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Review article

Cover up and cancer risk assessment: Prominent US scientists suppressed evidence to promote adoption of LNT

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ABSTRACT

This paper reports that William Russell, Oak Ridge National Laboratory (ORNL), conducted a large-scale lifetime study from 1956 to 1959 showing that exposure of young adult male mice to a large dose of acute X-rays had no treatment effects on male and female offspring concerning longevity or the frequency, severity, or age distribution of neoplasms and other diseases. Despite the scientific, societal and crucial timing significance of the study, Russell did not publish the findings for almost 35 years, nor did he inform governmental advisory committees, thereby significantly biasing decisions made during this period which supported the adoption of LNT for risk assessment. Of further significance, Arthur Upton, an ORNL colleague of Russell during this study and later Director of the US National Cancer Institute (NCI), was also fully knowledgeable of this study, its findings and its negative impact on the acceptance of LNT. Upton later worked along with Russell to publish these data (i.e., Cosgrove et al., 1993) to dispute the case-specific claim that children developed cancer because of the radiation exposure of their fathers as workers at the Sellafield nuclear plant. Thus, while Russell's data were available, but were not used to challenge the key radiation and leukemia paper of Edward B. Lewis, (1957) when LNT was being adopted by regulatory agencies, they were used in a major trial in the United Kingdom (UK) for the client (i.e., British Nuclear Fuels Plc) that hired Upton. While the duplicity of Russell's and Upton's actions is striking, the key finding of the present paper is that Russell and Upton intentionally orchestrated and sustained an LNT cover up during the key period of LNT adoption by regulatory agencies, thereby showing an overwhelming bias to enhance the adoption of LNT.

1. Introduction

Over the past decade, one of us (EJC) has published a series of papers that document the occurrence of numerous scientific errors, striking ideological biases at the highest scientific levels, and deliberate misrepresentations of the genetic toxicology research record, with a goal to establish and sustain the linear non-threshold (LNT) dose response model for cancer risk assessment. These numerous irregularities and falsifications of the research record now serve as the historical foundation of cancer risk assessment in the US and worldwide (Calabrese, 2011, 2012, 2015a,b, 2016a,b, 2017a,b, 2018a,b, 2019a,b,c, 2020, 2021a,b,c). Despite being founded in 1970 and now more than five decades in operation, the United States Environmental Protection Agency (US EPA) has served as an unwitting vehicle to implement such scientific deceptions due to its failure both to explore the historical foundations of cancer risk assessment, much of which occurred prior to its creation, and to take action to correct the errors once the ramifications were understood (Table 1). The present paper reveals a new and a pivotally significant cover up of key scientific findings, which is disturbing because the covered-up findings may well have prevented the acceptance of LNT

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in the critical period of the late 1950s to early 1960s, during which LNT came to be adopted by major scientific and regulatory advisory committees. The "discovery" of this new information occurred following recent discussions between Selby and Calabrese concerning the research career of Selby at ORNL which extended from his undergraduate involvement in 1966 to receiving a Ph.D. in radiation genetics under William L Russell in 1972, and his employment at ORNL following a three-year postdoc in Germany, and then a 20-year period working under the direction of William Russell's wife Liane, which was followed by more years of working in environmental risk assessment and toxicology while still at ORNL. These discussions extended earlier information exchanges between us that led to previous publications by Calabrese (2016a, 2016b) showing that a flaw in the Russells' reporting of their research results, with regard to a type of clusters of spontaneous mutations that ensured overestimation of risks from radiation-induced mutations, likely played an important role in the adoption of LNT by the Biological Effects of Ionizing Radiation (BEIR) I (National Academy of Sciences NAS/National Research Council NRC, 1956) Committee. These flaws in the reporting of the Russell research are important because the NAS BEIR I committee was created in 1970 by the US Federal Radiation Council (FRC) (itself created in 1959) to guide the US federal government on the health risks ostensibly associated with ionizing radiation. However, later that same year, President Richard Nixon abolished the US FRC, transferring its functions to the newly created US EPA. Thus, the NAS BEIR I Committee would then provide its recommendations on cancer risk assessment and radiation to EPA. In 1972, BEIR I offered its recommendations, which supported the adoption of LNT and thereby extended the recommendations of the Biological Effects of Atomic Radiation (BEAR) I Genetics Panel some 16 years earlier, although they acknowledged the critical error of that 1956 BEAR I Genetics Panel, which had rejected the concept of a dose rate effect resulting from the repair of radiation-induced mutations. The 1972 BEIR I Genetics Committee was chaired by James Crow, a member of that BEAR I Genetics Panel. In 1975, EPA (EPA, 1975) formally adopted the LNT recommendation, citing the significance of the Russell mega-mouse radiation studies as foundational in this decision (see Calabrese, 2019b).

The present paper does not discuss the substantial literature on the flawed historical foundations of cancer risk assessment. Instead, it documents an important case of a long-lasting scientific cover up by William Russell starting in 1959 that helped to ensure the rejection of the threshold dose response model in favor of the LNT.

2. Discovery of the cover UP

During recent conversations with Calabrese, Selby mentioned that he had testified in a major litigation (i.e., Hope and Reay vs British Nuclear Fuels Plc (BNFL) in the UK in 1993 concerning radiation and cancer risk assessment.[2] It is now understood that the process of potential Selby involvement began when Professor Arthur Upton, New York University (NYU), was visited by representatives of BNFL concerning this litigation. In that case, BNFL was being sued by Plaintiffs concerning cancers in the children of fathers who had been exposed to ionizing radiation decades earlier while working at a facility that was being operated by BNFL at the time of the lawsuit. In the course of his conversation with the team from BNFL, Upton revealed the existence of the unpublished Russell 1959 study, its findings, significance and relevance to the litigation. It seemed to be a perfect fit for the Defendants. Here they had "new" findings that could impact the outcome because the case involved cancers in the offspring of fathers occupationally exposed to radiation, and the unpublished results were said to be uniformly negative. This information led to BNFL sending a team to visit William Russell at ORNL.

An event about two years earlier is important for understanding how Selby became involved in this matter. Dr. Shirley Fry of Oak Ridge Associated Universities (ORAU) called Selby (PBS) in the spring of 1990 to see what he thought about the Gardner hypothesis regarding increased leukemia and lymphoma among young people near the Sellafield nuclear plant in West Cumbria, UK. Although Selby had been actively involved in hereditary risk estimation since 1977, he only rarely read any scientific papers related to epidemiology and knew nothing about the Gardner publications (Gardner et al., 1990a, 1990b). However, having just submitted a detailed critical review (Selby, 1990) on the induction by radiation and chemicals of dominant mutations in mice, which included rather detailed reviews of numerous experiments that claimed to show effects on cancer and longevity in first-generation progeny, Selby expressed interest in looking into the matter. This contact resulted in a seminar that he gave at ORAU on June 13, 1990, entitled "Paternal irradiation and childhood leukemia: Are the epidemiological findings in the Sellafield Study biologically plausible?" He concluded that the Gardner hypothesis was not biologically plausible and described numerous research findings (including several of his own related to the induction by ionizing radiation of dominant mutations affecting the mouse skeleton) upon which his opinion was based. William Russell was aware that he gave this seminar as well as with the contents of his long historical review of the subject.

