The U.S. National Toxicology Program of the U.S. National Institutes of Health Radiofrequency Carcinogenicity Research Study
Review by Environmental Health Trust

The U.S. National Toxicology Program (NTP), released a partial report on parts of the world's largest, most thorough and well-designed study of its type - at a cost of $25 million - on the potential carcinogenicity of cell phone radiofrequency radiation in rats and mice.

What did the study find?
The study found adverse effects after long term exposure to cell phone radiation:

- Increased incidences of glioma (a rare, aggressive and highly malignant brain cancer) as well as schwannoma (a rare tumor of the nerve sheath) of the heart were found in both sexes of rats, but reached statistical significance only in males.
- Increased incidences of rare, proliferative changes in glial cells of the brain and in Schwann cells (nerve sheath) in the heart of both sexes of rats, while not a single unexposed control animal developed these precancerous changes.
- DNA damage was induced with both modulations of radiofrequency radiation (RFR) in both rats and mice (mixed results in tissues and brain regions).
- Results from this study clearly show that biological impacts occur at non-thermal exposures like those that take place from cell phones today.

Data analyses in mice are ongoing. The complete results from these rodent studies will be available in NTP Technical Reports by the end of 2017.

Why is this study considered a "landmark" study?
1. The NTP findings of brain tumors (gliomas) and malignant Schwann cell tumors of the heart in the NTP study - as well as DNA damage in brain cells of exposed animals - present a major public health concern because these tumors occurred in the same types of cells that had been reported to develop into tumors (gliomas and acoustic neuromas) in epidemiological studies of long term cell phone users.

2. In 2011, the International Agency for Research on Cancer of the World Health Organization (IARC/WHO) classified radio frequency radiation as a Class 2B "possible carcinogen" largely based on the epidemiological studies linking long term cell phone use to increased glioma and acoustic neuroma. The NTP findings provide significant new animal evidence which supports the human epidemiological data and indicates that a higher carcinogenicity classification is appropriate for radiofrequency radiation.

3. The NTP results show adverse biological effects from RFR at non-thermal or minimally thermal (non-heating) exposure levels. Current international radio frequency exposure limits and mobile phone regulations are based on avoiding thermal (heating) effects and to protect the public from acute thermal effects. Therefore, the NTP findings indicate that current regulations do not adequately protect public health.

Are studies in animals relevant to humans and useful for assessing human risk?
Yes. Animals and humans exhibit similarities in biological processes of disease induction, and the pharmaceutical industry relies on the results of animals studies prior to conducting clinical trials of new drugs in humans.

- It is unethical to intentionally expose humans to environmental agents that cause cancer in animals.

- Every agent that is known to cause cancer in humans has been shown to be carcinogenic in animals when adequately tested.
- Almost one-third of human carcinogens were identified after carcinogenic effects were found in well-conducted animal studies.
- The careful control of exposure conditions in animal studies can eliminate the potential impact of confounding factors on the interpretation of study results.

Due to rodents' short lifespan in comparison to humans, animal studies can eliminate the need to wait for a high incidence of human cancers (which may clinically manifest as much as 30 years from the time of first exposure) before implementing public health–protective strategies. Placed in the context of the large body of evidence on RFR, this animal study lends critical evidence in understanding the human health risk of cell phone and wireless radiation.

How were the animals exposed?
NTP animals were carefully exposed to RFR in reverberation chambers. A reverberation chamber is a large, shielded room containing an excitation antennae and ventilation panels. In this chamber, field exposures emanate from all directions, while rotating paddles distribute the fields within the chamber to create a statistically homogeneous electromagnetic environment. An advantage of this approach is that animals are able to be exposed in an unrestrained state for extended periods of time. During this time, RFR exposure was turned on and off at particular intervals. Prior to the start of the toxicity/carcinogenicity studies, specific exposure intensities were identified which would not cause measurable increases in body temperature. To maintain relatively uniform exposures to all body organs, rats were exposed to 900 MHz RFR and mice were exposed to 1900 MHz RFR.

Did the NTP study mimic human exposure?
Rats and mice were exposed to frequencies and modulations currently used in cellular communications in the United States specifically to mimic humans' long term low level exposures. Rats were exposed for 10-minute on, 10-minute off increments, totaling 9 hours a day of exposure from before birth to slightly more than 2 years of age. Exposures of mice began at 6 weeks of age and followed the same exposure pattern as rats. Based on the increased use of cell phones over the past 10 years and the extensive use of multiple wireless devices which emit RFR, these daily exposure durations are not unreasonable.

For the NTP studies of rats and mice, the full body exposure values were 1.5 Watts per kilogram (W/kg), 3 W/kg, and 6 W/kg. These exposures are similar to or only slightly above regulatory threshold levels for cell phones which range from 1.6 W/kg (head/torso) to 4 W/kg (ears, hands, wrists). Rats and mice were exposed to two types of RFR, called CDMA and GSM for each exposure intensity.

For exposure to RF energy from wireless devices, the allowable US Federal Communications Commission Specific Absorption Rate (SAR) limit is 1.6W/kg, averaged over one gram of tissue (and averaged over 30 minutes). The limit of 2 W/kg averaged over 10 grams of tissue as specified by the International Committee on Non-Ionizing Radiation Protection (ICNIRP) guidelines is used in Europe and many other countries (and averaged over 6 minutes). In addition, for body parts such as ears, hands, feet, wrists, and ankles the threshold limit is 4 W/kg averaged over 10 g. In addition there is a 30% uncertainty in the measurements (which could mean that a value over 1. 231 W/kg could exceed the 1.6 W/kg limit as noted in IEEE 1528-2013). In this context, the NTP rodent exposures are more than reasonable and the results are suitable for assessing human cancer risk.

