells by the National Committee on Radiation Protection and Measurement (NCRPM) and applied to cancer risk assessment (Whittemore 1986 – Page 608, Footnote 260). This perspective was widely adopted in numerous countries by various regulatory and public health agencies (e.g. International Committee for Radiation Protection-ICRP) and continues to the present (Calabrese 2009, 2011a, 2013)

Historical reassessment of the BEAR I Genetics Panel report and its scientific foundations has revealed a series of key scientific concerns, flaws, and misrepresentations that challenge the basis of the original linearity recommendation (Calabrese 2011b, 2013). These findings provide substantial evidence

that the switch from threshold to linearity occurred due to ideologically-based deceptions of key papers on ionizing radiation induced mutation by leaders in the radiation genetic community, most notably Hermann J. Muller, Nobel Prize winner, and Curt Stern, University of California-Berkeley professor.

The current paper extends this historical re-evaluation into the activities of the BEAR I Genetics Panel with particular focus on the key publication of that panel in Science, entitled "Genetic Effects of Atomic Radiation". The Science paper represents the "technical" publication (Anonymous 1956) of the panel whereas a "popular" version (NAS/NRC 1956) was written for the media and public and included summaries of each of the NAS BEAR I Committee Expert Panels. Each of the technical Panels published a separate article in the journal Science in 1956. The present paper originated as a result of an unexpected observation that the Science paper of the Genetics Panel reported genetic risk estimates of only six of the 12 geneticist members of the Panel. Yet, an investigation of the personal correspondence and unpublished technical writings of the Genetics Panel uncovered detailed assessments from nine members of the Panel. This previously unrecognized discrepancy led to a further investigation resulting in the present paper.

Estimating radiation induced genetic risk

A key finalizing activity of the Genetics Panel was to provide an estimate of the total number of offspring (including embryonic/fetal deaths/stillbirths and those born but unable to reproduce) that would be adversely affected by mutations (i.e. often referred to as "genetic deaths" –adversely affected offspring that could not reproduce) assuming the entire adult reproducing population received a single dose of 10 roentgens (R) (0.1 Gy) to the gonads. The specific charge to the Genetics Panel was given by the chairman, Warren Weaver of the Rockefeller Foundation, the organization which funded the assessment. This finalizing topic was extensively discussed on Feb. 6, 1956 in the Panel meeting, occupying about 40 transcript pages (NAS 1956a). On Feb. 8, 1956 a memo was sent by Weaver to the Genetics Panel with the subject heading of "Reminder" (Weaver 1956a). He stated the following:

"At the Chicago meeting it was agreed that every geneticist on the panel was invited and indeed urged to undertake an estimation of the expressed damage due to detrimental mutations. The estimation was to apply to the total number of children (say 160 million ?) which will in the future be born to persons now alive in the U.S.; and to their children and so on. At least three estimates are desired: 1) expressed damage to the first set of 160 million children due to a dose of 10r to the persons now living; 2) expressed damage to the F1 through F10 generations of children due to a single dose of 10r to the persons now living; 3) expressed damage to F1 through F10 due to a dose of 10r per generation.

It would be most helpful also to have comparable estimates for 2) and 3) above when the dose is 50r. Linearity applies to 1), so that it is trivially easy to adjust that estimate to any dose.

It was agreed that each would state the range which applies to the estimates entering the calculation, and the range applying to the final result; and would state his reasoning in enough detail so that the other members could intelligently weigh, criticise (criticize), and compare the various estimates.

May I urge you that you undertake this <u>as promptly as possible</u>, and that you duplicate your report and send it to every member of the panel?"

The basis for the charge conferred upon the geneticists by Weaver was a discussion of a written position statement of geneticist Panel member Tracy Sonneborn that was read into the transcription record on Feb. 5, 1956. In addition to a statement of genetic risk assessment principles, Sonneborn raised the question as what would be the risk communication message for the general public based on their Panel deliberations. This led Weaver to trace three possible options with the most desirable, being the most explicit. That is, he wanted the Panel to provide reproductive risk estimates to the general

public that were specific and quantitative, estimates that would build upon the belief that all doses of radiation were harmful, cumulative, and irreversible.