Sometime around late February of 1992, Russell told Selby that a team of lawyers and scientists from BNFL would be visiting him in a few weeks, specifically on March 9. Russell said that Arthur Upton was working as an expert witness for BNFL in a lawsuit and had told this BNFL team about an experiment that Russell had done long ago, and they had become so interested in it that they were coming to Oak Ridge to meet with Russell. Because Russell had also learned from Upton that the lawsuit was somehow related to the claims of Gardner, Russell asked Selby to give the BNFL team essentially the same talk that he had given at ORAU in the summer of 1990. He told Selby to present mainly the details as to why he considered the Gardner hypothesis to lack biological plausibility and indicated that he doubted that the visitors would be interested in any parts of Selby's research other than those directly related to the question of biological plausibility.

A complication in travel plans delayed the meeting until May 10, when the BNFL team consisting of three lawyers and two scientists met with Russell and Selby in the conference room of the Mouse House at ORNL. Russell first told the group many more details about the experiment completed in 1959 and answered their questions. He also told them that he had been in contact with Gerald Cosgrove, who was the pathologist who examined the mice in the study after they died, and that he, Upton, and Cosgrove were willing to prepare a paper for publication on which they had begun working. He noted that Cosgrove's involvement would be minimal because of serious illness. Selby then gave the talk that Russell had requested. This meeting was Selby's introduction to Russell's experiment conducted between 1956 and 1959 that failed to confirm the strong conclusions that Russell had reported in his 1957 paper concerning the effects of radiation on longevity in a mouse model. As Russell would have known, Selby had briefly mentioned that Russell

[2] On October 8, 1993, the High Court of Justice in London ruled that the evidence was "decisively" against preconceptional irradiation being a material contributory cause of infant leukemia and non-Hodgkins lymphoma in young adults, whose fathers had received comparatively large preconceptional doses at the Sellafield nuclear installation in West Cumbria, England. The findings of this case were reported by Wakeford and Tawn (1994) in considerable detail. Of relevance to the present paper was a summarization of the testimony of Selby for the Defendants concerning the Cosgrove … Russell (Cosgrove et al., 1993) paper. Also, there is substantial documentation regarding the testimony of Upton for the Defendants.

1957 paper in two long reviews that he had published dealing with mutational research in mice (Selby, 1981, 1990).[3]

During that meeting on March 10 it became apparent that the Gardner hypothesis was central to the arguments made by the Plaintiffs in the case and that arguments about biological plausibility would be of considerable importance. The BNFL team was also concerned about arguments that they expected the Plaintiffs to use related to the extensive research of Taisei Nomura, and they were particularly interested that Selby had provided some criticisms of Nomura's experiments during his talk. The BNFL team eagerly tried to get Russell to agree to serve as an expert witness for them, along with Arthur Upton and other well-known scientists. However, Russell said that, even though he was willing to help by preparing the desired paper, he was unwilling to work for them as an expert witness. The BNFL group indicated that there was more to discuss and asked to continue the meeting the next day. On that second day, they asked Selby if he would be willing to work as an expert witness. With no indication of disapproval from Russell, and having had a fascinating and positive experience in 1979 as an expert witness in an evidentiary hearing related to hereditary effects of radiation, Selby agreed to work as an expert witness as long as the Administration of the ORNL Biology Division would approve his working on the case outside of his regular job, which it did. Russell's willingness to have Selby become involved may have been influenced by the obvious interest he had shown in hearing Selby's accounts of happenings in that earlier legal action.[4]

It is now known from documents in our possession that Upton first contacted Russell in 1991 (probably late that year) to tell him about his involvement with BNFL in the court case and to urge him to publish the results of his experiment with Cosgrove. Cosgrove had moved to California decades earlier but had maintained contact because he and Russell had been friends. Russell communicated with Cosgrove by phone once in late 1991 and again in early 1992 (Russell, 1992). Some correspondence regarding the old experiment was exchanged between Cosgrove and Russell and also between Cosgrove and Upton in the weeks before and after the beginning of 1992. Also, some type of table along with a summary of the old study was released by Upton and Russell to BNFL before the meeting of the BNFL team with Russell and Selby at ORNL in March 1992. The Plaintiffs were also given some of this early information as was necessitated by disclosure requirements for court proceedings. The preparation of the manuscript, however, proceeded slowly during 1992, partly because of the time required for Russell to care for his wife, who had a serious health issue that year. A letter sent from Richard Wakeford (the epidemiologist on the BNFL team) to Selby on July 2, 1992, asked him to urge Russell and Upton to hurry up with the paper and stated that the paper will be a "body blow" to the Plaintiffs' genetics case. Cosgrove died on August 20, 1992. Patrick Pennal (the lead solicitor in the case for BNFL) wrote to Russell on December 4, 1992, urging him to hurry to complete the paper because the trial was proceeding faster than expected. The Defendants considered it essential that the paper be submitted for publication before Upton was called to testify, which was expected to be on March 1, 1993. In early February 1993, Russell and BNFL both urged Selby to assist in helping to speed up the preparation of the manuscript, and he became involved in the analysis, in the typing of revisions, and even at one point had an extremely long conversation by phone with Upton.[5] A February 19, 1993, faxed letter from Pennal to Selby, that was shared with Russell, highlighted the urgency of having the paper submitted by the time Upton was to testify on March 1, 1993, and stated that it would be helpful if Selby could be added to the paper as a co-author. (He would be testifying a few months after Upton, and Pennal thought that because of possible problems with getting the paper submitted on time, it might prove helpful to have Selby listed as an author so that he could testify in regard to the paper.) On Friday, February 26, Selby faxed Pennal a copy of the submitted manuscript that would be mailed within a few hours to Michael Shelby, an editor of *Mutation Research*, along with assurances to Pennal that because that editor lived in the adjacent state of North Carolina, Pennal could safely assume that the manuscript would be officially submitted on March 1, 1993, which was now definitely known to be the day of Upton's testimony. When Russell gave Selby the final manuscript, Russell told him that he had made him the second author because of the crucial role that he had played in getting the paper ready by the deadline, and that is how Selby came to be an author of a paper that reported an important experiment which had been conducted when he was between 11 and 14 years old.

It is unknown whether Russell was paid by BFNL for his considerable effort in getting that old experiment published or whether he just did it as a favor for his longtime friend Upton, or possibly because he somehow now felt obligated to let the public know about that experiment. He obviously considered the results important and relevant and seemed genuinely interested in making them public, and he clearly realized the importance of submitting the paper in time to be of maximum benefit for

[3] Selby had presented and discussed a long review by Green (1968) in which Russell's 1957 report of a decrease in life span was listed as one of a great number of experiments with the goal of determining the extent of damage to populations caused by irradiation. Green had concluded that while most of those experiments showed no effect, application of the studies that did show effects was uncertain for numerous stated reasons. Selby included the following cautionary quotation from the Green review, which he considered particularly relevant: "the generally negative results of these studies may be due to the nonexistence of induced mutations having only moderate individual effects in heterozygotes, to the failure to find the right indicator trait, or to relatively small sizes of the experiments so far conducted and their relative lack of power for discriminating small genetic differences in the presence of large amounts of nongenetic variability."

