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Dr. Lawrence J. Marnett
Editor, Chemical Research in Toxicology
Department of Biochemistry
Center in Molecular Toxicology
850 Robinson Research Bldg.
Vanderbilt University School of Medicine
Nashville, TN
37232-0146

Re: Letter to the Editor - Portrayal of Industry Research in *Chem. Res. Toxicol.*, **2010**, *23* (10), pp 1586–1595.

Dear Dr. Marnett:

CropLife America (CLA) is very concerned about the portrayal of industry research in the journal Chemical Research in Toxicology. In the introduction to the recent article, "Glyphosate-Based Herbicides Produce Teratogenic Effects on Vertebrates by Impairing Retinoic Acid Signaling," the authors opine and directly challenge the integrity of research conducted by industry. This commentary text is not appropriate within your esteemed journal. It reflects a misconception that some academic researchers have about industry funded research. Thus, we offer the following information to inform your readers as to the level of scrutiny that regulatory studies conducted by industry undergo for crop protection chemicals.

CLA is the not-for-profit trade organization representing the nation's developers, manufacturers, formulators and distributors of plant science solutions for agriculture and pest management in the U.S. Our member companies produce, sell and distribute virtually all the crop protection technology products used by American farmers. CLA comments on issues that can have broad scientific and regulatory implications, which sometimes occur in the context of chemical-specific or product-specific regulatory reviews, decisions, and actions. CLA is focused on helping feed a hungry world and advancing agriculture.

The Environmental Protection Agency (EPA), together with state agencies, registers or licenses pesticides for use in the United States. Pesticide registration is the process through which EPA examines the ingredients of a pesticide; the site or crop on which the pesticide is to be used; the amount, frequency and timing of pesticide use; and storage and disposal practices. EPA evaluates the pesticide to ensure that it will not have

unreasonable adverse effects on humans, the environment and non-target species. Specifically, under the Federal Insecticide Fungicide Rodenticide Act (FIFRA), EPA is required to ensure that each pesticide "will perform its intended function without unreasonable adverse effects on the environment." Additionally, Federal Food Drug and Cosmetic Act (FFDCA) further requires EPA to make the determination that there is a "reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue" in foods. Updates to FIFRA and FFDCA including the Food Quality Protection Act of 1996 have modernized the chemical evaluation process for EPA. Pesticides must be registered or exempted by EPA's Office of Pesticide Programs before they may be sold or distributed in the U.S. Once registered, a pesticide may not legally be used unless the use is consistent with the approved directions for use on the pesticide's label or labeling.

Under mandates of FIFRA and FFDCA, developers and manufacturers seeking registration of pesticide products must submit data that covers specified areas as defined in the Harmonized Test Guidelines, all of which have been extensively validated. The study guidelines are accessible at the following web site (URL: http://www.epa.gov/ocspp/pubs/frs/home/guidelin.htm). Over 200 different studies are required on chemical pesticides before registration by EPA. Of this total, 49 tests address a wide array of health effects and 51 address ecological effects. These studies are best characterized as regulatory toxicology studies which are designed to be comprehensive in identifying adverse effects that could result from single or repeated-administration in mature as well as developing organisms. Treatment-related responses are characterized in multiple species and at a range of exposure-levels to define the most sensitive effect as well as the No-Observed-Adverse-Effect-Level (NOAEL) which is then typically used for the purposes of risk assessment with the inclusion of appropriate uncertainty factors.

All of these studies are required to be conducted according to Good Laboratory Practice (GLP) Standards (U.S. EPA, 2008). For over 2 decades, GLP Standards have required that there be detailed written testing protocols, well documented and characterized test substances, trained personnel, calibrated equipment, an independent quality assurance unit and many other provisions to rigorously document and ensure quality of studies for pesticide registration. Additionally, GLP Standards allow EPA to independently audit the generation of all pieces of data as well as determine if studies were conducted according to pre-written protocols. Every data point within a GLP study can be tracked, audited, and validated by EPA. Regular EPA audits of testing facilities verify compliance and provide enforcement of GLP Standards. EPA [along with other organizations such as U.S. Food and Drug Administration (FDA), the National Toxicology Program (NTP) and the Organisation for Economic Co-operation and Development (OECD)] require studies to be conducted in accordance with GLP.

In contrast, academic toxicology research focuses on the scientific method and the testing of a new hypothesis. Academic research is typically focused on learning more about the mechanisms of a given effect; academic research does not typically focus on the

threshold of the effects. While full data records are made available for EPA review for industry conducted research, such details are rarely made available as part of the peer-review process for publishing a manuscript in a scientific journal. Under GLP, meticulous attention is provided on validating data and ensuring compliance with written protocols. This review is often not part of the scrutiny of academic research. In fact, given the level of detail available to the Agency in an industry funded GLP study, EPA often excludes research not conducted under GLP in making regulatory decisions.

The United Nations (U.N.) predicts world population will exceed 9 billion by mid-century and has called for a 100 percent increase in world food production by 2050 (U.N., 2007). According to the U.N., this doubled food requirement must come from virtually the same land area as today. The U.N. Food and Agriculture Organization (FAO) further states that 70 percent of this additional food must come from the use of new and existing agricultural technologies (U.N. FAO, 2002). Therefore, the need for innovation through new technologies is essential for the future of citizens, communities and natural resources. The crop protection industry is totally committed to providing farmers with technologies that are both safe and efficacious, and we will continue to do our part to better feed the world, through continued investment in research and science-based regulatory systems. The significant role of industry in supporting scientific research and providing GLP data to authorities such as EPA should not be undermined by editorializing in respected scientific journals including American Chemical Society publications. We would encourage the editorial staff of Chemical Research in Toxicology to ensure that future articles published in the journal do not contain biased and inaccurate statements. Such statements are unprofessional, add nothing to the scientific merit of a publication and frankly diminish the good reputation of the Journal.

Please note we are willing to work with you and the journal staff to edit this 'Letter to the Editor' for publication within Chemical Research in Toxicology. If there are further questions, please contact Dr. Wendelyn Jones at wjones@croplifeamerica.org or +1 202-872-3885).

Sincerely,

Wendelyn Jones, Ph.D.
Senior Director, Human Health Policy
CropLife America

Barbara P. Glenn, Ph.D.
Vice President, Science and Regulatory Affairs
CropLife America

References:

United Nations, Food and Agriculture Organization. 2002. World Agriculture: toward 2015/2030. Rome. ftp://ftp.fao.org/docrep/fao/004/y3557e/y3557e.pdf

United Nations. 2007. World Population Prospects: The 2006 Revision. U.N. Population Division, NY

U.S. EPA. 2008. Good Laboratory Practice Standards. 40 CFR 792.