Benefits and Safety of Glyphosate

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Glyphosate is a versatile herbicide used by farmers, land managers and gardeners to simply, safely and effectively control unwanted vegetation. Since their introduction in 1974, glyphosate-based products have become the most commonly used herbicides in the U.S. This widespread adoption is the result of glyphosate’s ability to control a broad spectrum of weeds, its extensive economic and environmental benefits and its strong safety profile. Glyphosate is currently undergoing registration review by the US Environmental Protection Agency (EPA or the Agency) and it is essential that farmers, land managers and gardeners retain access to this important tool for weed control.

Herbicide use on US crops increased steadily between the introduction of synthetic herbicides in the mid-twentieth century until the 1980s, driven by the ability of herbicides to reduce labor, fuel and machinery needs. With the adoption of glyphosate-tolerant crops beginning in the mid-1990s, glyphosate began to replace alternative herbicides. In the absence of a crop tolerant to a specific herbicide, growers had to rely on tillage or hand weeding, complicated herbicide application schemes or accept that some weeds would not be controlled. