BEFORE

THE STATE OF CALIFORNIA

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY (Cal/EPA)

OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT (OEHHA)

COMMENTS OF MONSANTO COMPANY

ON

OEHHA'S SEPTEMBER 4, 2015 NOTICE OF INTENT TO LIST GLYPHOSATE

October 20, 2015

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1.0 Glyphosate Should Not Be Listed Under Proposition 65.

On September 4, 2015, California's Office of Environmental Health Hazard Assessment (OEHHA) provided notice of intent to list the herbicide glyphosate as known to the state of California to cause cancer under the state's Safe Drinking Water and Toxic Enforcement Act of 1985 (Proposition 65). This action is unsupported by science, law, and policy. Following multiple intensive reviews of the unusually large dossier of studies on glyphosate, no regulatory authority in the world has ever determined that glyphosate causes cancer. Indeed, OEHHA itself has closely reviewed the science and concluded: "Based on the weight of evidence, glyphosate is judged unlikely to pose a cancer hazard to humans."[1] If anything, glyphosate is known to the state of California **not** to cause cancer. OEHHA should withdraw its September 4, 2015 notice and should not list glyphosate under Proposition 65.

The notice states that OEHHA has determined that glyphosate and three other herbicides meet the criteria for listing by the so-called Labor Code listing mechanism based on the actions of the International Agency for Research on Cancer (IARC).[2] OEHHA asserts that these are "ministerial listings" and that all comments should therefore be limited to whether IARC has identified the specific chemical or substance as a known or potential human or animal carcinogen. OEHHA also asserts that it "cannot consider scientific arguments concerning the weight or quality of the evidence considered by IARC when it identified these chemicals and will not respond to such comments if they are submitted."

As a leading manufacturer of glyphosate, Monsanto Company (Monsanto) cannot accept this limitation on the content of its comments and believes it would be both irresponsible and unlawful for OEHHA to ignore such comments. Global regulatory authorities and independent experts all agree that glyphosate is not carcinogenic. Indeed, OEHHA itself, after reviewing the very same scientific data on animal carcinogenicity considered by IARC, concluded in 2007 that glyphosate is unlikely to pose a cancer hazard to humans. A refusal by OEHHA to consider comments concerning the weight of the scientific evidence, notwithstanding its own assessment in 2007 that glyphosate is unlikely to be a carcinogen, would be unreasonable and unlawful.

Further, OEHHA's implementation of the Labor Code listing mechanism grants enormous authority -- rulemaking authority -- to a foreign entity that is not under the control of any California state entity and that can make decisions without any due process safeguards, in violation of the United States and California Constitutions as well as well-established principles of government and public policy. Specifically, with respect to the proposed listing of glyphosate, OEHHA's policy will cause the agency to overlook errors in IARC's process and flaws in the faulty document that served as the primary scientific basis for IARC's review of animal carcinogenicity, which was the main factor in its classification decision.

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[1] OEHHA, Public Health Goals for Chemicals in Drinking Water: Glyphosate (June 2007) ("OEHHA Assessment"), page 1, *available at* http://oehha.ca.gov/water/phg/pdf/GlyPHG062907.pdf (last visited October 2015).

[2] More specifically, OEHHA has stated that it is relying on the following documents published by IARC: "Agents classified by the IARC Monographs, Volume 1-112" (IARC, 2015a); and the glyphosate monograph in Volume 112 of the IARC Monographs series (IARC, 2015b). OEHHA further stated that IARC concluded that glyphosate is classified in Group 2A ("probably carcinogenic to humans") and that there is sufficient evidence of carcinogenicity in experimental animals for glyphosate (Guyton et al., 2015 IARC, 2015a & b), *available at* http://oehha.ca.gov/prop65/CRNR_notices/admin_listing/intent_to_list/090415LCset27.html (last visited October 2015).

As discussed below, OEHHA can only implement Proposition 65 consistent with law and with sound public policy by reviewing these errors and withdrawing the proposed listing of glyphosate.

2.0 Glyphosate Is Widely Used, Has a Long History of Safe Use, and Is Economically and Environmentally Beneficial to California.

Glyphosate was first commercialized as an herbicide in 1974. It is a non-selective, foliar acting, translocated herbicide. It is absorbed by green leaves and stems and transported within the plant to the growing points in shoots and roots. There, glyphosate blocks the activity of the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS)—an enzyme found only in plants and some microorganisms.[3] Inhibition of this enzyme prevents the plant from synthesizing the aromatic amino acids essential for protein synthesis and plant growth. Glyphosate has extremely low volatility, meaning it is highly unlikely to move off-site as a vapor to damage off-site vegetation during application. After application, glyphosate binds very tightly to most soils and sediments in the environment. Because of its strong soil-binding properties in most soils, glyphosate is not available for uptake by roots of nearby plants. As a result, glyphosate poses negligible risk to non-target plants with unexposed roots in the application zone and exhibits limited movement through the soil, reducing the risk of movement into groundwater.

Since being first introduced in 1974, glyphosate "has become the world's most widely used herbicide because it is efficacious, economical and environmentally benign."[4] It is marketed under a number of trade names, both by Monsanto and others, in various herbicide products and is registered in more than 160 countries. Glyphosate is a highly effective active ingredient controlling a wide range of weeds. A plethora of uses has been developed to manage unwanted vegetation either overall or by selective application to protect desirable vegetation. It is important to both the California agricultural economy and the efficient use of public agencies' budgets in California. Indeed, glyphosate is approved for use in more than 250 agricultural crop applications in California, as well as in weed control applications in non-cultivated settings. No other active ingredient compares in terms of number of approved uses.