[4] A summary of the Class Action complaint can be found at https://law.justia.com/cases/federal/appellate-courts/F2/621/578/184958/. Before Selby became involved in that evidentiary hearing, Wilson Horde, the head legal counsel of Union Carbide, the contractor at the time for ORNL, called Selby to request that he set up an urgent meeting (with an unstated agenda) with him and Russell. At that meeting, Horde said that the U.S. Government was one of the numerous Defendants in a large class action lawsuit that involved serious hereditary effects. He knew nothing else about the case, but he had been given a short list of experts in the field, on which Russell and Selby both appeared. He asked if Russell and Selby would be willing to help the U.S Government as expert witnesses. Russell said that he was not willing. Selby's only question was what would happen if, when he learned the details, he agreed that the Plaintiffs were correct. Horde assured Selby that because the Government was the Defendant, in that instance the Government would try to negotiate a fair settlement. Selby, with Russell having no apparent problem with Selby becoming involved, then agreed to call the number provided to find out what the case involved. He soon learned the details of the lawsuit and became heavily involved including submitting two affidavits and assisting Department of Justice lawyers for 9 days during their cross examinations, which helped to discredit the Plaintiffs' case. Incidentally, the results of Russell's experiment completed in 1959 would also have been highly relevant to that earlier trial if they had been available.

[5] During this whole process, and even though Upton visited Russell once to work on the manuscript in person, Selby's only contact with Upton was by phone and faxed letters.

the Defendants.[6]

The reason for the historical reawakening of the 1959 Russell research was that the data were uniformly negative, with no adverse effects reported, and that they could become pivotal during the case, especially given both the study's relevance and its uniquely "surprise" nature to an unsuspecting Plaintiff. However, the data needed to be published in a top journal to be maximally useful. Thus, nearly 35 years following the completion of the study in 1959, Russell and his colleagues, including Selby and Upton, published it in *Mutation Research*, in 1993.

During the course of several long phone and zoom conversations between the two of us (Calabrese and Selby) over the past few years, Selby on a few occasions, in passing, mentioned his involvement in a trial in England in 1993 and the curious fact that an experiment of importance in the trial resulted in his becoming one of the authors of a paper that reported on an experiment that began when he was in grade school. When this was mentioned, and likely not the first time, I (Calabrese) became curious and asked for the reference. By reading that 1993 paper and seeing what the study was about, I was immediately struck by the fact that this experiment was started in 1956 at the time of the BEAR I Genetics Panel meetings and finished in 1959. I realized that the study was substantial, had excellent pathology, high statistical power and other impressive features. In fact, that a paper developed in the 1950s could pass peer review at a top journal in the 1990s was an indication of its quality. However, it was now clear that Russell had never published this substantial study on key public health endpoints such as longevity and cancer. This study would have been considered one of the most relevant and substantial of the 1956–1959 era had it been published. This led me to wonder why this significant study had not been published, especially since it was undertaken by a US national lab, with public financing, and thus with the public having the right to be made aware of the results. Even though this represented a major finding, one that could have enlightened debate on the reasonableness of assuming LNT as well as numerous other scientific questions, it had no impact whatsoever at the time because Russell did not publish his findings until 34 years later (Cosgrove et al., 1993), and there is no evidence that he shared his findings with members of the BEAR Committee or with any other advisory committees or even with colleagues at ORNL. Given its practical and research importance, Russell had a responsibility to try to get it published, unless there were scientific flaws. So why didn't Russell publish this study?

To better understand the situation, it may be helpful to provide some context [drawn mainly from three sources (Rader, 2006; Krause, 1980; Hewlett and Duncan, 1969)] for this experiment that was not reported until decades later. Much of what follows would not have happened without the vision and leadership of Alexander Hollaender, who immigrated to the USA from Germany as a child with his family after World War I, returned to his homeland for college, and then returned to the USA for good after the 1925 elections in Germany in which Hindenburg (and by extension, Hitler) would come to power. In 1946, Hollaender was offered the opportunity by the U.S. Surgeon General to develop the biology program at post-war Oak Ridge, Tennessee, in the ruins of what was then called The Clinton Laboratory. He was offered a temporary position as the director of the new Biology Division. Hollaender had experience with the radiation genetics of *Drosophila*; however, soon after moving to Oak Ridge he decided that there should be a big project since, as he put it "in the long run, it was absolutely essential that we prove whatever we found on mammals which are close in comparison to man." With the empty buildings available to him[7] and connections that he had, he believed that such work could be done at Oak Ridge. Early in 1947, he happened to hear that a promising young geneticist named William Lawson Russell was needing to leave The Jackson Laboratory, and he established contact with him. Russell was needing to find a job somewhere else because he had gotten himself into an awkward situation involving a messy and professionally contentious situation that would end in his divorce from Elizabeth (Tibby) Schull Russell in September, 1947.[8] He applied for positions at some universities as well as at the Biology Division, where he visited Hollaender, probably in early 1947, and pitched his proposal for what he called the specific-locus test (SLT) for studying whether there was induction of recessive mutations at seven genes in mice by X-rays. Hollaender was impressed by Russell and by his proposal and thought that, if it worked, it would be advantageous for the Atomic Energy Commission (AEC) genetics program as well as for basic genetics research. In October 1947, Hollaender presented Russell's plan to the AEC's Director of Research as an "effort to obtain information on the possible genetical implications of bomb explosions," and he concluded confidently: "we believe the information can be obtained."

Nonetheless, Hollaender also clearly recognized the risks[9] involved in undertaking such a massive experiment, and before committing AEC resources to such a project, he subjected Russell's proposal to peer

[6] A set of preserved letters provided by Selby indicates that Upton was in possession of some of the computer files of the Cosgrove et al. (1993) study data during an early meeting with the BNFL representatives. This suggests that Upton had either obtained these data files while he was employed at ORNL and retained them over about 35 years, or possibly that they had been sent to him by Cosgrove after Upton became involved in the litigation. At that time, the longevity, but apparently not the autopsy records, were in possession of Russell. The letters indicate that the first choice for a journal was *Proceedings of the National Academy of Sciences (PNAS)* but there was concern over whether it would publish data that was over three decades old. There was also concern over the fact that technical requirements for tables and figures were quite high with PNAS, and it might take too much time to meet those requirements, thereby delaying submission until after Upton's testimony. It was also learned from a discussion with Michael Fry, who worked in the Biology Division and was the Editor of the journal *Radiation Research*, that *Radiation Research* would not be likely to give this manuscript a special publication priority. There was the suggestion of asking Upton to use his influence with Fry in an attempt to make this happen. In the end, Russell decided to submit the manuscript to *Mutation Research*. Michael Shelby, one of its editors, was a friend of Russell and his wife and provided much financial support for ongoing specific-locus experiments on chemicals as well as other research in the Biology Division. There was much strategizing about publication. It should also be noted that Upton cited the Cosgrove et al. paper in his written testimony (i.e., his expert report), in which he cited a preliminary version of the paper with a 1992 date.