Most importantly to understanding the relevance of the NTP study, the carefully controlled radiation levels in exposed NTP rodents remained *non-thermal.* The finding of carcinogenic effects at *non-thermal* levels is of great scientific relevance and represents a serious public health concern.

Does the gender difference mean the findings of carcinogenicity can be dismissed?
As the American Cancer Society explains, "It's important to note that these sorts of gender differences often appear in carcinogenic studies, so the fact they show up here should not detract from the importance of the findings." In addition, gender differences in cancer rates also exist in humans. For example, brain cancer mortality rates are approximately 50% higher in men than in women, and for many human cancers (e.g., colorectal, liver, soft tissue including heart, kidney, non-Hodgkin lymphoma, etc.) the incidence and mortality rates are much higher in men than in women. Thus, the different response between male and female rats in the NTP study of RFR does not diminish the relevance of the cancer findings.

Were the results peer reviewed?
The brain and heart tumors and the pre-cancerous lesions observed in the NTP study were reviewed by nearly 20 pathologists. In addition, because the results from this study provided evidence-based consistency and support for the IARC conclusions, the overall partial findings were subjected to an accelerated peer review by three individuals with expertise in evaluating experimental cancer data, plus six NIH scientists. Dr. John Bucher, Director of the National Toxicology Program Division, has stated that "the majority" of NIH reviewers to the data set agreed with the report's conclusions.

Is the statistical power strong?
Typically, carcinogenicity studies use 50 animals per group. For this study 90 animals of each sex were included per exposure group. Though this study had more power than most other carcinogenicity studies, an increased incidence of about 5% compared to controls was necessary to achieve statistical significance for rare tumors.

Does the shorter lifespan of the controls mean they just did not live long enough to develop cancers?
The answer to this question is no, for at least two reasons. First, there was no statistical difference in survival between control male rats and the exposure group with the highest rate of gliomas and heart schwannomas. Second, no glial cell hyperplasias (potential precancerous lesions) or heart schwannomas were observed in any control rat, even though glial cell hyperplasia was detected in exposed rats as early at week 58 of the 2-year study and heart schwannomas were detected as early as week 70 in exposed rats. Thus, survival was sufficient to detect tumors or pre-cancerous lesions in the brain and heart of control rats. Both control and experimental animals were kept in special housing that blocked out all other EMF exposures; no other animal carcinogenicity studies block this potential confounding exposure.

Have any other animal studies shown a link to cancer?
Yes. With the results of the NTP, there are now three important animal studies within the past six years showing increased development of cancers after RF-EMF exposure. A German study published in 2015 replicated 2010 research which showed carcinogen-induced tumor rates were significantly higher in the lung and liver of animals exposed to RF-EMF along with a known carcinogen.

What are the limitations of the study?

The study only followed the animals up to 2 years and not for a full lifetime. The study only tested one modulation at a time and yet humans are often exposed to multiple frequencies at various intensities. The effects to the reproductive system, hormones and to brain development were not addressed in the study design; nor were cognitive and behavioral effects on the exposed animals.

What are the policy implications of these study results?
This study adds significant evidence of cancer risk from cell phone RFR. Other agents such as formaldehyde, some pesticides and engine exhausts that have been shown to cause cancer are the subject of serious efforts to reduce and restrict human exposure. Public health agencies do not need to insist on absolute proof of human harm before implementing steps to prevent damage by taking precautionary measures. Given the large number of cell phone users in the US and worldwide, even a small increase in cancer risk at exposure intensities close to what humans experience could result in a large number of individuals developing an RFR-induced tumor with long term exposures. The current message to take precautionary measures "if you are concerned" is inadequate.

For children the cancer risks may be greater than those for adults due to increased penetration and absorption of cell phone radiation within the brains and bone marrow of the skull of children. Furthermore, the developing nervous system of children is more susceptible to tissue damaging agents, and children have a longer life ahead of them during which adverse effects can develop. Based on this new information, regulatory agencies around the world are making strong recommendations for consumers to take precautionary measures and to avoid close contact with their cell phones and wireless devices, and especially to restrict or avoid use of wireless devices by children.

NATIONAL TOXICOLOGY PROGRAM (NTP) LINKS
NTP Report of Partial findings from the National Toxicology Program Carcinogenesis Studies of Cell Phone Radiofrequency Radiation in Hsd: Sprague Dawley® SD rats
NTP Press Release: NTP Cell Phone Radiofrequency Radiation Study: Partial Release of Findings
New NTP/NIEHS Webpage on Cell Phones
Powerpoint Slides of NTP Study BIOEM 2016 Conference
Video of Presentation by NTP at NIEHS June 2016 on the Study Findings

NEWS MEDIA COVERAGE
Wall Street Journal: Debate Renews Over Health Risks from Cell Phone Use
Wall Street Street Journal: Cell Phone Study Fans Cancer Worries
Consumer Reports: Does Cell Phone Use Cause Brain Cancer? What the New Study Means For You
Science Magazine: Questions abound after study links tumors to cellphone radiation
PBS: How Might Cell Phone Signals Cause Cancer May 30, 2016
Scientific American: Major Cell Phone Radiation Study Reignites Cancer Questions: Exposure to radiofrequency radiation linked to tumor formation in rats

SCIENTIFIC RESPONSE
American Cancer Society Press Release:New Study Linking Cell Phone Radiation to Cancer
American Academy of Pediatrics Responds to National Toxicology Program study
Barcelona Institute for Global Health, GROWING EVIDENCE FOR THE LINK BETWEEN MOBILE PHONES AND CANCER
BERENIS - Swiss expert group on electromagnetic fields and non-ionising radiation, September 2016 Newsletter Review of the NTP Study
Dr. Eitan Kerem, Chair of Pediatrics at Hadassah Hebrew University Hospital