- Glyphosate-based herbicides are used in agricultural applications, for example, because they offer a simple, cost-effective way to control weeds that can otherwise persist for years. Additionally, their broad-spectrum effectiveness allows farmers to control weeds with minimal tilling of the soil, a practice known as conservation tillage. This conserves valuable topsoil, reduces soil movement into streams and other surface water, helps retain soil moisture, and reduces trips across farm fields, conserving time and fuel.

- In addition to agricultural uses, herbicides containing glyphosate are used to control vegetation in utility rights-of-way, on roadsides, along railways or in places around the home such as

[3] Franz, J. E. , Mao, M. K., Sikorski, J. A. (1997). Glyphosate: A Unique Global Herbicide, ACS Monograph No. 189. American Chemical Society, Washington, DC. Among other awards, John E. Franz received the 1987 National Medal of Technology, the highest honor in the United States for technological achievement, bestowed by the President of the United States for outstanding contributions to America's economic, environmental and social well-being, for the discovery of glyphosate.

[4] Powles S B, 2008. Evolved glyphosate-resistant weeds around the world: lessons to be learnt. Pest Management Science. 64:360-365, a*vailable at* http://onlinelibrary.wiley.com/doi/10.1002/ps.1525/epdf (last visited October 2015).

sidewalks and gardens. Herbicides containing glyphosate are also used by wildlife organizations to protect and restore wildlife habitats threatened by invasive, non-native vegetation. For example, a Monsanto glyphosate-based herbicide was selected to control *arundo donax* (giant reed) in the Central River Valley and the San Francisco Bay area. This highly invasive weed threatens California's riparian ecosystems by outcompeting native species, such as willows, for water.

- Some glyphosate-based herbicides are approved for vegetation control in aquatic environments, including ponds and reservoirs, waterfowl sanctuaries, and recreational waterways. Very few herbicides have such favorable toxicological and environmental characteristics that allow them to be directly applied to aquatic vegetation, and conservation groups have chosen glyphosate-based formulations for these reasons.[5] As noted above, glyphosate-based herbicides have been used in California to control *arundo donax*, an invasive weed known to clog rivers, streams and flood control channels. Glyphosate is also used for many other difficult to control aquatic weeds in California, including cattails, bulrush, water primrose and water hyacinth.

- By using glyphosate-based herbicides, growers of tree, nut and vine crops, as well as industrial and aquatic vegetation managers, can avoid mechanical and labor intensive methods of weed removal to protect these high-value crops. Further, ditch banks, steep hillsides and many non-crop areas are not accessible with mechanical means such as heavy equipment or mowers, and use of glyphosate reduces the risk of injury for workers who otherwise must frequently re-enter the area to maintain mechanical control of tall-growing vegetation.

- All municipal, county, and state government agencies in California have limited budgets for vegetation management, and glyphosate-based herbicides have helped these agencies use their budgets effectively on behalf of taxpayers and ratepayers. Use of such herbicides reduces the cost and labor resources needed to control weedy vegetation in a timely manner to protect infrastructure, water flow, irrigation, and public safety and health from the negative impacts of uncontrolled weedy vegetation.

- As the amount of uncontrolled vegetation increases, there is an increase in the amount of dry fuel which aids in the rapid spread of wildfires during drought and California's arid summer months. Glyphosate is widely used by government agencies in California to control vegetation and establish fire breaks during the wet months of the year. This integrated approach to vegetation management with glyphosate helps municipalities and other government agencies

[5] Glyphosate has undergone extensive toxicological, ecotoxicology and environmental testing over the last 40 years to acquire global regulatory approvals. This testing has shown that glyphosate does not produce acute or chronic toxicity to higher organisms including wild mammals, birds, fish, aquatic invertebrates, and terrestrial invertebrates such as earthworms and honeybees at environmentally realistic exposure levels. It also has shown that glyphosate-based formulations, when used according to label directions, do not cause unacceptable adverse effects to wildlife and that glyphosate showed no effects on soil biomass or microbial respiration. Giesy, J.P. et al., (2000). Ecotoxicological risk assessment for Roundup® herbicide. *Rev. Environ. Contam. Toxicol.* 167:35-120, *available at* http://www.usask.ca/toxicology/jgiesy/pdf/publications/JA-228.pdf (last visited October 2015); Hart, M.R. et al., (1996). Soil microbial biomass and mineralization of soil organic matter after 19 years of cumulative field applications of pesticides. *Soil Biol. Biochem.* 28:1641−1649, *available at* http://www.sciencedirect.com/science/article/pii/S0038071796002490 (last visited October 2015).

protect valuable resources, property and the public from the uncontrolled spread of wildfires in California.

Many of the glyphosate uses are on municipal property, and many municipalities prohibit the use of Proposition 65 listed chemicals. Fundamentally, if glyphosate is de-selected due to its listing under Proposition 65 (due to municipal prohibitions or unfounded concerns about its carcinogenicity), farmers and public agencies will be forced to utilize mechanical means with dramatically increased costs, safety concerns, and risks to the environment.

3.0 No Regulatory Agency Considers Glyphosate To Be A Carcinogen.

Glyphosate has been the subject of hundreds of toxicological, ecotoxicological, and environmental studies during its nearly 40 years of use. Because glyphosate products are used in so many different ways (agriculture, ornamental, aquatics, wildlife habitat, residential, etc.), glyphosate is perhaps the most studied of any herbicide molecule. Many scientists – from industry, governmental agencies, universities, and independent institutions – have conducted experiments, laboratory studies and field research with glyphosate herbicides.

To get a clear picture of the environmental and toxicological characteristics of glyphosate, it is important to consider the total weight of evidence provided by this extensive body of research. The U.S. Environmental Protection Agency (EPA), the European Commission (EC), the Health Canada Pest Management Regulatory Agency (PMRA), and many other regulatory bodies and science organizations, including programs under the World Health Organization (WHO), have reviewed this data. Their overwhelming consensus is that there is no evidence that glyphosate causes cancer, even at very high doses, and that it is not genotoxic.[6] Most recently, and after IARC's classification of glyphosate, Germany, as the 'Rapporteur Member State' for glyphosate within the framework of EU re-evaluation, assessed glyphosate as non-carcinogenic.[7]

Furthermore, IARC is one of four programs within the WHO that have reviewed the safety of glyphosate, and the IARC classification is inconsistent with the assessments of the other programs. Two of the WHO programs (the Core Assessment Group of Joint Meeting on Pesticides Residues—"JMPR"—and the International Programme on Chemical Safety) previously concluded glyphosate is not carcinogenic.[8] WHO Guidelines for Drinking-Water Quality concluded glyphosate does not represent a hazard to human health.[9]

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[6] Appendix 1 provides details on the national regulatory reviews and conclusions of Australia, Canada, Japan, Germany (on behalf of the EU), and the United States, as well as other programs within the WHO.

[7] Germany Federal Institute for Risk Assessment. Does Glyphosate Cause Cancer? (2015), *available at* http://www.bfr.bund.de/cm/349/does-glyphosate-cause-cancer.pdf (last visited October 2015).

[8] JMPR (WHO/FAO). Pesticide Residues in Food. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group. Part II-Toxicology, Glyphosate: 96-169. Rome, Italy 20-29 September (2004), *available at* http://whqlibdoc.who.int/publications/2006/9241665203_eng.pdf?ua=1 (last visited October 2015);
WHO International Programme on Chemical Safety Environmental Health Criteria No. 159: Glyphosate. World Health Organization, Geneva. (1994), *available at* http://www.inchem.org/documents/ehc/ehc/ehc159.htm (last visited October 2015).

[9] WHO, Guidelines for Drinking-water Quality, 4th edition (2011), p. 374, a*vailable at* http://apps.who.int/iris/bitstream/10665/44584/1/9789241548151_eng.pdf (last visited October 2015);

In fact, as shown in the following table, 17 reviews by regulatory bodies and associated WHO programs have considered the same studies that IARC relied on, and each has come to the opposite conclusion -- that the four long-term carcinogenicity studies of glyphosate do not show that the small number of tumors identified in the rodents subjected to treatment with glyphosate were related to glyphosate. These four studies are shown in the table as:

1. **MON Mouse**: Knezevich, A.L. & Hogan, G.K. (1983). A chronic feeding study of glyphosate (Roundup Technical) in mice. [cited by IARC as EPA (1985a, b, 1986)]
2. **MON Rat 1**: Lankas, G.R. & Hogan, G.K. (1981). A lifetime study of glyphosate (Roundup Technical) in rats. [cited by IARC as (EPA, 1991a, b, c, d)]
3. **MON Rat 2**: Stout, L.D. & Ruecker, F.A. (1990). Chronic study of glyphosate administered in feed to albino rats. [cited by IARC as (EPA, 1991a, b, c, d)]
4. **CHEM Mouse**: Atkinson, C., et al. (1993). Glyphosate: 104 week dietary carcinogenicity study in mice. [cited by IARC as (JMPR, 2006)]

Date	Entity Considering Whether Tumors Are Related to Treatment	Tumors Related to Treatment?			
		MON Mouse	MON Rat 1	MON Rat 2	CHEM Mouse
1987	WHO/JMPR	No	No	-	-
1991	US EPA Cancer Classification	No	No	No	-
1991	Canada PMRA	No	No	No	-
1993	US EPA RED	No	No	No	-
1994	WHO/IPCS	No	No	No	-
1999	Japan FCS	No	No	No	-
2000	FAO Specifications	No	No	No	-
2002	EU Annex I	No	No	No	No
2004	WHO/JMPR	-	-	No	No
2005	WHO/Water Sanitation Health	No	No	No	-
2007	OEHHA	No	No	No	No

Glyphosate and AMPA in Drinking-water Background document for development of WHO Guidelines for Drinking-water Quality. (2005), a*vailable at* http://www.who.int/water_sanitation_health/dwq/chemicals/glyphosateampa290605.pdf (last visited October 2015).

Date	Entity Considering Whether Tumors Are Related to Treatment	Tumors Related to Treatment?			
		MON Mouse	MON Rat 1	MON Rat 2	CHEM Mouse
2008	US EPA Effects Determination	No	-	No	-
2010	Japan FCS	No	No	No	-
2012	US EPA Human Health Risk Assessment	No	No	No	-
2013	Australia	No	No	No	No
2015	EU Annex I Renewal (BFR)	No	No	No	No
2015	Canada PMRA Registration Rev	No	No	No	No
2015	US EPA Registration Rev	-	-	-	-
2015	WHO/IARC	Yes	Yes	Yes	Yes

The consistent opinion of these entities, spanning reviews for over 20 years, is that glyphosate is not carcinogenic. It is clear that the outlier among these entities is IARC.

4.0 OEHHA Itself Does Not Consider Glyphosate To Be A Carcinogen.

In 2007, OEHHA conducted a risk assessment of glyphosate for purposes of setting a Public Health Goal (PHG) for glyphosate in drinking water.[10] As part of that assessment, OEHHA evaluated the carcinogenicity of glyphosate using the "best available toxicological data in the scientific literature" and concluded: "Based on the weight of evidence, glyphosate is judged unlikely to pose a cancer hazard to humans."[11] OEHHA's proposal to list glyphosate as known to the state of California to cause cancer, notwithstanding the Agency's own determination in 2007 that glyphosate is unlikely to be a carcinogen, makes no sense. It is troubling (and, as discussed below, unlawful) for OEHHA to ignore its own careful analysis and allow an unrepresentative group of scientists, acting under the aegis of a foreign body and relying on selective studies and ignoring the full body of evidence, to overrule the determination of California's designated scientific officials.

Notably, OEHHA, in finding glyphosate *not* to be a carcinogen, considered the very same scientific studies that IARC relied upon in reaching the conclusion that there is "sufficient evidence" in experimental animals for the carcinogenicity of glyphosate. Specifically, IARC made the following findings with respect to the animal carcinogenicity data: (i) "[t]here was a positive trend in the incidence of renal tubule carcinoma and of renal tubule adenoma or carcinoma (combined) in males in one feeding study in CD-1 mice"; (ii) "there was a significant positive trend in the incidence of

[10] OEHHA, Public Health Goals for Chemicals in Drinking Water: Glyphosate (June 2007) ("OEHHA Assessment"), *available at* http://oehha.ca.gov/water/phg/pdf/GlyPHG062907.pdf (last visited October 2015).
[11] OEHHA Assessment, page 1.

haemangiosarcoma in male CD-1 mice" in a second feeding study of mice; and (iii) two studies in rats "showed a significant increase in the incidence of pancreatic islet cell adenoma in males."[12] As described below, each of these studies — two in mice and two in rats — also was reviewed by OEHHA in its 2007 assessment of glyphosate.

- Renal Tubule Carcinoma/Adenoma. IARC cited a 1983 study—Knezevich A, Hogan G (1983)[13] — for its finding that "[t]here was a positive trend in the incidence of renal tubule carcinoma and of renal tubule adenoma or carcinoma (combined) in males in one feeding study in CD-1 mice."[14] OEHHA evaluated this same study (referenced by OEHHA as Bio/Dynamics, Inc. (1983)), but, in contrast to IARC, did not find the data to support a finding of carcinogenicity. OEHHA noted, for example, that "[a]fter reviewing the data, the FIFRA Scientific Advisory Panel noted that age-adjusted tumor incidence data did not demonstrate a statistically significant increase based on concurrent controls. . . ."[15]

- Haemangiosarcoma. IARC cited a single study discussed in a 2004 Joint FAO/WHO Meeting on Pesticide Residues ("JMPR") report[16] for its finding that "there was a significant positive trend in the incidence of haemangiosarcoma in male CD-1 mice."[17] OEHHA also cited the JMPR report, but reached a different conclusion, stating: "In its 2004 review of the toxicity of glyphosate, WHO (2004) found the chemical has no genotoxic potential and there is no evidence of carcinogenicity in rats or mice."[18] And indeed, OEHHA's conclusion in 2007 was supported by the findings of the JMPR report, which stated in regard to the relevant study that the "administration of glyphosate to CD-1 mice for 104 weeks produced no signs of carcinogenic potential at any dose."[19]

- Pancreatic Islet Cell Adenoma. IARC cited two studies in rats—Stout & Ruecker (1990) and Lankas (1981)[20]—for its finding that there was an "increase in the incidence of pancreatic islet cell adenoma in male[]" rats.[21] OEHHA reviewed these same studies (referenced by OEHHA as Monsanto, 1990c and Bio/Dynamics, Inc., 1981a/Monsanto, 1984) and did not find sufficient evidence of an increased incidence of pancreatic islet cell adenoma.

[12] IARC Monograph Vol. 112, page 76 (summary of animal carcinogenicity data), *available at* http://monographs.iarc.fr/ENG/Monographs/vol112/mono112-02.pdf (last visited October 2015).
[13] EPA (1983). Review of Knezevich A, Hogan G (1983). A chronic feeding study of glyphosate (Roundup Technical) in mice.
[14] IARC Monograph Vol. 112, pages 30, 76 [cited by IARC as EPA (1985a, b, 1986)].
[15] OEHHA Assessment, page 13.
[16] JMPR (WHO/FAO). Pesticide Residues in Food. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group. Part II-Toxicology, Glyphosate: 96-169. Rome, Italy 20-29 September (2004), page 122, *available at* http://whqlibdoc.who.int/publications/2006/9241665203_eng.pdf?ua=1 (last visited October 2015). The study cited therein is Atkinson, C., et al. (1993). Glyphosate: 104 week dietary carcinogenicity study in mice.
[17] IARC Monograph Vol. 112, pages 33, 76, *available at* http://monographs.iarc.fr/ENG/Monographs/vol112/mono112-02.pdf (last visited October 2015).
[18] OEHHA Assessment pages 20, *available at* http://oehha.ca.gov/water/phg/pdf/GlyPHG062907.pdf (last visited October 2015).
[19] JPMR (2004), page 122.
[20] IARC cited a series of US EPA reviews (EPA, 1991a, b, c, d) on the toxicity/carcinogenicity of glyphosate that addressed these two studies, Monograph Vol. 112, page 36.
[21] IARC Monograph Vol. 112, pages 36, 40, 76.

