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No Validity to No Safe Dose: Part VI – An End to the Linear No Threshold Model of Carcinogenesis

A Commentary by Mark G. Zellmer of Husch Blackwell LLP

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An era in regulatory analysis on carcinogenesis and plaintiff's claims in toxic tort cases should finally be over. For decades, some regulatory agencies and plaintiffs' attorneys and experts have claimed that carcinogens, such as asbestos, will cause cancer at any level of exposure without any threshold of a safe dose. On August 28, 2025, with the publication of the letter of Edward Calabrese and Paul Selby in the journal *Science*, this concept is laid bare of scientific validity and should be coming to an end.¹

In 1927, Hermann J. Muller found phenotypic changes in subsequent generations while conducting experiments in which he subjected male fruit flies to high dose X-rays. Muller published his finding as proof of "artificial transmutation of the gene," or, in other words, gene mutations.² Although Muller's studies used very high doses of radiation, he assumed that the dose response was linear down to a single radiation event at the lowest dose. So began the long and sordid history of the linear no threshold model of carcinogenesis ("LNT"). A full explanation of that history is not the point of this article and may be found elsewhere.³

The LNT model of carcinogenesis postulates that every exposure to a carcinogen regardless of the amount of exposure or the time over which the exposure occurs will increase the risk of

cancer in direct proportion to the amount of exposure. Although science in the 1940s and 1950s followed a threshold view of the risk of cancer from exposure to carcinogens, some scientists substituted LNT, a no threshold view, to explain the risk of cancer from radiation exposure.⁴ In 1956, the extremely prestigious journal *Science* published the work of The Committee on the Genetic Effects of Radiation entitled "Genetic Effects of Atomic Radiation."⁵ This 1956 report provided the basis to switch to a no threshold view of carcinogenesis from radiation. As a result, it is a key moment — if not the key moment — in the acceptance of LNT in a number of regulatory and legal circles. Thereafter, the EPA in the 1970s as well as other regulatory agencies took LNT from radiation science and applied LNT to essentially all carcinogens.⁶ In the process, the agencies admittedly "waved aside" any difference between radiation and other carcinogens.⁷

For years, Edward Calabrese, Professor of Toxicology Emeritus at the University of Massachusetts, Amherst, and others have presented overwhelming evidence demonstrating that LNT lacks scientific validity.⁸ Recently, on August 28, 2025, the argument over LNT took a major turn. Calabrese, along with co-author Paul Selby, at one time a research scientist at Oak Ridge National Laboratory, published a letter in the journal *Science*, the same journal that published the 1956 report.

The letter explained that the evidence is "unequivocal" that the 1956 report was based upon "incorrect data provided by William Russell," a member of the Committee writing the 1956 report. Russell's experiment involved millions of mice, but he badly miscalculated the rate of mutation of the control mice not exposed to ionizing radiation. When the miscalculation was corrected, exposure to radiation only caused mutational damage after the dose exceeded clear thresholds. It becomes clear that it "is long past time to correct flawed regulatory policies and practices that are presently based on the unreliable information from the [1956] report."¹⁰

The significance of this letter cannot be doubted. The publication of this letter is already spreading in scientific circles.¹¹

The terms of the letter are appropriately critical, even unforgiving, of the errors in the 1956 report. This is not any ordinary letter to an editor in a scientific journal; its publication is an acknowledgement of the errors in the 1956 report by the present-day editors at the journal *Science*, the same journal that published the original 1956 report central to the adoption of LNT. The letter is close to an admission by the journal *Science* that the 1956 report should not have been published. Without this 1956 report the concept of LNT would be far less likely to have become a part of the lexicon of regulations on carcinogenesis and legal cases on the cause of cancer.

This letter emphasizes that the attack on LNT must not be truncated for simplicity, but, rather, should include that the origins of LNT arise from the study of radiation because those origins powerfully show that LNT has no scientific basis. For defense attorneys in toxic tort cases, when the cause of cancer is at issue, this letter should be a key part of the attack on LNT.

Endnotes

¹ Calabrese, E. J. and Selby, P. Letter to the Editor: “Mistakes Discovered: Cancer Risk Assessment Challenged.” *Science* (August 28, 2025).

² Muller, H.J. “Artificial Transmutation of the Gene.” *Science* Vol. 66, Number 1699 (1927) at 84.

³ Calabrese, E.J. “The linear No Threshold dose response model: A comprehensive assessment of its historical and scientific foundations.” *Chemico-Biological Interactions*. Vol. 301 (2019) at 6-8; Zellmer, M. “No Validity to No Safe Dose: Part I - The Flawed Linear No Threshold Model of Carcinogenesis.” *Asbestos*, HarrisMartin publications (August, 2021).

⁴ Calabrese, *supra*.

⁵ Committee on the Genetic Effects of Radiation. “Genetic Effects of Atomic Radiation.” *Science*, vol. 123, no. 3209 (June 29, 1956).

⁶ Albert, R. E. “Cancer Risk Assessment in the US Environmental Protection Agency.” *Critical Review of Toxicology*. Vol. 24 (1994) at 75-85.

⁷ *Id.*

“The significance of this letter cannot be doubted. The publication of this letter is already spreading in scientific circles. The terms of the letter are appropriately critical, even unforgiving, of the errors in the 1956 report.”

⁸ See, for example, articles published in *Chemico-Biologic Interactions* 301 (2019).

⁹ Calabrese, Selby letter, *supra*.

¹⁰ Calabrese, Selby letter, *supra*.

¹¹ Goldhaber, S. “The Ripple Effect of Fraudulent Science.” *American Council on Science and Health*.
<https://www.acsh.org/news/2025/09/03/ripple-effect-fraudulent-science-49704> (Sept. 3, 2025).

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