[7] In the old Y-12 area of the Oak Ridge facilities during the Manhattan Project, there were several large buildings that the Manhattan District had hastily constructed in 1945 for the chemical extraction of uranium 235 but had never used. The Contractor, Union Carbide, which had become responsible for the Y-12 area, urged Hollaender to take the buildings off of its hands. By the end of 1946, Holaender, who by then had decided that he wanted to stay in Oak Ridge, had drawn up a comprehensive research proposal for the new Biology Division of the Clinton Laboratories (Hewlett and Duncan, 1969), and he had likely already begun to think that one of those large buildings could house a huge mouse research facility.

[8] The month during which Russell's divorce from Tibby Russell occurred, and the need for William Russell to leave the Jackson Laboratory, were both made clear in a letter from C.C. Little, William Russell's boss at the Roscoe B. Jackson Laboratory, to Dr. M. Demerec dated August 5, 1947. Tibby Russell, William Russell, and Liane Brauch, whom Russell would soon marry, all eventually became members of the National Academy of Sciences.

[9] As stated in the book Atomic Shield—A History of the United States Atomic Energy Commission, Volume II (Hewlett and Duncan, 1969), "The prospects of bringing Russell to Oak Ridge were interesting, but there was a real gamble involved in the mouse project. Even Russell could not deny the difficulties of genetic experiments in mammals. To provide reliable results, the project would have to be the largest mouse experiment ever undertaken. That would mean high costs, a considerable fraction of the division's budget. It might take ten years to get results, and a failure after that investment might well destroy all of Hollander's plans for Oak Ridge. Many geneticists thought that the project was much too difficult and that they had already acquired all the essential data in experiments with Drosophila. Others saw the future of genetics in studies of microorganisms."

Table 1
LNT Chronology: From mutation to cancer risk assessment (Based on Calabrese, 2019b).

Statement	Year
Muller report on X-ray induced mutation in Science	1927
Oliver (Muller student) dissertation showing linear dose response for radiation induced mutations	1930
Muller proposes Proportionality Rule	1930
Timofeeff-Ressovsky et al. propose single hit model and link to Muller's linear dose response mutational data	1935
Ray-Chaudhuri (Muller's student) dissertation supports total dose/linear theory	1939
Manhattan Project-genetic mutation study starts at U. Rochester with Curt Stern directing project	1943
Ernst Caspari's data support threshold rather than linear dose response	1946
Stern published Warren Spencer and Caspari papers in Genetics	1948
Stern and Uphoff publish mini-meta analysis of Manhattan Project mutation research in Science	1949
National Academy of Sciences BEAR I Genetics Panel	1955–1956 recommend switch to LNT, 1956
NCRP applies LNT model for cancer risk assessment	1958
William L. Russell (Oak Ridge National Labs) published first evidence of dose rate for mutations with ionizing radiation, suggesting the existence of DNA repair	1958
NAS BEAR II Genetics Panel, report acknowledges dose rate in mouse and Drosophila	1960
NAS creates BEIR I (1970) which retains LNT while rejecting total dose; it switches to use of Russell mouse data from fruit fly reliance.	1970
EPA adopts LNT based on the use of the Russell data	1975
Paul B Selby reports error in Russell control group in 1995; error confirmed by the Russells and corrected in the scientific literature separately by Russells and Selby	1996 and 1998
Calabrese applies Russells' and Selby corrections to BEIR 1972 risk assessment and reports that a threshold or hormesis response would have been reported if the control group error had been detected and corrected at the time of BEIR I	2017

review by two famous geneticists whose opinions he valued, namely H.J. Muller and Sewall Wright. Probably a few days before Thursday, October 23, 1947 (significance of date to be explained below), and a few days after Russell and Liane[10] had been helping to fight the huge forest fire then raging on Mount Desert Island near Bar Harbor, Maine, Russell was in Oak Ridge to attend this fateful meeting with Hollaender, Muller and Wright[11]. In discussions between Russell and Selby during the almost 25 years when they were close friends and colleagues, when they would often discuss applications of Selby's experiments on dominant mutations affecting the mouse skeleton to hereditary risk estimation, Russell would sometimes refer to that meeting in October of 1947. Russell said that at that meeting Sewall Wright (who had been Russell's Ph.D. dissertation advisor at the University of Chicago) argued that the most important experiment needed to provide meaningful evidence of hereditary risk in humans should involve some type of damage to the health of mice in the first generation after the radiation exposure. Selby does not know what, if any, specific types of damage Wright might have suggested; however, it is obvious that such an experiment would involve looking for effects relevant to humans caused by radiation-induced dominant mutations.[12] Russell said that he agreed with Wright; however, he countered that, with the level of understanding about induction of mutations by radiation in mice at that time, it was very uncertain how a successful experiment of the type preferred by Wright could be done. He pointed out that he had already developed stocks of mice in preparation for the large-scale specific-locus experiment that he was proposing, and that his proposed experiment would provide a good chance of determining whether recessive mutations were being induced by X-rays in mice, as they had been in *Drosophila*. He suggested that if he was successful in demonstrating convincingly that X-rays did induce recessive mutations in mice, an effort could then be made to proceed along the lines of what Wright had suggested should be done first. Wright then agreed with the possibilities of Russell's proposal and urged Hollaender to proceed. Muller was slower than Wright to appreciate the possibilities of Russell's proposal, but he did eventually give his enthusiastic support, even telling Hollaender that he should try to get an animal facility three times the size of Russell's initial request. With the support of these two famous geneticists, Hollaender then persuaded the AEC to support the project. Once he had a commitment from the AEC, Hollaender hired Russell to set up a large mouse research program at Oak Ridge. One condition insisted upon by Russell before accepting Hollaender's offer was that Liane also be hired even though she was years away from earning her Ph.D.

Hollaender was courageous to proceed in this way because, as he noted: "Muller and Wright were the only two geneticists who backed the mouse genetics study. The rest of the geneticists thought we were wasting our time and money!" A noteworthy and tragic event occurred soon after that meeting. On the morning of October 23, the strong wind shifted and blew the fire rapidly toward Bar Harbor, Maine, where most of the city as well as the Jackson Laboratory were destroyed. All of Russell's research records were entirely destroyed[13] as well as all of the stocks of mice that Bill and Liane Russell had prepared to allow the

[10] William and Liane Russell were married on September 23, 1947.

[11] This meeting thus involved four of the 16 members of the historically important US NAS/NRC Biological Effects of Atomic Radiation (BEAR) I Genetics Panel.

[12] It is obvious that some types of dominant mutations would not have been what Wright had in mind as being useful for estimation of damage occurring from induced mutations already in the first generation after exposure, which is usually considered to be the generation for which a risk estimate is most needed. For example, dominant visible mutations have been reported in many experiments after, and even before, Wright's opinion was given. Russell (1951), as an example, is one of many geneticists to explain why frequencies of induction of dominant visible mutations in mice cannot be used reliably to estimate hereditary risk of radiation exposure in humans. Examples of types of dominant mutational damage that have been applied by committees in attempts to estimate hereditary risk in humans already in the first generation are skeletal malformations (United Nations Scientific Committee on the Effects of Atomic Radiation [UNSCEAR] Scientific Annexes in 1977 and later) and cataracts (UNSCEAR Scientific Annexes in 1982 and later).