In other words, OEHHA, the "lead state agency for the assessment of health risks posed by environmental contaminants,"[22] reviewed the exact same set of animal studies relied upon by IARC and determined that glyphosate is **not** likely to be a carcinogen. OEHHA's proposal to list glyphosate as known to the state of California to cause cancer, notwithstanding the Agency's own assessment that glyphosate is not likely carcinogenic, reflects a disregard for principles of good government and sound public policy.

5.0 IARC's Classification Contradicts Sound Science.

The IARC Category 2A classification is not supported by the scientific data and standard scientific methodology. It is imperative for society that conclusions about a matter as important as safety (food, applicators, consumers, etc.) should be objective, thorough and based on quality science that adheres to internationally recognized standards. IARC's review of glyphosate does not meet the quality standards used by regulatory authorities around the world, and IARC's misclassification should not be used by OEHHA to list glyphosate under OEHHA's interpretation of Proposition 65.

IARC's monograph does not present new research or data. The IARC monograph is not a 'study'. The key studies considered by IARC in their monograph have been recently reviewed in 2015 in a more comprehensive toxicology assessment by the EU Rapporteur Member State and the Canadian PMRA for the re-registration processes in the EU and Canada respectively, neither of which found glyphosate to pose a carcinogenic risk.

Unlike regulatory agencies, IARC did not conduct a total weight-of evidence evaluation or follow standard toxicological practice and evaluation frameworks.[23] It is clear from the references listed in the Monograph that the information actually selected for consideration by the panel represents only a subset of the vast dataset available on glyphosate. Consideration of the complete dataset, as is done by regulators globally, overwhelmingly supports the conclusions of safety and lack of carcinogenic potential of glyphosate.

The IARC panel did not conduct an overall evaluation of all data; instead it conducted an evaluation of selected studies, selected data points, and IARC's interpretation of the data within each of the four areas of evidence the panel considered (animal carcinogenicity, exposure, genotoxicity, and epidemiology). This is in striking contrast to regulatory authorities, other WHO programs, independent experts and even the authors themselves of the studies used by IARC in the assessment. Highlighted below are some key examples of IARC's surprising conclusions (a full analysis by Dr. Donna Farmer is submitted herewith and incorporated herein):

- *Animal carcinogenicity*: In reaching its conclusion of "sufficient evidence" of carcinogenicity in animals, the IARC panel reinterpreted isolated findings of tumor incidences in particular studies,

[22] OEHHA Website, OEHHA Department Description, *available at* www.oehha.ca.gov/about/description.html, (last visited October 2015).

[23] Adami H.O. et al., (2011). Toxicology and epidemiology: improving the science with a framework for combining toxicological and epidemiological evidence to establish causal inference. *Toxicol. Sci.* 122(2):223-34, ***available at*** http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3155086/, (last visited October 2015); Lewis R.W. et al., (2002). Recognition of Adverse and Nonadverse Effects in Toxicity Studies. *Toxicol. Pathol.*, vol 30, no 1, pp 66–74, *available at* http://mysop.washington.edu/images/stories/pharmaceutics/restricted/PCEUT587/587-article-2.pdf (last visited October 2015).

focusing on numerical increases in tumor incidence in treatment groups, but ignoring the lack of a dose-response, background tumor incidences in historical control animals, and pathology expert opinions -- all of which typically provide context to toxicologists in their assessment of whether there is a possible relationship to treatment. IARC's approach is non-standard and at odds with basic toxicological practices. Other experts and regulators have long concluded that the isolated tumors discussed by IARC were spontaneous and not related to glyphosate treatment. Moreover, multiple other long-term toxicology studies conducted according to international standards were not reviewed by IARC but clearly corroborate the lack of carcinogenic potential of glyphosate.

- *Epidemiology*: In reaching its conclusion of "limited evidence" in humans for the carcinogenicity of glyphosate, the IARC panel used case-control studies with design limitations and diverse methods for the estimation of glyphosate exposure as well as an inappropriate statistical model. IARC ignored the findings from the largest and single most important study into the health of pesticide applicators in the US, which found no link between glyphosate and non-Hodgkin's lymphoma or any another cancer.

- *Genotoxicity*: In reaching its conclusion of strong evidence that glyphosate and commercial formulations can be genotoxic and produce oxidative damage, the IARC panel selectively relied on non-standard studies with adverse effects, which used methods that have not been validated and/or were not conducted according to international guidelines. Furthermore, IARC disregarded a plethora of more relevant data, including the 2004 JMPR review, peer-reviewed literature reviews, and opinions of numerous other scientists who have carefully considered all the available data including those required by regulators and concluded glyphosate is not genotoxic.

- *Exposure*: The IARC monograph considered an incomplete literature review, citing old references where more recent ones exist, and selectively used references and data. IARC cites detections of glyphosate in different matrices (urine, serum, soil, air, water, and food) without placing the levels and potential exposures into the proper context. In reality, regulatory authorities and the JMPR establish Average Daily Intakes (ADIs) and Acceptable Operator Exposure Levels (AOELs) to account for potential human exposures and establish safe exposure levels. When regulatory agencies consider exposure in the proper context, they consistently conclude that there are no health concerns with exposure to glyphosate.