On page 244 of the Feb. 6, 1956 transcribed proceedings of the Panel (NAS 1956a), Weaver stated his desire to obtain the independent views of the geneticists for the prediction of radiation induced genetic damage for subsequent generations of humans, using the US population as the working example. This was viewed as a means to define the range of informed judgment and to ascertain how much the Panel geneticists were in agreement, a key factor needed to support policy recommendations of the Panel. On page 257 of that same transcript Sonneborn stated **"that the thing of most value in all this calculation would be to show how one can use different methods to make estimates, and see to what extent methods, if possible, variations in approach, lead to different answers. So that if they converge, or tend to converge, then we might have more willingness to put them forth."** Weaver and Sonneborn were, of course, mindful of the fact that the geneticists brought differing technical abilities, research experiences and judgments to the Panel. Panel geneticists were experts with Drosophila, bacteria, paramecia, mice and human population genetics. Some of the Panel members were far more mathematically oriented than others. Each was expected to independently consider the problem and then document in writing their methods, assumptions and their estimated population-based radiation induced genetic harm. These estimates were to be collectively summarized and would define the range of expert agreement/disagreement using the different but complementary approaches of each contributing expert geneticist.

The Genetics Panel

There were 13 *bona fide* geneticists who were members of the Genetics Panel. These included: George W. Beadle – California Institute of Technology; James Cotterman – Baylor University; James F. Crow – University of Wisconsin; Milislav Demerec – Carnegie Institution of Washington; H. Bentley Glass – Johns Hopkins University; Berwind P. Kaufmann – Carnegie Institution of Washington; Clarence C. Little – Roscoe B. Jackson Memorial Laboratory; Hermann J. Muller – Indiana University; James V. Neel – University of Michigan; William L Russell – Oak Ridge National Laboratory; Tracy Sonneborn – Indiana University; Alfred Sturtevant – California Institute of Technology; and Sewall Wright – University of Wisconsin. Other members of the committee were the chairman Warren Weaver, Rockefeller Foundation, a mathematician; C. Failla, Columbia University, a health physicist; Alexander Hollaender, a physical chemist and administrator of Oak Ridge National Labs; and Shields Warren, New England Deaconess Hospital, a physician, who was also a member of the NAS BEAR I Pathology Panel. After the meeting in Chicago (February 5/6, 1956), Cotterman resigned from the Panel due to academic work load issues, leaving 12 geneticists on the committee. Of the 12 geneticist members, estimates of nine members have been obtained via searching past committee communications and letter exchanges from all members of the committee. The three members not providing estimates were Little, Neel, and Sonneborn. While there is no record of Little's actions on this matter, Sonneborn and Neel refused the request of Weaver to provide estimates of genetic damage since they did not believe that they could be reliably made. In fact, Neel argued that the scientific basis for such estimates were so uncertain that providing them would be a violation of his obligation as a scientist to society, an unethical condition. On April 6, 1956 he specifically addressed his concern with Chairman Weaver (Neel 1956a):

"The geneticist has social responsibilities, but he also has responsibilities as a scientist. One is that in an area as critical as this one is, he must beware of letting his conjectures get too far in advance of his facts. It is to me an exceedingly tenable position, having stated the general genetic argument, to say flatly that we know so little about the quantitative aspects." In fact, Neel was so adamantly opposed to the decision to develop and provide such genetic estimates of damage that he wrote Weaver on March 8, 1956 stating that he would **"go down with flags flying and guns booming to the last"** (Neel 1956b).

Organizing the estimates

The nine estimates were provided by the end of February, 1956. At a March 1, 1956 meeting of the Genetics Panel, a decision was made on how the estimates would be processed. In a March 2, 1956 brief summary (Weaver 1956a) (Muller manuscripts (mss), Lilly Library) of the March 1 meeting, Weaver indicated that **"Jim Crow was made the chairman of a sub-committee (he can commandeer help on this if he wishes) to go through all the damage estimates, compare them, and display assumptions, methods, input, and results in some sort of chart or graphic form."** This description did not indicate that Crow was authorized to exclude individual contributions, nor to make judgments as to which estimates were the most/least credible. Crow's role as sub-committee Chair was to organize and integrate the submitted estimates in a coherent manner so that the entire Panel could intelligibly, efficiently and objectively view the submitted estimates.

The Science journal article

In the Genetics Panel Science paper it was stated that **"Six of the geneticists of this committee considered the following problem: suppose the whole population of the United States received one dose of 10 roentgens of radiation to the gonads. What is the estimate of the total number of mutants which would be induced by this radiation dose and passed on to the next total generation of about 200 million children? Each geneticist calculated what he considered to be the most probable estimate, and then bracketed this by his minimum and maximum estimates. Each thus said, in effect: I feel reasonably confident that the true value is greater than my minimum estimate and less than my maximum. My best judgment, as stated in a single figure, is what I have labeled the most probable estimate."** Note that authors published an errata one month later indicating that the 200 million number of children should have been 100 million (Errata-Science, Volume 124, page 170, 1956). The paper goes on to state that **"the most probable estimates as thus calculated by the six gentcists (geneticists) do not differ widely. They bunch rather closely around the figure 5 million. Four of the six estimates are very close to that figure, and the other two differ only by a factor of 2.**

These six geneticists concluded, moreover, that the uncertainty in their estimation of the most probable value was about a factor of 10. That is to say, their minimum estimates were about 1/10, and their maximum estimates about 10 times the most probable estimate."

Inconsistencies emerge from the Science paper

A detailed evaluation of the Genetics Panel article in Science reveals a number of anomalies and concerns.

1. The invitation to provide estimates was made with some urgency to all geneticists on the panel. The reader is informed that only six provided estimates. The specific six geneticists were not identified in the Science paper. The Science paper did not provide any description of the biological models and methods used by the six geneticists to obtain their respective estimates. While only six geneticists were stated as having **"considered the …problem"**, all 12 geneticists were urged to take on this task. We also know that the number of geneticists providing written assessments was nine. Based on a letter from James Crow to Warren Weaver on May 21, 1956 (Crow 1956a), he listed the names of six geneticists on the Panel who provided estimates. These geneticists included Beadle, Crow, Glass, Muller, Russell and Sturtevant. It is this group of six that the Science article values were based upon. However, detailed mutational estimates were provided in a professional and timely manner consistent with the request of Weaver by three other Panel geneticists [Demerec (2/14/56 letter; 2/11/56 document; and stamped received 2/16/56) (Demerec 1956); Kaufmann (2/27/56 letter to Weaver and stamped received 2/29/56) (Kaufmann 1956); and Wright (2/22/56 letter to Weaver and stamped received on 2/24/56 (Wright 1956)]. Each of these three documents (Demerec, Kaufmann and Wright) were obtained from the Lilly Library, papers of Hermann J. Muller at the University of Indiana as well from the

files of multiple other members of the Panel. It therefore seems that Weaver received the assessments and that they were distributed to Panel members, as expressly recommended in the Weaver memo (Weaver 1956b). Thus, it is likely that all or most Genetics Panel members saw the three assessments that were excluded from the reporting in the Science publication. The question needs to be raised as to why didn't the Science article incorporate the independent findings from the other three Panel geneticists since they were professionally addressed and completed in a timely manner?

2. The estimates of the six Panel geneticists were summarized by James Crow in three letters [March 12, 1956 (Crow 1956b); March 29, 1956 (Crow 1956c); and May 21, 1956 (Crow 1956a)] to Weaver. The March 12, 1956 letter provided a graph showing the minimum, maximum and best estimates for total genetic damage expected from all descendants of the first generation of parents exposed to 10r, the cumulative damage through ten generations for a single generation exposed to 10r or the damage at the 10th generation from 10r per generation up to that time. In this letter, Crow stated that he made a decision to exclude the estimates of Drs. Wright and Demerec while the non-cited report of Kaufmann was not mentioned. However, the estimates of Wright were included in the March 12, 1956 graph. More specifically, in the final paragraph of this letter, Crow writes that he did not provide **"Dr. Wright's methods which are greatly different, but clearly given in his letter."** In the next sentence he then writes that **"I haven't included Dr. Demerec's estimate on the graph for it, too, is based on quite different assumptions that lead to a greatly different value than the others obtained".** The only specific comment that Crow offered for the Demerec estimation was that it **"was based on bacterial mutation rates"**. As for the Wright estimates, Crow stated that he **"counted only mutations causing conspicuous effects in postnatal life"**. However, the Wright document states that his analysis included the **"conspicuous detrimental effect on viability or fecundity"**. Thus, the effects estimated by the Wright analysis would not have been restricted to only those occurring in postnatal life, thereby contradicting the statement of Crow. Furthermore, the postnatal effects estimated by Wright were not restricted to an age of the offspring to display the harmful effect. However, Crow accepted the analysis of William Russell (1956) which restricted the age of expressing damage to only three weeks, a limitation that Russell noted. The actions of Crow to exclude the Wright and Demerec estimates are at variance with the instruction that he present **"all the damage estimates, compare them, and display assumptions, methods, input, and results in some sort of chart or graphic form."**

