

# **The Linear No Threshold (LNT) Model -- Time for Evidence-Based Cancer Risk Assessment?**

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# Presentation Overview

- LNT role in environmental regulations
- Historical aspects of LNT endorsement & use
- Evidence for radiation linearity
- Regulatory & Economic implications of LNT
- Radiation data
- Chemical data
- Conclusions
- Path forward

# On-going Economic & Societal Consequences of LNT-Driven Regulations

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- The LNT model plays a substantial role in many sweeping environmental regulations
- Staggering economic consequences and costs
- While originally intended for cancer risk assessment LNT now used for non-cancer risk assessment as well
- Many recent, on-going, and future EPA Rulemakings have an LNT-driven component

# EPA Rulemaking Timelines with Likely LNT-Driven Component

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- 2010
  - PM NAAQS
  - SO<sub>2</sub> NAAQS
  - Oil & Gas NSPS & MACT
- 2011
  - Boiler MACT/GACT; New Air Toxics
  - Carbon monoxide & Ozone NAAQS
  - PM NAAQS
  - Refinery Risk Rule
  - Utility Power Plant Risk NSPS

# EPA Rulemaking Timelines with Likely LNT-Driven Component

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- 2012

- PM SIP control
- PM NAAQS
- Secondary NO<sub>2</sub>/SO<sub>2</sub> NAAQS
- Carbon monoxide NAAQS
- H<sub>2</sub>S HAP Listing

- 2013

- Ozone NAAQS
- Refinery MACT/GACT
- Auto/Truck Painting & Polymer & Resins RR Rule
- Iron & Steel Foundries and Aluminum RR Rule

# The On-going Evolution of Chemical & Radiation Cancer Risk Assessment

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- 1940s
  - First use of nuclear weapons
  - Doomsday clock starts ticking
  - Nuclear physicists & biologists declare there is no safe threshold for radiation-induced DNA mutation and cancer
- 1970s
  - President Nixon creates EPA
  - Congress passes Clean Air Act, Safe Drinking Water Act (SDWA) & Toxic Substances Control Act (TSCA)
  - National Academy of Sciences creates Safe Drinking Water Committee (mandated by SDWA)

# The Ongoing Evolution of Chemical & Radiation Cancer Risk Assessment

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- 1977-1980s
  - NAS SDWC debates whether, like radiation, chemicals that damage DNA have no safe threshold for exposure
  - Committee concludes (reluctantly) that chemicals should be treated like radiation
  - “Linear-no-threshold model” (LNT) enshrined as basis for chemical cancer risk assessment
- 1980s to Present
  - EPA uses LNT model for all potential cancer-causing chemicals regardless of whether they damage DNA
  - Now used for non-cancer effects as well

# The Ongoing Evolution of Chemical & Radiation Cancer Risk Assessment

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- 2000s
  - Modern toxicological methods demonstrate that radiation & chemicals have thresholds showing the LNT is scientifically invalid
- 2007
  - NAS develops a “Vision and a Strategy” for toxicity testing in the 21<sup>st</sup> century based on “toxicity pathways” which show that cells can adapt to chemical stresses, up to a point, i.e., toxicity has a threshold
- 2011
  - Evidence emerges that available data in the 1940s showed a threshold for radiation-induced DNA damage & cancer
  - This suggests the SDWC endorsement of the LNT model for chemical cancer risk assessment was not scientifically valid



# Prolog

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- A key conclusion from the NAS Committee on Biological Effects of Atomic Radiation (BEAR I 1956) replaced threshold model for assessing radiation risks with a linear no threshold (LNT) model.
  - *Any radiation dose, however small, can induce some mutations. There is no minimum amount of radiation dose which might be exceeded before any harmful mutations occur.*
  - *...if we increase the radiation that reaches the reproductive glands by X percent, the number of mutations caused by radiation will also be increased by X percent.*
- These conclusions generalized to radiation-induced cancer one year later by National Committee on Radiation Protection (NCRP) & in 1977 for genotoxic chemical carcinogens by NAS SDWC.

# NAS Safe Drinking Water Committee (SDWC 1977)

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- Vol. 1 of “*Drinking Water & Health*” (DW&H), developed under contract with EPA’s Office of Drinking Water as mandated by Safe Drinking Water Act of 1974.
- First time LNT model endorsed & used for chemical environmental cancer risk assessment.
- Based on radiation data assumed that chemically induced DNA mutations and cancers would also not have a threshold.
- Substantial collective skepticism & reluctance for adopting LNT approach.

# NAS Safe Drinking Water Committee (SDWC 1977)

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- Underlying skepticism concerning the LNT continued.
- Vol. 4 of DW & H (1982), the SDWC rescinded its endorsement of the LNT model.
  - *“more confidence could be placed in mathematical models for extrapolation if they incorporated biological characteristics of the animal studies...premature at this stage to recommend any single approach....”*
- Vol. 5 of DW &H (1983) the LNT model again relied upon & its use became the default methodology for chemical cancer risk assessment.