[13] Before the fire burned down his office at the Jackson Laboratory, the scientist with whom Russell shared that office managed to move all of his own files to a safe location. Russell attributed the fact that scientist did not also rescue Russell's records to that scientist being upset with him about the divorce because he was a friend of Tibby Russell. As explained elsewhere (Selby, 2020), the fact that Russell had once lost his records in a fire was likely a reason why the Russells computerized a large portion of their SLT records in the mid-1960s. Had they not done so, the circumstances almost certainly never would have occurred that led to Selby's discovery of the complication about FCGM clusters in the Russells' SLT data, which is discussed later.

proposed SLT experiment get off to a fast start. The Russells moved to Oak Ridge late in 1947 (Krause, 1980).[14]

By 1951, Russell had published the preliminary findings of the first specific-locus experiment (Russell, 1951), thus establishing that specific-locus mutations were induced by ionizing radiation in mice at a frequency many times higher than in *Drosophila*. Within a few years it would be stated that the mutation rate was about 15 times higher in mouse spermatogonia than in Drosophila spermatogonia (Alexander, 1954; Russell, 1981; Krause, 1980). Not surprisingly, in view of such dramatic findings, the program in the Mouse House expanded rapidly and, within two decades, vast amounts of information on radiation mutagenesis in mice were gathered and published, with many notable discoveries (Krause, 1980; Russell, 2013).

Just a few years after publishing that X-rays induced specific-locus mutations in mice at a surprisingly high frequency, and undoubtedly influenced by the previously referenced early discussion with Sewall Wright, Russell did an experiment that looked for a possible effect of radiation-induced dominant mutations on the longevity of the offspring of irradiated male mice. To make the experiment especially applicable to radiation from atomic bombs, the partially shielded mice were exposed to neutron and gamma radiation from a nuclear detonation. It was in February of 1953 when William Russell and a co-worker drove the mice to the Nevada desert where they were exposed to radiation from an above-ground bomb test. During transit to the desert, the mice were held in cages arranged on a plywood structure constructed to fit on the floor in front of the back seat of a Ford sedan. When the bomb was detonated, the mice were in the air-conditioned interior of 7″-thick lead hemispheres placed on the desert floor at various distances from the bomb tower. After the mice were retrieved, William Russell brought the mice back to Tennessee in a military plane (Russell LB, 2013). Dosimetry was reported in units of rep,[15] with this unit being approximately equal to 1 rad. Although huge sample sizes are needed when looking for mutations at only 7 genes, Russell thought that there might be so many genes affecting longevity that huge samples might not be needed. After determining how many days the first-generation offspring of the irradiated (5 dose levels) and unirradiated control mice lived, a regression analysis provided strong evidence of shortening of life in the offspring of exposed males, $P < 0.01$ (Russell, 1957). Russell suggested that his results were so extreme that it "seems quite possible that shortening of life is an effect that might be detectable in studies of the offspring of exposed parents in human populations." He referred to the 1956 BEAR I Genetics Panel Report and stated that "no data of this nature were ready for consideration prior to the writing of the 1956 report of the National Academy of Sciences Committee on Genetic Effects." Feeling justified in making an extrapolation of his results to predict risk in people, he argued that a comparable decrease in the lifespan of a human would be 20 days/rep with 95% confidence limits of 5–35 days/rep. He also stated that the shortening of life in first-generation progeny was almost the same as that in the exposed mice themselves—a remarkably bold claim—and that such dominant mutations affecting longevity "would, to a certain, and probably large degree, be transmitted to later generations." Sewall Wright was the member of the National Academy of Sciences who communicated Russell's (1957) paper for publication on January 31, 1957. Such claims should have seemed much more alarming to those estimating hereditary risk at that time than any other data then available on rates of induction of recessive mutations in mice, flies, or other organisms. Before this paper was submitted, Russell in collaboration with Cosgrove (whose supervisor was Upton) initiated the much larger follow-up experiment, the subject of this paper.

The period of 1955 to the early 1960s would prove to be transformative for cancer risk assessment. Most critical during this period was the highly influential publication of the NAS BEAR I Genetics Panel (National Academy of Sciences NAS/National Research Council NRC, 1956) that recommended a switch from the threshold model to LNT. There is no indication that Russell's experiment on longevity published in 1957 was discussed at the meetings that resulted in the BEAR I report. Russell probably was not far enough along with the study to discuss it at that time. The BEAR I report (National Academy of Sciences NAS/National Research Council NRC, 1956) received enormous publicity and was widely distributed. It was also eagerly anticipated by multiple high level national and international advisory committees, such as the National Committee on Radiation Protection (NCRP) and the International Committee on Radiation Protection (ICRP), which soon lowered recommended exposure standards for ionizing radiation for workers and the general public by about 2/3 (Walker, 2000). These developments then led to the US Congress holding hearings on health concerns of ionizing radiation, involving most of the BEAR I Genetics Panel members and Edward B. Lewis who had become an important figure following his paper in *Science* that had received a strongly supportive editorial (DuShane, 1957). The Hearings converged in time with a new paper by Lewis (May 17, 1957), occurring in early June 1957. The Lewis paper was the first cancer risk assessment for radiation and leukemia that was based on the analysis of multiple exposed groups, which ranged from victims of the bombings in Japan to patients treated with X-rays and even radiologists themselves, and with all groups showing enhanced risks of leukemia that Lewis claimed followed the LNT dose response model. Lewis argued that he had provided the necessary link between his work and that of the BEAR Panel, using a mutational mechanism based on Drosophila research (Uphoff and Stern, 1949) that would underlie the linear dose response features of his cancer risk assessment. The 1957 testimonies of the BEAR members and Lewis would be followed by a second round of Congressional Hearings in 1959 in which the LNT conclusion would be even more strongly asserted.

William Russell was also active in the Congressional sessions, offering his own unique expertise with his massive mouse studies from ORNL. In addition, Russell and several other members of the BEAR Genetics Panel would serve as advisors for the NCRP and the new federal organization called the Federal Radiation Council (FRC) (Walker, 2000). In fact, in 1961 (published in 1962) the FRC would adopt the LNT perspective for radiation, offering risk estimates. In that report, the FRC stated that "Much available evidence indicates that **any** (emphasis added) radiation is potentially harmful … …it is virtually certain that genetic effects can be produced **by even the lowest doses**." (emphasis added) based on the advice of Russell and his other geneticist colleagues, with all acknowledged by the FRC, 1961). For example, the Federal Radiation Council (1962) provided the estimated number of children that would be expected to develop fallout-induced birth defects and malignancies over the next 70 years.

Of importance at this 1956–1960 time period is that two major studies were completed that challenged the LNT recommendation of the BEAR Panel and the Lewis (1957) cancer risk estimates. The first was by James V. Neel, a BEAR Panel member, but also the director of the 10-year-long study on birth defects following the atomic bombings in Japan (Neel and Schull, 1956). The findings involved 75,000 children who were followed for ten years, showing no radiation treatment related effects. Lewis (1957) would ignore these human mutational data in favor of 10-year-old fruit fly data from highly compromised studies in which the flies were exposed to "chronic" doses of irradiation that were

[14] The forest fire destroyed the Jackson Laboratory and its entire mouse population. Several inbred strains were needed to conduct the SLT experiment as well as numerous stocks of mice that carried the mutant alleles at the seven genes of interest, which would be essential for determining if any mutants found in their experiment were actually mutations at the expected locus. After much effort, the Russells were able to import the needed inbred strains from other laboratories; however, their luckiest break came when they found a mouse fancier in Florida who just happened to have numerous stocks carrying the coat color mutations that were most needed for their effort, and he was willing to ship them to the Russells (Russell, 2013).