3. In the March 29, 1956 letter to Weaver, (Crow 1956c), Crow stated: **"The limits presented on our estimates of genetic damage are so wide that the reader will, I believe, not have any confidence in them at all."** He then makes the statement that **"I recommend one of two things: omit the estimates entirely, or b) give a single best estimate of the number of mutations, or a narrow range of estimate, based on direct extrapolations from mouse and Drosophila."** Crow then inexplicably states that **"We then state that these are based on mouse data and let the reader add his own uncertainty factor."** Basing estimates on Drosophila and mice and then telling the reader that the estimates are based only on mice is deceptive. Asking the reader to construct their own uncertainty factor with what is highly censored data lacking upper and lower bounds is disingenuous. This recommendation followed from his earlier comment in the March 12, 1956 letter (Crow 1956b) that **"...the groups differ widely in their confidence in the best estimate, as indicated by their grossly discrepant minimum and maximum estimates."** In the May 21, 1956 letter, he again provided mutational estimates of the six geneticists, including their best estimates and ranges (Crow 1956a). He stated in the letter

that he did not support publishing the table. This issue was eventually considered for a vote by the entire committee and the table was not included, only the summary statement as given above.

4. Table 1 reveals that the best (i.e., most probable) estimates of affected children after 10 generations ranged from 2 to 10 million, a five-fold range. The range of uncertainty varied considerably amongst the geneticists. Beadle and Glass, for example, gave a 2,000 fold uncertainty range while Muller's estimate was 10-fold. In the Science paper, it was stated that the uncertainty estimates were within 10-fold of the best estimates (i.e., 100-fold range). However, in the case of Beadle, the bounded values range from 20-fold below to 100-fold above his best estimate. For Glass, his range was from 40-fold below to 50-fold above his best estimate. In the case of Muller, his bounded values were 4-fold below and 2.5-fold above his best estimate. Similarly large variation in uncertainty estimates was also presented by Crow in his March 12, 1956 (Crow 1956b) letter to Weaver for the damage expected in the first offspring generation. In fact, the estimated number of affected individuals ranged from 5000- 20,000,000, a 4000 fold value. It is not possible to discern how the minimum and maximum values were derived in some cases. In the case of Beadle, for example, the values are provided without any explanation. As for Russell the best estimate was derived but lower and upper bound estimates are not included. It is not known how Crow derived such values. The case of Crow's own estimate may also be instructive. He stated on March 29, 1956c (Crow 1956c) **"I shall use as a minimum estimate a direct extrapolation from Drosophila and as a maximum some calculation from the sex-ratio data in the Japanese cities. An estimate from mouse data turns out to be just about half way between these, so I shall use it as the most probable estimate."** With such non-sequitur biological reasoning guiding the genetic risk estimates as well as with estimates lacking any documentation, it is not surprising that the committee members did not want to share their procedures with others. Furthermore, there was an absence of criticism of the bizarre approach offered by Crow as well as the lack of documentation for upper and lower bound estimates by Beadle, Russell and others despite the high priority placed on such values. Even Sturtevant, whose lower and upper bound estimates were exactly ± 10-fold, stated on February 20, 1956 to Weaver (Sturtevant 1956), **"After going through these calculations I come out with a feeling that they are rather futile. At almost every step it has been necessary to make a guess, often with little to go on, and with no real basis for setting limits within which the true value probably lies".** This statement raises the question that Sturtevant may even have been open to the possibility that the true estimate was not even within his derived lower and upper bounds. The statement of Sturtevant contradicts the earlier statement in the Science article which claimed that **"Each thus said, in effect, I feel reasonably confident that the true value is greater than my minimum estimate and less than my maximum."** In fact, the term guess was also used by other reporting geneticists. For example, Russell referred to his extrapolation process also as a "guess" (Russell 1956).

5. According to Neel the closeness of the best estimates of the six geneticists selected by Crow was due to the fact that they used essentially the same assumptions for gene number, mutation rates, and other parameters (Neel 1956c). Neel thought that their scientific "agreement" was illusionary since there was little independence of thought. In fact, once each of the six had to think far more independently on the problem as with the case of estimating upper and lower uncertainty bounds their "apparent" agreement strikingly disappeared, supporting the Neel perspective. However, knowing that he had been overruled on genetic risk estimations, Neel

asked to be dissociated with any aspect of the report that provided quantitative estimates of genetic damage or a recommended permissible dose (Jolly 2003 - page 359).