# Evidence for Radiation Linearity

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- Recent Calabrese papers review experimental history & claims of LNT radiation response for DNA mutation & cancer.
- Call into question underlying basis for endorsement of LNT model by the SDWC in 1977.
- Prior to acceptance talk, Nobel-laureate H.J. Muller knew of high quality data directly contradicting linearity for radiation-induced DNA mutation.

# Evidence for Radiation Linearity

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- However, in his Nobel Prize Lecture Muller unequivocally stated there was “*no escape from the conclusion that there is no threshold*” for ionizing radiation germ cell mutation.
- As documented by Calabrese, extensive correspondence discovered in DOE archives between Muller & authors of contradictory studies show data were suppressed to maintain reliance on the LNT for radiation.
- This suggests 1977 endorsement of LNT model by SDWC was based on highly questionable data.
- David Hoel, a key proponent of the LNT in 1977, now believes that radiation-induced cancer is a non-linear phenomenon at environmental exposures.

# Regulatory Implications of LNT Model

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- EPA states, on numerous occasions, that chemical regulations are based on science alone (i.e., not policy); opens door for evaluating the science underlying the LNT.
- LNT implications go well beyond cancer risks as suggested in NAS (2009) *Science and Decisions* (i.e., “*Silver Book*”) which recommended LNT concept for non-cancer chemical effects.
- Recent regulatory actions rely on LNT to assess non-cancer health risks, e.g.,
  - Ozone & mercury based on the Clean Air Act (CAA), i.e., Mercury and Air Toxic Standards (MATS)
  - Maximum Achievable Control Technology (MACT) standards

# Economic Implications of LNT Model

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- Economic aspects of numerous EPA policies the subject of intense national debate
- This suggests the role of the LNT in assessing potential cancer or non-cancer risk be critically evaluated.
- Recent EPA report on costs & benefits of 1990 Clean Air Act rules
  - Annual costs of compliance estimated at \$65 billion
  - Value of benefits estimated at almost \$2 trillion
- The LNT also distorts priority setting by over-estimating the number of lives saved (i.e., benefits) than if science-based approaches are used

# Radiation Data

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- Radiation-induced cancer risk still based on atomic bomb survivor data extrapolation (Biological Effects of Ionizing Radiation [NAS BEIR VII] report).
- Substantial data from DOE Low Dose Program (> 700 papers) on radiation-induced mutation & cancer show thresholds for these effects *in vivo*.
- The collective results from DOE (in addition to other data on radiation & chemicals) demonstrate that the LNT:
  - Does not conform with newest experimental data using modern toxicological tools
  - Is an artificial construct & needs replacement.



# Chemical Data

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- NAS (2007) “*Toxicity Testing in the 21st Century*” called for new ways to test chemicals by using human cells rather than whole animals.
- Detect effects in key “adverse outcome” pathways that, when sufficiently perturbed, lead to adverse health outcomes, i.e., computational toxicology.
- EPA recently stated that , “...computational toxicology data used for decisions...need to be ‘*solidly ground-truthed*’ science.”
- Since “adverse outcome pathways” will show thresholds, it seems logical that the LNT be “solidly ground-truthed” in science as well.
- As long as the LNT remains an unchallengeable default, achieving the goals of the NAS vision will be impossible since the LNT & NAS vision are mutually incompatible.

# Conclusions (1 of 2)

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- The rationale for adopting the LNT in 1977 for risk assessment of carcinogens now called into question by historical radiation data and modern studies with chemicals & radiation.
- Little, if any, supporting empirical data for assuming that chemical- or radiation-induced cancer are linear no-threshold phenomena.
- Given the lack of an evidentiary basis for the LNT, it is time for a critical reassessment of its continued use today for chemical or radiation risk assessment.

# Conclusions (2 of 2)

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- Repeated assertions that regulations are science-based opens the door for assessing the LNT since this default plays a central role in cancer & non-cancer risk assessment.
- Following sufficient analysis of salient science, another different NAS committee (i.e., not BEIR) should address cancer & non-cancer risk assessment approaches for chemicals & radiation not based on LNT concept.

# Path Forward

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- Multi-phased disciplined approach to “ground-truth” the underlying science of the LNT
  - Critical multi-author peer reviewed science analysis of all relevant data; particular emphasis on DOE Low Dose data
  - Critical multi-author peer reviewed economic analysis/case studies with & without LNT-driven “benefits” calculations
  - Advocacy/Communications/Public Outreach
- Congressional hearings

# Path Forward

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- Appropriations for DOD/DOE request for a different NAS committee to address non-LNT cancer risk assessment approaches
- Widespread support for challenging LNT model
  - Numerous industry trade associations
  - Individual companies
  - State regulatory agencies
  - Animal rights organizations
  - House Energy & Commerce Committee

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