Glyphosate Research Scoping

Background Materials:

NTP Technical Report on Toxicity Studies of Glyphosate (CAS No. 1071-83-6) Administered in Dosed Feed to F344/N Rats and B6C3F$_1$ Mice, NTP Toxicity Reports Series No. 16, (1992)
http://ntp.niehs.nih.gov/results/pubs/shortterm/reports/abstracts/tox016/index.html

IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Vol 112 (2015)
http://monographs.iarc.fr/ENG/Monographs/vol112/index.php

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Glyphosate (CAS No. 1071-83-6) is a broad-spectrum herbicide widely used in agriculture and residential settings. Glyphosate inhibits an enzyme in an amino acid biosynthetic pathway that is specific to plants; i.e., it is absent in mammals. Glyphosate-based herbicide formulations contain various other substances, classified as inert ingredients, that aid in delivery and absorption of the active ingredient to target plants. Over the past 25 years, use of glyphosate has risen dramatically due to development of glyphosate-resistant genetically modified crops, and today, glyphosate is the most heavily used herbicide worldwide.

Glyphosate was first nominated to the NTP for testing in 1981. The NTP conducted a series of short-term studies including 13-week toxicity studies of glyphosate administered in dosed feed to male and female mice and rats (NTP, 1992). Few toxicological effects were observed and there was no evidence of genetic toxicity, and NTP did not elect to conduct further testing with glyphosate.

In 2015, the International Agency for Research on Cancer (IARC) published Monograph Volume 112 on glyphosate and 4 other pesticides. Based on the review of the publicly available scientific literature, IARC concluded that glyphosate is a probable human carcinogen. The IARC evaluation of glyphosate included an assessment of the available data on glyphosate-based formulations. Two of the key factors used to inform the IARC classification were studies suggesting that glyphosate and various formulations were genotoxic and induced oxidative stress. Furthermore, where glyphosate was compared directly to glyphosate-based formulations, the formulations were generally more toxic than glyphosate alone.

Later in 2015, the European Food Safety Authority (EFSA) released its scientific assessment of glyphosate, concluding that glyphosate is unlikely to pose a carcinogenic hazard to humans. The US Environmental Protection Agency (EPA) is currently undertaking a registration review of glyphosate which will include a risk assessment and ultimately a decision on whether glyphosate satisfies regulatory requirements for continued use.

Due to the different conclusions in the various human health assessments conducted to date and the significant public concern regarding glyphosate use and exposure, the NTP began to consider whether additional investigations into the potential toxicity of glyphosate and its formulations were warranted. The initial focus is on genetic toxicity and cancer, particularly studies that would inform mechanisms and pathways relevant to carcinogenicity.

Internal scoping activities in progress are aimed at identifying critical research questions and specific approaches that could aid the interpretation of existing literature on glyphosate. Envisioned are a series of robust dose-response studies utilizing a battery of in vitro and in vivo screening assays to evaluate genotoxicity, oxidative stress, and other key characteristics of carcinogens for glyphosate, its metabolites, and multiple glyphosate-based formulations. As an initial step in considering whether additional research is warranted to better understand non-cancer health outcomes, NTP plans to conduct a screening-level analysis of the existing literature using text mining and machine-learning approaches.[1]

This presentation will briefly describe 1) activities NTP has undertaken to date to identify critical research gaps, and 2) research approaches currently under consideration by the NTP to provide additional information to support human health assessments of glyphosate and glyphosate-based formulations.

[1] Howard, B.E., J. Phillips, K. Miller, A. Tandon, D. Mav, M. R. Shah, S. Holmgren, K. E. Pelch, V. Walker, A. A. Rooney, M. Macleod, R. R. Shah and K. Thayer (2016). "SWIFT-Review: a text-mining workbench for systematic review." Syst Rev **5**(1): 87.