[15] The Röntgen equivalent physical (rep) is a legacy unit of absorbed dose introduced by Herbert Parker in 1945.

delivered at about a 100,000-fold greater dose-rate than background (Uphoff and Stern, 1949; Calabrese, 2011b; 2019a). Neel gave his study to the BEAR I Genetics Panel at the start of its proceedings in late November 1955 (Calabrese, 2020). In what could only have been a major shock and disappointment to Neel, the NAS BEAR I Genetics Panel, led by Hermann J, Muller, refused to give scientific standing to this massive effort, and it was never reviewed by the BEAR I Genetics Panel. Neel would provide it to a similar Genetics Panel in the UK that formally thanked Neel for sharing the report, praised its scientific value and was guided by its findings in their own risk assessment activities (Calabrese, 2020). Russell clearly would also have been acutely aware of the subsequent intense dispute between Muller and Neel concerning this study, its significance and publication in a major WHO report. So acrimonious had the interactions between Muller and Neel become that Russell's supervisor, Alexander Hollaender, attempted to facilitate a reconciliation between Muller and Neel at the Biology Division in Oak Ridge in January 1957. That attempt proved to be unsuccessful (Calabrese, 2020). Because Russell was present at those meetings, he must have been aware of the hostilities directed toward the younger Neel who was challenging his peers with negative mutation findings. Muller used this debate to threaten Neel's standing and career (Calabrese, 2020). The message that Muller was sending was not lost on Russell.

All of this troublesome controversy was occurring while Russell's experiment with Cosgrove was in its early stages. By sometime in 1959 (likely early in the year in view of the average lifespan of mice and the experiment's start in 1956) it became obvious that the exciting findings published in 1957, which had been communicated to PNAS by Wright, had not been confirmed. Those findings of Russell, which addressed the issue of longevity and cancer risk, would have provided a strong complement to Néel's report. However, as is now known, Russell failed to share these negative findings with the scientific community and continued to promote the LNT agenda of the BEAR Panel. Russell had to have known about the findings of his 600 R experiment with Cosgrove before the 1960 BEAR Genetics Panel Report was published, yet there is no mention of this experiment in that report. Indeed, the following wording appeared near the front of the report in what was said to be a list of important information known at that time: "There is some shortening of life in the progeny of irradiated male mice, as well as in the irradiated mice themselves." It is curious that he permitted that important statement to remain in the report unmodified. So why would Russell not publish these major findings from his study completed in 1959 that provided no support for the strong conclusions that he had drawn regarding longevity in his 1957 paper? What made the negative paper special so that it was set aside, ignored, hidden and/or suppressed (yet not forgotten)?

Some additional perspective seems helpful. In 1951, Russell claimed that his mouse model was significantly more sensitive to the mutational effects of ionizing radiation than the standard fruit fly genetics model. This perspective was supported in follow-up research in showing about a 15-fold difference (Alexander, 1954; Krause, 1980). Russell (1956) used these and related data to argue that the mouse was much more susceptible to induction of recessive mutations than *Drosophila*, thereby gaining considerable attention from other radiation geneticists, including those comprising the BEAR Genetics Panel (Muller, 1963). As noted earlier, most geneticists had considered Russell's effort to be a waste of time and money. The belief that mice were much more susceptible than fruit flies to radiation mutagenesis was materially important to the field, and Russell was off to an impressive start in building a substantial career with a major research program. Hollaender's gamble with Russell appeared to be very successful. The use of a standard mammalian model for human risk assessment purposes was very attractive, compelling and necessary. It became quickly evident that the Russell findings might lead to a major shift away from the reliance on *Drosophila* for estimating human risk, with it giving way to the Russell work with mice. The Russell research was also unique because the SLT required massive numbers of mice, which was research on a scale that could only be undertaken at what was becoming a major government research center such at ORNL. No other location in the US offered such research facilities and only two other locations worldwide undertook such research (UK and Germany) albeit with much smaller operations. By showing the enhanced susceptibility of his model, Russell had achieved a transitionally significant leadership position, a type of changing of the guard in concept and in personal leadership. However, there was a serious problem in the Russell research that had not been disclosed. Russell knew that there were serious undisclosed complications in the interpretation of SLT results caused by the occasional presence of large clusters of spontaneous mutations, with a large one not being reported that had been found as early as his first experiment in 1951[16] (Selby, 2020). The problem was that Russell refused to include these findings in his publications or otherwise disclose them. The issue of unreported clusters of this type in the Russells' historic mouse research became an issue 45 years later within the DOE, resulting in an investigation mandated by the DOE by an external committee with four members that consisted of one scientist picked by each of the following: DOE (with its pick chairing the committee), the Biology Division, the Russells, and Selby. Numerous details about this investigation and about the issue involved are published (Selby, 2020) and the official report of the Ethics Investigation Committee is available upon request (contact PBS). The Committee concluded that the Russells had made a mistake over the entire history of their research in not reporting this type of cluster. Clusters of other types were reported, but perhaps not always, with the reported clusters resulting mainly from treatments that caused such extensive killing of spermatogonial stem cells that the testes were repopulated from rather few stem cells. The Russells were told that they must make the information on those unpublished clusters available. Selby argued that the data from the Russells' experiments, which extended over almost half a century, should be put into the public domain and that there should be an independent reevaluation of their results; however, the Committee agreed with the Russells that they should keep the data to themselves and provide their own analysis of the

[16] The issue of the cluster mutations was first brought to the attention of DOE by Paul Selby who made this unexpected discovery in 1994.–The first male known to sire a large cluster of mutations of the type causing the complication was unirradiated H-stock male 8751. He was born on August 10, 1950, and died on January 12, 1953. The first of many T-stock females with which he was mated was T-stock female 13,803. She was born on September 31, 1950, and put into a pen with H-stock male 8751 on February 8, 1951, and remained there until August 1, 1951. She produced 6 litters, with 35 total offspring being observed for specific-locus mutations. Among them were 8 offspring having the same spontaneous mutation at the *c* locus. Although no mutants were found in her first two litters, her third litter contained 8 offspring, of which 3 males and 1 female had that same mutation. Thus, the Russells knew very early in their first SLT experiment, for which initial results were published in 1951 (Russell, 1951) with no mention of finding a cluster, that their experiment involved a major complication. As noted earlier, this cluster was never associated by them with a mutation experiment until they were forced to disclose it in 1996. In an attempt to better understand the reason for that first cluster in 1951, they began pairing up H-stock male 8751 with numerous other females, starting during the period when T-stock female 13,803 was still in a pen with him. In their standard procedure at that time, there were only pair matings, with females being replaced when they became too old to produce offspring. The 402 offspring that H-stock male 8751 sired included a cluster of 90 mutants. Although FCGM clusters can occur in any mice, experimental or control, H-stock male 8751 was in the control. When Russell (1963) reported that all data for control groups in experiments on males up to that time had yielded 28 mutants among 531,500 offspring, there was no mention of any clusters of any kind in the control in the male or even in vast amounts of SLT data from numerous fractionation and low-dose-rate experiments in both sexes. Interestingly, the word cluster did occur in that paper, but it was in relation to the control for females, with that cluster being the only FCGM cluster that the Russells ever mentioned in their SLT experiments before 1996. It was mentioned with regard to the way in which it complicated statistical comparisons with experimental data.

