

February 27, 2020

Jeffrey Shuren, M.D., J.D.
Center for Devices and Radiological Health
U.S. Food and Drug Administration
Email: jeff.shuren@fda.hhs.gov

RE: FDA Literature Review on Radiofrequency Radiation and Cancer

Dear Dr. Shuren,

I am writing this letter to detail major incorrect statements and omissions of relevant data in the FDA document titled “Review of Published Literature between 2008 and 2018 of Relevance to Radiofrequency Radiation and Cancer.” I led the design of the National Toxicology Program’s (NTP) toxicity and carcinogenicity studies on cell phone radiation and I strongly believe that the anonymously written FDA document misrepresents the utility of the NTP study for assessing human health risks. In addition, the report’s casual dismissal of both the mechanistic findings and the numerous results from epidemiological studies that have shown increased cancer risks associated with exposure to radiofrequency radiation (RFR) are inconsistent with the FDA’s stated core mission “to protect and promote the public health.”

Regarding the NTP studies on cell phone RFR, an expert peer-review panel discussed the results for 3 days and concluded ([NTP TR-595](#); [Peer-Review Report 2018](#)) that this carefully designed and conducted study provided “clear evidence of carcinogenic activity.” In contrast to the NTP and peer-review conclusions, the FDA claims that whole-body exposures used in the NTP study cannot be related to the local RFR exposures a human receives while using a cell phone. The dismissal of the NTP study results by the FDA is rather peculiar since it was the FDA’s Center for Device and Radiological Health that requested the toxicity and carcinogenicity of RFR in experimental animals ([CDRH nomination of RFR](#)) “to provide the basis to assess the risk to human health,” and FDA scientists were fully aware of the exposure methodology that was used in the NTP study long before those studies were begun.

The NTP study was designed to provide accurate organ-specific dosimetry that could be used to quantify risks for any adverse effect that might be identified. Most people who check on the RF emissions from their cell phones learn that the Federal Communication Commission (FCC) requires that local tissue exposures be lower than 1.6 W/kg averaged over any one gram of tissue. In the NTP study, the exposures to the brain of rats were approximately 1.5, 3.0, and 6.0 W/kg – close to the FCC’s local exposure limit. For experimental studies in small groups of laboratory animals, these values are unusually close to allowable local tissue exposures in humans and require minimal extrapolation to estimate human cancer risk.

The FDA report complains that the whole-body exposures in the NTP study at 6 W/kg was 75 times higher than the exposure limit for the general population (the lower doses were 38- and 19-times that limit for the general population, but only 8- and 4-times the exposure limit for workers). However, whole body exposures provide little information on organ-specific exposure levels. When an individual holds a cell phone next to their head, the important exposure for consideration of health risk is the local exposure. That is why the NTP study design focused on the local exposure intensities. If the animal studies had used the whole-body exposure limit of 0.08 W/kg, then the exposure to the brain of

exposed animals would have been 20-fold less than the FCC's local exposure limit for the general public, i.e., a useless study for assessing human risk. It is misleading for the FDA document to ignore the local exposure limit of 1.6 W/kg and its importance for assessing organ-specific cancer risk.

The FDA document criticizes studies that did not perform histopathology evaluations blinded to the dose group, including the NTP study. However, as was pointed out previously¹, the final diagnosis of lesions in the NTP study was done by a group of pathologists who did not know whether the slides they were examining came from an exposed or an unexposed animal. In addition, for anyone questioning the diagnosis of any tissue in this study, all of the slides from the NTP studies are available for examination at the NTP archives.

The FDA document also suggests without evidence that the carcinogenic effects in rats exposed to 6 W/kg were due to the loss of their ability to maintain their body temperatures during the exposures. However, measured body temperatures were within 1 °C of their normal body temperature, there were no differences in body weights between exposed and sham control rats in the 2-year study, there was no indication of tissue damage in the 28-day study, and there were no exposure-related clinical observations in the 2-year study ([NTP TR-595](#)). Thus, it is clear that animals tolerated the exposure levels used in the NTP study. The peer reviewers of the NTP studies were fully aware of all issues raised in the FDA document, yet still concluded that the results of those studies showed clear evidence of carcinogenic activity. FDA scientists had opportunity to offer criticisms of the NTP study prior to and during the 3-day peer-review, but did not. Did the FDA somehow have an epiphany regarding the human relevance of the NTP cancer data or was there some other factor influencing their decision to dismiss those results?

Lastly, the FDA document misstates the results of the genetic toxicology tests in animals from the NTP study. For example, the FDA document claims there were “no statistically significant increases in DNA damage in female rats or either mouse sex” and the increases in DNA damage in male rats “was not statistically significant,” when in fact there were significant increases and significant trends in DNA damage in the frontal cortex of male mice exposed to GSM or CDMA modulated RFR and in the frontal cortex and hippocampus of male rats exposed to CDMA ([NTP TR-595](#)).