If OEHHA moves forward to list glyphosate based solely on the IARC classification, it will do so as a result of incomplete and misinterpreted data and in contradiction to the overwhelming weight of evidence from more than 800 studies on glyphosate safety and the consensus of regulatory agencies around the world. Moreover, OEHHA would be making a decision to list without the benefit of the sound, science-based assessment currently being conducted by competent regulators, including the U.S. EPA, and contradicting OEHHA's own prior review of the science regarding glyphosate.

6.0 It Is Improper to List Glyphosate Under the Labor Code Mechanism.

Monsanto has serious concerns about OEHHA's over-reliance on the Labor Code listing mechanism. Monsanto believes that OEHHA's implementation of the Labor Code listing mechanism constitutes an unlawful abdication of the authority delegated to the agency by the voters in enacting Proposition 65 and rests on an interpretation of the statute that improperly delegates law-making authority to an

unelected, undemocratic, foreign body. That body convenes ad hoc groups of scientists, chosen in a non-transparent process, to review and summarize scientific research and make extremely consequential decisions, without even taking public comment. OEHHA's statement in the proposed listing that it must blind itself to sound science is particularly troubling and remarkable in light of OEHHA's mission and personnel.

Not surprisingly, IARC explicitly disavows any policy- or law-making role, and does not intend its determinations to carry the force of law. In its Preamble, IARC states:

> The evaluations of IARC Working Groups are scientific, qualitative judgements on the evidence for or against carcinogenicity provided by the available data. These evaluations represent only one part of the body of information on which public health decisions may be based. Public health options vary from one situation to another and from country to country and relate to many factors, including different socioeconomic and national priorities. Therefore, ***no recommendation is given with regard to regulation or legislation***, which are the responsibility of individual governments or other international organizations.[24]

As such, it is all the more inappropriate for OEHHA to rely on the determinations of IARC—or, more accurately, the small group of individuals appointed by IARC to review any individual substance—to make decisions that have the effect of placing chemicals on the Proposition 65 list following only a "ministerial" process that does not involve any consideration whatsoever of the weight or quality of the scientific evidence. That impropriety is all the more clear in a situation, such as this, where OEHHA itself has determined, based on a searching analysis of the same scientific studies, that the chemical is not likely to cause cancer.

The abdication by OEHHA of any substantive role in listing a substance under the Labor Code mechanism rests on an interpretation of Proposition 65 that improperly delegates the People's authority to a foreign body without any safeguards for due process, public involvement, or control by the People's representatives. This violates the United States and California Constitutions. *See, e.g.*, *Carter v. Carter Coal Co*., 298 U.S. 238, 310 (1936) (striking down law that empowered industry associations to draw up regulatory codes that carried the force of law); *Natural Resources Defense Council v. EPA*, 464 F.3d 1, 9 (D.C. Cir. 2006) ("[A]ssigning law-making functions to international bodies . . . would raise serious constitutional questions in light of the nondelegation doctrine, numerous constitutional procedural requirements for making law, and the separation of powers."); *Carson Mobilehome Park Owners' Assn. v. City of Carson*, 35 Cal. 3d 184, 190 (1983) ("An unconstitutional delegation of authority occurs only when a legislative body (1) leaves the resolution of fundamental policy issues to others or (2) fails to provide adequate direction for the implementation of that policy."); *Bagley v. City of Manhattan Beach*, 18 Cal. 3d 22, 26-27 (1976) (employing non-delegation doctrine to invalidate voter initiative that would have allowed wages to be set by an arbitrator, and holding that "the city possessing no power under existing state statute to provide for arbitration of wage rates, such power cannot be created by local initiative"); *Int'l Assn. of Plumbing & Mech. Officials v. Cal. Bldg. Standards Comm'n*, 55 Cal. App. 4th 245, 253-54 (1997) ("IAPMO") (upholding delegation of authority to the California Building Standards Commission, a governmental entity, to adopt as law model codes prepared by private entities, but only because the Commission was vested with discretion subject to adequate safeguards and was not required to adopt the standards approved by a private entity).

[24] IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Preamble (emphasis added), page 3, (2006), *available at* http://monographs.iarc.fr/ENG/Preamble/CurrentPreamble.pdf (last visited October 2015).

Here, OEHHA's implementation of the Labor Code mechanism delegates to an unelected, foreign body the authority to set regulations under California law. IARC is not subject to any procedural safeguards or oversight by a California governmental body. IARC can change its procedures at any time. It need not consider any comments. It could appoint patently unqualified scientists, with undisclosed conflicts of interest or from backgrounds biased against certain industries or fields. It could act by majority vote, or by dictate of those appointed by governments who provide the organization with the most funding. It could be controlled by the chemical industry, the consumer products industry, or by activists with any number of agendas. Because there are no safeguards on IARC's processes, OEHHA's unwillingness even to review IARC's scientific determinations and consider comments on them only furthers the injury to the democratic process and to the use of sound science in regulatory decision-making. OEHHA has a responsibility to interpret and implement Proposition 65 in a manner that carries out the voters' mandate consistent with the United States and California Constitutions, and OEHHA's unwillingness to consider scientific comments shirks that responsibility and overlooks the significant limitations and errors in IARC's process identified above that resulted in the misclassification of glyphosate.