impact of this complication. Following the Committee's encouragement to do so, Selby (1998 a,b) also published the results of his large-scale computer simulation analysis, which he had made in an attempt to determine the impact of the complication on risk estimation, which he argued could not reasonably be made from experimental data. A summary of some of the curious happenings that occurred after the Ethics Investigation Committee completed its report is found elsewhere (Selby, 2020). The ramifications of the situation appear likely to become more extreme in view of recent insights that the two of us have had.

The Russells promptly completed a massive reanalysis of their data and published it in a paper in PNAS (Russell and Russell, 1996), which was followed by important additional information that was published, without any discussion, in a correction in PNAS (Russell and Russell, 1997). According to the Russells' reanalysis, their estimate of the spontaneous SLT mutation frequency per generation based on their results should be multiplied by 2.2 to correct for the previously unreported clusters that resulted from what they term "masked mosaics" (which Selby refers to as "first cleavage gonadal mosaics" [FCGM]). The spontaneous mutation frequency per generation for specific-locus mutations in mice is of importance for those wanting to use the doubling-dose method of hereditary risk estimation. Other ways to express this 2.2-fold error would be to say that there was an error of underestimation in the spontaneous mutation rate per generation of 120%, or that the Russells reported a spontaneous mutation frequency per generation that was only 45% (i.e., [1 ÷ 2.2] x 100%) of what it really was. Selby's opinion presently is that the error actually was at least 10-fold (i.e., that the Russells' reported frequency was 10% or less of what it really was).

Despite the availability now of the Russell "correction" of the research record, there is really no way to estimate the damage that this continuing error has done to the scientific and regulatory communities, especially organizations like NAS advisory committees and then organizations such as EPA that based recommendations and national carcinogen standards, in part, on the Russell findings. If these hidden data on clusters had been reported at the time they were first observed [at least 3 times before 1960 (Russell and Russell, 1996, 1997; Selby, 2020)], it is unclear what the impact would have been on the interpretation of the Russell data or even on the willingness of funding agencies to greatly expand the mega-mouse research, for which the SLT was always portrayed as a simple and straightforward method of studying mutagenesis in mice. During the years when the program in the Biology Division at ORNL was rapidly expanding, numerous arguments were raging about the interpretation of control data in *Drosophila* experiments, while—as far as the scientific community knew—control data were without complication in the SLT method in mice. General knowledge in 1951 of this complication would likely have substantially reduced the estimates of enhanced genetic risk claimed by Russell using his model (Calabrese, 2016a,b). Using the correction provided by Russell and Russell (1996), Calabrese (2016a,b) showed that the ionizing radiation risk assessment for cancer offered by BEIR I (NAS/NRC, 1972) would have most strongly supported a threshold dose response.

Not publishing the 1959 research on longevity thus marked the second time within the 1950s that Russell withheld important scientific information. In both cases the undisclosed information would have had profoundly important implications regarding the reasonableness of using LNT or thresholds and also on the significance of Russell's research approach. In these two cases there are two different concerns. In the case of his spontaneous mutations resulting from masked mosaics, which would be expected to cause complications in interpreting data in both control and experimental groups, Russell altered the research record by not reporting all the data, which suggests the possibility of research falsification. In the case of Russell not publishing highly relevant findings with regard to the experiment completed in 1959, it appears that he did not want: (1) to provide results that would detract from his bias for LNT, (2) to do anything that might hinder the growth of his research program, or (3) to do anything that would lead to conflict with powerful geneticists such as Muller. Each one of the three appears to be a serious breach of research ethics.

In 1959 the mouse SLT was widely viewed as being a simple and straightforward method for studying variables of importance for understanding radiation mutagenesis in mammals. The conclusion that the mouse was 15 times more sensitive than *Drosophila* was helping to rapidly expand the Russells research program in the Mouse House, and the Russells were known for making numerous important discoveries, with the most striking one probably being the presence of the dose rate effect in male and female mice, which led to Russell's repair hypothesis and the development of a whole new area of research. It was likely both troubling and disappointing to Russell when he realized that his 600 R experiment with Cosgrove had failed to support and confirm the bold conclusions that he had published on longevity in PNAS in 1957. Everything seemed to be going his way, and he may not have wanted to report these negative findings and thus kept them to himself.

There is also another important episode with Russell that has a bearing on his failure to share the 1959 data. In 1960, the BEAR II Genetics Panel had finalized its report, updating developments since 1956. When reviewing the draft report, Russell noticed that his major discovery on dose rate and genetic damage repair (Russell et al., 1958) had not been discussed. He and his supervisor Alexander Hollaender contacted George Beadle, the chair, and were permitted to write an appropriate section on this development for the report. However, Russell was also in possession of the highly significant negative 1959 data but failed to make this known to the BEAR Genetics Panel and neglected to highlight these findings in the report. It is relevant that unpublished developments that were important were noted in that 1960 report, such as Muller's confirmation of the dose rate effects of Russell with fruit flies. Thus, there was no reason to excuse the decision of Russell not to reveal the negative results of his study that was completed in 1959 based on the fact that he had not published the findings yet (Calabrese, 2017b).

In both cases, the actions of Russell had serious and long-lasting implications for cancer risk assessment, strongly biasing a conclusion toward LNT. It is also important to appreciate that Russell was a member of BEAR and BEIR committees and of advisory committees to federal agencies such as FRC while, at the same time, withholding data that was of high relevance. Yet, he would in 1992 authorize the publication of these data when they became relevant to win a court case for the Defendants. In addition, it seems important to note that Upton became the head of NCI at a critical time of LNT implementation within the federal government. During Upton's tenure as Director of the NCI, OSHA (1980) would hold major hearings on carcinogen risk assessment and policy in 1978 and yet Upton, as well as Russell, would never act (until 1992) to make the results of the Russell study completed in 1959 known. A detailed check of the many thousands of testimonial records of the OSHA Hearings indicates that Russell offered no comments while Upton was quite active, especially in his role at the NCI. A review of the Upton testimonies indicates that he repeatedly reaffirmed support for the LNT while never sharing with OHSA his knowledge of the 1959 Russell negative study. For example, in a 1980 paper Upton stated "We should regard any dose of a carcinogen as being capable of contributing some fraction to the total number of cancer cases observed in any exposed population group".[17] Of further interest is that the NAS invited Upton to chair BEIR V which published its report in 1990. The BEIR V committee advocated the use of a linear dose response for solid tumors and a linear-quadratic model for leukemia. Again, while Upton could have used that opportunity to share with another authoritative group his

[17] This 1980 LNT perspective of Upton contrasts with his (Upton, 1961) publication which stated that "it is not yet feasible to define the carcinogenesis or to prove the existence or absence of a threshold dose for carcinogenesis by extrapolation of the dose-response curve from regions of detectably significant dosage."

knowledge of the 1959 Russell study, he failed to do so.