6. The 100-fold range reported in the Science article to characterize the uncertainty about the best estimate strikingly conflicted with and misrepresented the range of uncertainty of this group of geneticists which had a mean value of 745 (uncertainty range 10-2000 – see Table 1) for the 10 generation estimate (median 180) and a mean of 756 (uncertainty range 100-2857) for the first generation (median 312.5) (data from March 12, 1956 Crow Letter to Weaver) (Crow 1956b).

Draft BEAR I Genetics Panel Report of March 19, 1956

In this draft report (NAS 1956b), Weaver stated that the **"estimates have been independently furnished by seven of the geneticists of this Panel. Each estimated the total damage (that is to say, the number of genetic deaths or extinctions) which would occur among our 100 million children. Each of the seven geneticists stated his result in terms of a range of values, giving what he considered to be a reasonable lowest figure and also a reasonable highest figure. Thus there were in all seven low estimates and seven high estimates. The lowest of the low estimates was 5,000 damaged individuals among our direct children. The highest of the high estimates was 20 million. This extreme range simply reflects our lamentable lack of information on human radiation genetics."** This range of high to low would indicate a 4000-fold range and probably reflected damage estimated in the first offspring generation. This draft differed from the May 21, 1956 table of Crow which showed a maximum 2,000 fold range, reflecting damage after 10 generations. There is also no explanation why there were seven geneticist estimates stated in this draft but only six were mentioned in the Science paper.

Chairman Weaver also raised the question that **"The public may well ask, why were there only seven such estimates when this Panel includes a larger number of geneticists? The answer is that many highly competent geneticists would not wish to undertake a calculation of this sort, either because they are not specifically experienced in the more mathematical aspects of genetics, or because they doubt that such a calculation is very useful at the present state of knowledge."** The response of Weaver failed to indicate that nine of the 12 geneticists provided estimates. He referred to seven Genetics Panel members as providing estimates. At some point one of the seven reports was reduced to six without explanation.

There were substantial differences as to what the trans-generational mutation risk might be, even amongst the six geneticist values that were used. The extent of the variation and the acknowledgment of the "futility" in making the given estimates undercut the confidence in the process and in its conclusions. Furthermore, this high degree of uncertainty would have been considerably greater if these geneticists were not constrained by Weaver (in his memo directions to the geneticists) to employ a linearity dose response assumption. The variability characterization estimates in the Science article provide a distinctly different impression than the actual estimates of the six geneticists, reflecting data censoring, and leading to false conclusions concerning the degree of uncertainty among the participating geneticists and the extent to which the experts agreed/disagreed amongst themselves on this matter.

On June 5, 1956 Chairman Weaver (1956c) wrote to the Genetics Panel informing them of the results of the voting on an unresolved aspect of the final report. One of the key questions was whether to include the table of Crow which showed the variation in genetic damage estimates between and within subjects. This decision was accomplished by a vote of 15 members of the Panel. The results were 7 against including the table, 6 for publishing it, with two designated as "indifferent". Thus, the recommendation of Crow prevailed and the table was not included. Based on incomplete obtained correspondence, it is known that Crow, Muller, Glass and Sonneborn voted against publishing the table.