7.0 OEHHA Should Withdraw Its Proposal to List Glyphosate.

A listing of glyphosate under Proposition 65 has the potential to deny farmers and public agencies the use of this highly effective herbicide, an herbicide whose use promotes the health, well-being, safety, and environment of Californians. As discussed herein, global regulatory authorities, including OEHHA itself, and independent experts all agree that glyphosate is not carcinogenic. Moreover, OEHHA's abdication of any substantive role in listing glyphosate under the Labor Code mechanism and refusal to consider comments concerning the weight of the scientific evidence would be unreasonable and a violation of the United States and California Constitutions, as well as established principles of good government and public policy. For the foregoing reasons, Monsanto urges OEHHA to withdraw its proposal to place glyphosate on the Proposition 65 list via the Labor Code mechanism.

Respectfully,

Monsanto Company

By: _____

Philip W. Miller
Vice President, Global Regulatory and Government Affairs

APPENDIX 1: Summary of Regulatory Decisions Globally

A. United States

In 2014, the U.S. Environmental Protection Agency (EPA) reviewed more than 55 epidemiological studies conducted on the possible cancer and non-cancer effects of glyphosate and concluded: "this body of research does not provide evidence to show that glyphosate causes cancer, and it does not warrant any change in EPA's cancer classification for glyphosate. This is the same conclusion reached in 2004 by the United Nations' Food and Agriculture Organization and affirmed this year by Germany's pesticide regulatory officials."[25]

In May 2013, the EPA found that all glyphosate exposures through food crops and water sources were no more than 13 percent of the average daily intake based on a highly conservative assumption that all crops are treated with glyphosate and carry maximum allowable levels.[26] The reality is that not all crops on all farms are treated, and those crops that are treated generally have well below the maximum allowable limit, leaving a wide margin of safety. This is confirmed by available monitoring data in humans, which indicate actual exposures are far below allowable intake levels.[27]

In 1993, the EPA, after reviewing studies conducted for re-registration of glyphosate, stated: "Several chronic toxicity/carcinogenicity studies…resulted in no effects based on the parameters examined, or resulted in findings that glyphosate was not carcinogenic in the study" and "Glyphosate does not cause mutations".[28] EPA rates all pesticides according to their potential to cause cancer.

In June 1991, EPA placed glyphosate in the agency's lowest cancer classification (Group E) "evidence of noncarcinogenicity for humans -- based on the lack of convincing evidence of carcinogenicity in adequate studies."[29]

B. Europe

On March 23, 2015, in response to the International Agency for Research on Cancer's (IARC) classification of glyphosate, the Germany Federal Institute for Risk Assessment (BfR) stated: "As the 'Rapporteur Member State' for the active substance glyphosate within the framework of EU re-

[25] Statement of Carissa Cyran, Chemical review manager for the Office of Pesticide Programs at EPA (2015). http://www.croplife.com/editorial/epa-plans-response-to-iarc-glyphosate-finding-but-not-just-yet/.
[26] Fed. Reg. Vol. 78, No. 84 (May 1, 2013). The EPA conservatively sets the acceptable daily intake (ADI) from all food and water sources at least 100 times lower than levels that have been demonstrated to cause no effect in animal testing. http://www.gpo.gov/fdsys/pkg/FR-2013-05-01/pdf/2013-10316.pdf
[27] Niemann, L., Sieke, C., Pfeil, R., and Solecki, R. (2015). A critical review of glyphosate findings in human urine samples and comparison with the exposure of operators and consumers. J. Verbr. Lebensm. 10:3–12.
[28] U.S. Environmental Protection Agency, Washington, DC. (1993), Registration Eligibility Decision (RED): Glyphosate, EPA-738-F-93-011. http://1.usa.gov/1J2vnlJ.
[29] *Ibid.*

evaluation, the Federal Institute for Risk Assessment (BfR) was responsible for the human health risk assessment and has assessed glyphosate as non-carcinogenic."[30]

In its 2014 Glyphosate Renewal Assessment Report, Germany, as Rapporteur Member State for the European Annex I Renewal of Glyphosate, stated:"…glyphosate was considered unlikely to pose a carcinogenic risk in humans …" and "In epidemiological studies in humans, there was no evidence of carcinogencity and there were no effects on fertility, reproduction and development or of neurotoxicity that might be attributed to glyphosate."[31] The studies reviewed included all those considered by IARC, plus many more.

A regulatory review was conducted by the European Commission's (EC) Health and Consumer Protection Directorate-General in 2002, after which glyphosate was re-registered for use in Europe. The EC review, like others around the world, concluded that there was "No evidence of carcinogenicity" and glyphosate is "Not genotoxic".[32]

C. Canada

On April 13, 2015, Canadian Pest Management Regulatory Authority (PMRA) proposed the continued registration of products containing glyphosate for sale and use in Canada, stating the following:

> The World Health Organization's (WHO) International Agency for Research on Cancer (IARC) recently assigned a hazard classification for glyphosate as probably carcinogenic to humans. It is important to note that a hazard classification is not a health risk assessment. The level of human exposure, which determines the actual risk, was not taken into account by WHO (IARC). Pesticides are registered for use in Canada only if the level of exposure to Canadians does not cause any harmful effects, including cancer.
>
> In consideration of the strength and limitations of the large body of information on glyphosate, which included multiple short and long term (lifetime) animal toxicity studies, numerous in vivo and in vitro genotoxicity assays, as well as the large body of epidemiological information, the overall weight of evidence indicates that glyphosate is unlikely to pose a human cancer risk. This is consistent with all other pesticide regulatory authorities world-wide, including the most recent, ongoing comprehensive re-evaluation by Germany (Rapporteur Member State for the European Union) that was published for public consultation in 2014.[33]