As unusual as this Russell and Upton story[18] appears, it was to become even more bizarre in 1991 when Upton convinced Russell that it was now time to dust off that old study and let the world know about it, which finally resulted in the manuscript that was submitted to Mutation Research on the very day that Upton was in the witness box in the huge trial that went on for months in London. It was published several months later (Cosgrove et al., 1993). That publication helped win the U.K. litigation. Thus, this almost 35-year-old study was of sufficient quality to pass peer-review. This suggests that it may have been an even more impressive study in the 1955–1959 time period if Russell had sought to publish the findings at that time. Certainly, key people such as Russell and Upton appreciated the study's findings and significance even though they were willing to deliberately not publish that information. Statements by Russell written about the time of the trial indicate that he refused to publish the study findings during the decades after it was complete for reasons that could be paraphrased as saying that he felt the general public was not capable of adequately understanding the results and of placing such findings into proper context.[19] Russell's actual words were as follows, as taken from the submitted version of the manuscript**: "It was, therefore, something of a surprise not to obtain a positive result in the experiment described here, and it was feared that publication of a negative finding could mislead the public into a false feeling of safety"**.[20]

Thus, Russell decided that he, and perhaps Upton, would keep the federal tax-payer funded study findings suppressed. However, the UK trial arose and the study data that was presented as evidence challenged assertions made by the Plaintiffs that low doses of radiation might induce heritable mutations that had a large effect on cancer risk in first-generation offspring. Yet, this story, which involved the extremely influential scientists Russell and Upton, is only now being shared with the scientific community, having somehow been missed by the regulatory agencies even though this trial was a major news story for many months in the U.K.

Now that it is understood that Russell's experiment completed in 1959, and finally published in 1993, failed to provide any support for Russell's bold and frightening conclusions presented in his 1957 paper, it is curious to note what Russell (1981) said about that study in a long paper in which he summarized and discussed many of his most important discoveries. He gave the following explanation as to why he never did a follow-up experiment to that longevity study: "As an example, I published one report indicating a shortening of life in the offspring of male mice exposed to neutron radiation from an atomic bomb (19) [Note: this refers to Russell, 1957]. Spalding (43) [i.e, Spalding, 1964] tried to confirm this with a laboratory neutron source and found no effect. I could point out that he irradiated a different strain of mice and a different germ-cell stage, and that the mean lifetime in his controls was much shorter than in mine, indicating a less viable strain or a less favorable environment – either of which might have accounted for the greater variation than in my experiment, and consequently have made it more difficult to detect an effect. But, without further replications, one cannot feel convinced that my results were unequivocally positive. Even if they actually were, the fact that the conditions of another experiment had obscured the effect would still demonstrate the difficulty of using F_1 lifespan as an end point." His statement continues: "Long before the Spalding report appeared, I had decided on the basis of my own experience that vital statistics, such as lifespan, have so much natural variability and are so easily affected by numerous factors, many of which are not under control, that a small increment of damage due to mutation is not easily detectable. Furthermore, even if a clear-cut positive effect on a vital statistic, such as longevity could be demonstrated in the mouse, how would one translate this into human detriment? Therefore, I decided to determine whether it would be possible to score radiation-induced mutations affecting one of the major body systems in the mammal." Russell then went on to describe how he suggested that Udo Ehling attempt to detect dominant mutations affecting the mouse skeleton, and then how Ehling's results led Selby, with Russells' strong encouragement, to considerably advance the study of dominant skeletal mutations.

If no one knew about the results of Russell's experiment completed in 1959, that quotation would seem to be a sensible explanation of why he never followed up on his experiment published in 1957. The quotation is baffling, however, in view of the fact that he did immediately follow up on that experiment in a large and well-done experiment, yet found no support for his earlier bold conclusions. Apparently, when he wrote that 1981 paper, Russell had no intention of ever publishing the Cosgrove-Russell experiment.

3. Final thoughts

The actions of Russell and Upton to have the 1959 research findings published after so many decades to win a case for the Defendant (BNFL), while refusing to act earlier when the health of the public was being debated, is of profound concern. While the behaviors of Russell and Upton are difficult to resolve, what is clear is that their actions appear to satisfy any reasonable definition of a scientific cover-up, preventing the scientific community and leadership advisory committees from pursuing crucial scientific truths. The story here seems to demand that the actions, and the lack thereof by Russell and Upton, warrant significant retrospective ethical, scientific, and regulatory inquiries. While this may await the judgment of history, the new findings also provide key evidence that LNT in its formative stages was the product of an ideological bias along with a significant component of self-interest. The US Congress, the Executive Administration, the scientific community and the general public placed considerable trust in leaders like Russell and Upton to be honest brokers in the search for truth as a means of guiding public policy. However, what society got was a complex and distorted hybrid of self-interest and ideology. The public came to believe these leaders and their messages because they were great scientists in trusted positions … …now we know that society was not served well.

4. Remaining questions

- When Russell submitted the Cosgrove et al. manuscript to *Mutation Research,* what was the response of the editor?
- What did Russell communicate to the *Mutation Research* editor as to the reason for the prolonged delay in submitting the manuscript?
- Did Russell reveal to the *Mutation Research* editor that the reason for publishing the results after so many years was to support one of the parties in a major litigation in the UK?
- Did the *Mutation Research* editor demand answers from Russell as to why he had waited almost 35 years to finally submit the paper?
- What were the comments of the peer reviewers and Russell's responses to those review comments?
- Is it likely that Alexander Hollaender had any role in the decision not to publish results of the key 1959 study?

[18] –this being a story that extended from the beginnings of the Biology Division at ORNL through 1990.

[19] Russell's supervisor at the ORNL during this period was Dr. Alexander Hollaender, also a member of the BEAR I Genetics Panel. It is not known whether Hollaender may have been involved in the decision to suppress the study findings.

[20] The wording from the submitted version of the manuscript is known because (see pp. 79–81) of the transcript from the trial on May 13, 1993. Mr. Spencer, a barrister for the Defendants, when taking the direct testimony of Selby, accidently read into the record most of the introduction in the submitted version of the manuscript before Justice French informed him that the text being read did not agree with the version that he had. Selby pointed out that some revisions had been made to the submitted version before the paper was accepted and that Justice French was reading from the version that was in press, from which Mr. Spencer then read.

- Did Liane Russell, an esteemed geneticist and William Russell's wife, know about his decision not to publish the findings of this 1959 study and its widespread implications?
- Considering the large risk that Hollaender and the AEC were taking in supporting Russell's experiments, including the fear that it might take 10 years to obtain meaningful results, would William Russell have dared to tell Hollaender about his puzzling finding of that large cluster early in 1951?
- At least 3 more definite FCGM clusters were found in other SLT experiments before 1960. How many months or years did it take after the spring of 1951 before the Russells began to understand why such clusters were occurring?

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The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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