The Missing Expert Geneticist Estimates

1) **What information did the three missing geneticist estimates provide?**
   Kaufmann: His report was six pages, providing a detailed mathematical derivation of mutation frequency based on human mutation rates, providing all assumptions used in his calculations. Three pages were text, two pages were tables and one page contained two summary figures. He provided genetic damage estimates over 10 generations and expressed the number of affected children per 200 million. Adjusting for 100 million, he reported 195, 000 affected children in generation #1. In his February 27, 1956 letter (Kaufmann 1956) to Weaver, Kaufmann stated that his **"calculations show that under the defined conditions the visible genetic damage resulting from chronic exposure to 10 r per generation is small in comparison with that of spontaneous origin."** Kaufman noted that his estimates, based on research of the geneticist Herman Moser, were quite complicated and he was not able to provide upper and lower confidence intervals. Note that Crow (1956b) included estimates of "Moser" which were subsequently dropped. These appear to be the estimates of Kaufmann.
   Wright: His report provided a nine page detailed assessment and mathematical derivation of genetic damage over 10 generations (Wright 1956). He also provided two estimates of damage based on assumptions related to the proportion of dominant mutations. The estimates provided in the report range from 34,000 to 67,000 (i.e. ~50,000 average) children affected in generation #1 based on the assumptions used. Upper and lower bound estimates were provided.
   Demerec: He provided a detailed, single spaced, three page assessment using *E. coli* as his model. He presented evidence for spontaneous mutation rates for 26 genes and X-ray induced mutation rates for the same genes. He also indicates that similar data existed for multiple chemical mutagens (Demerec 1956). The information that Demerec had developed on the *E. coli* model far exceeded that of any of the other models presented including Drosophila, mice and humans. His risk estimates were based on 160,000,000 as was originally proposed by Weaver. He estimated that there would be 14,200 affected children in generation #1 due to spontaneous mutation; in contrast, 8,320 additional children were estimated to be affected by the 10 r exposure to their parents. This value was adjusted to 5,200 for a 100 million population. Demerec stated that since he did not include "lethals" his estimate would need to be adjusted to some degree upward. He also stated that **"I do not wish to venture into speculations about the genetic damage that would be sustained by subsequent generations, for such speculations could only be based on assumptions not supported by experimental evidence."**
2) The three best estimates were 195,000 (Kaufman), 50,000 (Wright), and 5,200 (Demerec) (83,000 mean) for the first generation. On balance these are lower (~70 %) than for the other five geneticists (275,000 mean) (note that Beadle did not provide an estimate for generation #1). If all geneticist estimates for generation #1 were included, the generation #1 mean estimates would range from a low of ~ 5000 to a high of ~350,000, a ~70 fold difference, a value reflecting considerable variation amongst the geneticists.

Discussion

The present assessment indicates that the US NAS BEAR I Committee Genetics Panel Science paper included a series of significant misrepresentations relating to the central charge of the Panel, that is, predicting the public health risks of ionizing radiation from all sources, such as medical, fall-out and other means of exposure. The Panel knowingly reported that only six of the 12 geneticists provided estimates, when nine did. While reasons for this omission of data are speculative, two (i.e. Demerec and Wright) of the three excluded views offered notably lower estimates of risk than the six geneticists presented in the paper. If all geneticists' estimates were presented, it would have markedly altered the range of the best estimates; the range of the ~2-fold mean difference would increase to ~70-fold for

generation #1damage. If the experts were shown not to be in agreement, it would affect the credibility of their report and most likely weaken support for its policy recommendations.

The decision by Crow to exclude the estimates of Demerec and Wright overstepped his authority as given by Chairman Weaver. There was no documentation to support these actions. There is no indication of why the estimates of Kaufmann were omitted. Despite such actions of Crow to exclude these three, there is no evidence that such actions were disputed. This suggests that the affected members and the entire Panel accepted this decision. If this is the case, then it is even more problematic as the incorrect statement that only six geneticists provided estimates rather than the nine was known and agreed to by all. Whether this was due to internal pressure to conform to the goal of displaying highly consistent estimates is not known. Yet, the efforts of the three excluded geneticists were substantial, with no evidence that they withdrew their estimates.

The Panel also stated that the uncertainty range (i.e., upper to lower bound) was about 100-fold for the six geneticists used while the table of Crow had Beadle and Glass with ranges of 2,000 and a mean of 745, and uncertainty values that were even higher after the first generation. This misrepresentation, though different from omitted data, is consistent with the intention of creating the appearance of greater agreement amongst the geneticists than actually existed. Furthermore, the Science article failed to provide the reasons why three individuals (i.e., Little, Neel, and Sonneborn) did not provide estimates. Given the critical significance for Panel agreement with respect to the acceptance of policy recommendations, it was necessary to present the views of the entire group. In fact, the views of Sonneborn and Neel were that such estimates could not be reliably done, with Neel being particularly strident on this issue as quoted above. It is not clear what the opinions of Little were. Thus, if the broad spectrum of views and risk estimates had been summarized in the Science article, it would have undermined the conclusions and policy recommendations of the Panel even further. On this later matter, it is worthy of note that in his May 21, 1956 letter to the Panel (Crow 1956a), Crow states that **"Once again, I urge that we not include the table at all..."** He then displayed a table of the values of the six geneticists and stated that **"I include these values for Committee members' inspection because I believe the only thing worse than publishing the estimates at all is to publish the wrong values".** This recommendation was adopted and the table showing the extremely wide differences between the experts was dropped and was replaced with the above noted misrepresentation.