[30] Germany Federal Institute for Risk Assessment. Does Glyphosate Cause Cancer? (2015). http://www.bfr.bund.de/cm/349/does-glyphosate-cause-cancer.pdf.
[31] Annex I Renewal Assessment Report, Glyphosate (March 12, 2014). http://dar.efsa.europa.eu/dar-web/provision.
[32] European Commission, Report for the Active Substance Glyphosate, Directive 6511/VI/99, Jan. 21, 2002. http://ec.europa.eu/food/fs/ph_ps/pro/eva/existing/list1_glyphosate_en.pdf.
[33] Health Canada, Pest Management Regulatory Agency (2015), Proposed Re-evaluation Decision PRVD2015-01, Glyphosate. http://www.hc-sc.gc.ca/cps-spc/pest/part/consultations/_prvd2015-01/prvd2015-01-eng.php.

In 1991, PRMA concluded: "Health and Welfare Canada has reviewed the glyphosate toxicology database, which is considered to be complete. The acute toxicity of glyphosate is very low. The submitted studies contain no evidence that glyphosate causes mutations, birth defects or cancer."[34]

D. Australia

On March 23, 2015, in response to IARC's classification of glyphosate, Australian Pesticides and Veterinary Medicines Authority (APVMA), stated: "It is not the role of the IARC to consider how a formulated chemical product is used, or how human exposure can be minimised by following safety directions on a product label. In this regard, the findings of IARC cannot be directly compared to assessments conducted by regulatory authorities for the purposes of approval or registration of a pesticide product, in which are included appropriate risk mitigation measures to allow safe use."[35]

In its 2013 review of the Earth Open Source report "Roundup and Birth Defects: Is the Public Being Kept in the Dark?", the APVMA stated: "The APVMA currently has no data before it suggesting that glyphosate products registered in Australia and used according to label instructions present any unacceptable risks to human health, the environment and trade …" and "The weight and strength of evidence shows that glyphosate is not genotoxic, carcinogenic or neurotoxic."[36]

E. Japan

Glyphosate is currently being evaluated in Japan. Japan's 2000 evaluation of human health effects of glyphosate found no indication of carcinogenicity in the repeated dose studies and the results of all mutagenicity genotoxicity studies were negative (i.e., not genotoxic).[37]

F. World Health Organization (WHO)

The Joint WHO/Food Agricultural Organization (FAO) Meeting on Pesticide Residues ("JMPR") concluded in 2011 that the long-term and short-term intakes of glyphosate residues are unlikely to present a public health concern or risk to consumers.[38]

Similarly, in their 2004 report on pesticide residues in food, the JMPR stated: "Long-term studies of toxicity and carcinogenicity were conducted in mice and rats. In the study of carcinogenicity in mice, no

[34] Doliner LH. (1991) Pre-Harvest use of glyphosate herbicide [Preharvest application of glyphosate (Roundup) herbicide]. Discussion Document D91-01. 98 pp. Pesticide Information Division, Plant Industry Directorate, Agriculture Canada.
[35] Australian Government, Australian Pesticides and Veterinary Medicines Authority. Information about glyphosate use: The IARC assessment explained. http://apvma.gov.au/node/13891.
[36] Australian Government, Australian Pesticides and Veterinary Medicines Authority. (2013). http://archive.apvma.gov.au/news_media/docs/glyphosate_scitox_review_july_2013.pdf.
[37] Report of Evaluation by Food Sanitation Council Agricultural Chemicals Residue Committee, Shokuhin Eisei Kenkyu Vol.50, No.8 (2000).
[38] WHO/FAO, Pesticides residues in food -- 2011. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues (JMPR).
http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Report11/Glyphosate.pdf

toxic effects were observed at up to the highest dose tested (1000 mg/kg bw per day), and there was no evidence of carcinogenicity" and "Negative results were obtained in studies performed in compliance with current test guidelines. The Meeting concluded that glyphosate is unlikely to be genotoxic."[39] Despite the JMPR's findings of "no toxic effects," "no evidence of carcinogenicity," and "unlikely to be genotoxic," IARC cited this WHO report to support its finding of sufficient evidence of carcinogenicity in animals.[40]

The WHO's International Programme on Chemical Safety in its 1994 review of glyphosate studies, states: "Animal studies show that glyphosate is not carcinogenic, mutagenic…"[41]

In 1986, the JMPR, in their report on pesticide residues in food stated: "The chronic toxicity of glyphosate is low; the only significant toxicity seen in a number of animal bioassays was mild hepatotoxicity at high doses in mice. There is no evidence of carcinogenicity." and "Glyphosate was without mutagenic activity both in vitro and in vivo."[42]

[39] WHO/FAO, Pesticides residues in food -- 2004. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues (JMPR). http://whqlibdoc.who.int/publications/2006/9241665203_eng.pdf?ua=1

[40] Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate, Lancet Oncol (March 20, 2015) (citing 2004 Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues (JMPR)). http://www.thelancet.com/journals/lanonc/article/PIIS1470-2045%2815%2970134-8/fulltext.

[41] WHO International Programme on Chemical Safety (1994), Environmental Health Criteria No. 159: Glyphosate. World Health Organization, Geneva. http://www.inchem.org/documents/ehc/ehc/ehc159.htm.

[42] WHO/FAO, Pesticides residues in food – 1986. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues (JMPR). http://www.inchem.org/documents/jmpr/jmpmono/v86pr08.htm.