The FDA document also claims there is a “lack of biological mechanistic plausibility,” while eight *in vivo* studies cited in that document provided evidence of increased oxidative stress associated with exposure to RFR and 15 studies provided evidence of genotoxicity. In addition, many relevant *in vivo* studies showing evidence of oxidative stress were not reported in the FDA document and there are many *in vitro* studies that have found oxidative stress associated with exposure to RFR². A true risk analysis should consider both *in vivo* and *in vitro* studies when ascertaining biological mechanistic plausibility. A characteristic of many human carcinogens is the induction of oxidative stress that can subsequently lead to mutations, chromosomal translocations, and genetic instability.³ Thus, there does exist a biologically plausible mechanism for the induction or progression of tumors associated with

1 Melnick RL (2019). Commentary on the utility of the National Toxicology Program study on cell phone radiofrequency radiation data for assessing human health risks despite unfounded criticisms aimed at minimizing the findings of adverse health effects. *Environ Res.* 168:1-6.

2 Yakymenko I, Tsybulin O, Sidorik E, et al. (2016). Oxidative mechanisms of biological activity of low-intensity radiofrequency radiation. *Electromagn Biol Med* 35: 186-202.

3 Smith MT, Guyton KZ, Gibbons CF, et al. (2016). Key characteristics of carcinogens as a basis for organizing data on mechanisms of carcinogenesis. *Environ Health Perspect.* 124:713-721.

exposure to RFR. For studies that did not show evidence of carcinogenicity or genotoxicity, the FDA document did not comment on whether or not those studies were adequately designed with respect to animal group size, exposure levels and duration of exposure.

Regarding human studies, the FDA document cites the study by Little (2012) in which it was reported that glioma trends in the US between 1997 and 2008 have remained relatively constant, but omitted the study by Philips et al. (2018)⁴ that reported a doubling in incidence of glioblastoma (frontal and temporal lobes) in England between 1995 and 2015. The latter study was published in June 2018, which is within the timeframe (August 2018) for epidemiological studies included in the FDA document.

The FDA document identified several human studies that reported risks of glioma, acoustic neuroma, and other tumor types that were increased among cell phone users. In each case, the document focused on limitations in those studies to raise doubt about their reliability for assessing cancer risk. Two limitations specified for most case-control studies included selection and recall bias. However, the FDA document neglected to discuss the impact of the study by Momoli et al. (2017),⁵ which re-analyzed the Canadian data that was included in the Interphone study and showed that there was no effect on the risk of glioma after adjustments were made for selection and recall biases; the odds ratios (OR) for glioma were significantly increased when comparing the highest quartile of use to those who were not regular users whether or not adjustments were made: OR = 2.0, 95% confidence interval 1.2–2.4 without adjustment; OR = 2.2 95% confidence interval 1.3–4.1 with adjustments. Evidently, selection and recall biases do not explain the elevated brain cancer risks associated with use of cell phones in that study.

Thus, while there are reliable animal studies, mechanistic studies, and animal studies showing increased cancer risks associated with exposure to cell phone RFR, the FDA document dismisses nearly the entirety of those studies to enable the agency to conclude that there is insufficient evidence to support a causal association between RFR exposure and tumorigenesis. According to the FDA, animal studies are not useful for studying potential effects in humans (though animal studies are used in drug development) and the human studies “were subject to flaws and inaccuracies.” Yet, every known human carcinogen is carcinogenic in animals when adequately tested. Public health agencies including the NTP, US EPA, IARC, and the FDA have a long tradition of relying on the relevance of rodent toxicology/carcinogenicity studies to identify hazardous agents and assess human health risks in order to implement public health protective policies. The statement in the FDA report that “if any risk does exist, it is extremely low” is very misleading since the FDA has not performed a quantitative risk assessment on any of the available data sets and, because of the widespread use of cell phones in the US and world-wide, even a small increase in cancer risk would have a serious public health impact.

Based on the FDA review, which is not a risk analysis as stated in the document, the message for the general public appears to be that precautionary measures for use of cell phones are not necessary in spite of the fact that numerous studies have provided compelling evidence of increased cancer risk

4 Philips A, Henshaw DL, Lamburn G, O’Carroll MJ. (2018). Brain tumours: rise in glioblastoma multiforme incidence in England 1995-2015 suggests an adverse environmental or lifestyle factor. *J Environ Public Health*. Article ID 7910754,

5 Momoli F, Siemiatycki J, McBride ML, et al. (2017). Probabilistic multiple-bias modeling applied to the Canadian data from the Interphone study of mobile phone use and risk of glioma, meningioma, acoustic neuroma, and parotid gland tumors. *Am J Epidemiol*. 186:885-893.

associated with exposure to cell phone RFR. This is an irresponsible message for a government agency that claims its mission is to protect consumers and promote the public health.

The statement on the FDA website (<https://www.fda.gov/radiation-emitting-products/cell-phones/do-cell-phones-pose-health-hazard>) that there is a “scientific consensus on cell phone safety” is totally wrong and should be removed since there is no scientific consensus supporting this claim. In contrast, numerous experts in the field have reported evidence that current levels of cell phone radiation can be harmful to human health.

In conclusion, the FDA document has serious flaws and inaccuracies, as well as omissions of relevant data. Hence, in consideration of public health, it is important that FDA immediately retract their review on radiofrequency radiation and cancer.

Sincerely,

A handwritten signature in dark ink, reading "Ronald L. Melnick". The signature is written in a cursive, flowing style.

Ronald L. Melnick, Ph.D.
Retired toxicologist NTP, NIEHS