While the estimates of the panel members were clearly efforts in risk assessment speculation, they contributed to the appearance of confident conclusions throughout the Science article. In retrospect it appears that the exclusion of the Demerec and Wright estimates occurred because the derived values were “different”, that is, far lower than the other six. This was assumed to be due to the use of other methods, models or approaches. However, the charge of the Panel was to present the range of independent estimates and to describe them along with their assumptions. If complementary methods and models could be shown to have considerable agreement, it would bring added confidence to the recommendations of the Panel as noted above by Sonneborn. However, if the expert estimates were widely or wildly divergent, then it was feared that it would undermine acceptance and use of their report. In many ways, the future course of action would be affected by the degree of concordance of their estimates. When the estimates were found to be extremely variable, Crow and the other members of the Panel refused to show this variability/uncertainty and in fact acted to exclude low estimates and mischaracterize the estimates retained.

When placed in perspective what does this story reveal? The geneticists of the Panel firmly believed their genetics mutation-credo of nearly always harmful, cumulative, irreversible, and linear at low dose. However, when challenged by Weaver to translate this credo into independent estimates of societal harm, using their own research methods and experience, the results were unanticipated. That is, the estimates revealed much quantitative variability and uncertainty between and within the experts. So great was the range of estimates that actions were taken to prevent this from being exposed,

deliberately creating the false impression of agreement that was not warranted, as seen in the omission and mischaracterization of estimates. Comparing the message of the Science paper with the internal correspondence of the Panel members, reveals a striking dichotomy and dishonesty of the Panel. The falsification of the research record provided the vehicle for the acceptance of the Panel's goal, that is, the use of the LNT for risk assessment and ultimately its acceptance worldwide by regulatory and public health agencies and within the legal system. In a highly ironic twist to the present story, it should be noted that the US National Academy of Sciences building in Washington, D.C. has a statute of Albert Einstein, which is accompanied by a series of his famous quotes. One of these captures of the essence of the present paper and the intolerable actions of the Genetics Panel. "The right to search for truth implies also a duty; one must not conceal any part of what one has recognized to be true." In a retrospective statement some 40 years later concerning the actions of the BEAR I Genetics Panel, Crow (1995) confessed that he and especially Muller exaggerated the dangers of low level radiation and should accept significant blame for an irrational emphasis on such matters by the public and regulatory agencies.

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Table 1. Trans-generational estimations of the NAS BEAR I Genetics Panel – Subcommittee –
The values represent "the total genetic damage expected among all descendants (through 10 generations) of a single (i.e., first) generation exposure to 10r". Source: Crow, 1956b - March 12, 1956 of Crow to Weaver; Letter of Crow provided the four columns to the right.

Min to Max Range (uncertainty range)	Minimum	Most Probable	Maximum	Author
2,000-fold	100,000	2,000,000	200,000,000	Beadle
2,000-fold	100,000[a]	4,000,000	200,000,000	Glass
260-fold	250,000	5,000,000	72,000,000	Crow
100-fold	600,000	6,000,000	60,000,000	Sturtevant
100-fold	700,000	7,000,000	70,000,000	Russell
10-fold	2,500,000	10,000,000	25,000,000	Muller

[a] On May 21, 1956 Glass wrote to Weaver indicating that his minimum estimate was in error and should be 200,000 rather than 100,000. He stated that the reason for the error was that he based his estimate on 1 r rather than 10 r in his calculations. He stated that his most probable and maximum values were correct. Coincidently, Crow (1956d) wrote to Muller on that same day (May 21, 1956) with copies to Weaver and Glass indicating that Glass's minimum estimate needed to be adjusted to a 10 r exposure (rather than 1 r), which when normalized to a population of 10^8, his value was 100,000, the same as Glass originally reported. No changes were needed for his most probable and maximum values. Thus, the memo of Crow did not agree with the recommended change in damage estimate of Glass. This technical point was not resolved since the Panel decided not to provide the Table in their final report/ Science paper based on a vote by the Panel on May 29, 1956. Note that Glass received the copy of Crow's letter as it was in his files. Glass's May 21, 1956 (Glass 1956) letter explanation seems unlikely as his original genetic damage estimates included values for both 1 and 10 r, with the expected 10-fold damage difference.

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