

## Update on NTP Studies of Glyphosate

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Glyphosate is the active ingredient found in herbicide formulations worldwide and is toxic to plants by disrupting the shikimate amino acid synthesis pathway. The intensive use of glyphosate began with the introduction of glyphosate-resistant crops in the late 1990s. Although glyphosate has a low toxicity profile for humans and mammals, conflicting reports exist as to whether it poses a cancer risk for humans. The USEPA and European regulatory agencies have described glyphosate as unlikely to pose a carcinogenic hazard to humans. However, the International Agency for Research on Cancer (IARC) and the California EPA have classified glyphosate as “probably carcinogenic to humans” and “known to the State of California to cause cancer,” respectively. Oxidative stress and genotoxicity are proposed mechanisms by which glyphosate could potentially cause cancer. To address these hypotheses, the NTP is testing glyphosate in human cells using several assays that detect reactive oxygen species (ROS) and genotoxicity (see information on research program at <https://ntp.niehs.nih.gov/go/glyphosate>). The NTP will also compare and contrast the potency and efficacy of glyphosate to several glyphosate formulations in all assays. The formulations were chosen from a list of recommended products approved for agricultural use provided by the USEPA. Several products registered for home use were also evaluated.

Initial studies on glyphosate and its formulations are focused on evaluating several assays for detection of ROS in HepaRG, HaCaT, and TK6 cells. The HepaRG cells were chosen because they express significant xenobiotic metabolism. The HaCaT cells were chosen because studies identified by IARC as demonstrating strong evidence of oxidative stress by glyphosate and its formulations used these cells. The TK6 cells are the standard cell line NTP uses to screen for genotoxicity, and companion studies at the NTP will use these cells to evaluate in vitro genotoxicity of glyphosate and select formulations. In addition to ROS, cell viability and mitochondrial function will also be evaluated in these cells. The formulations were chosen from a list of recommended products approved for agricultural use provided by the USEPA. In addition, several products registered for home use were also evaluated. Detailed descriptions of the assays as well as the status of the project will be provided at the Board of Scientific Counselors meeting.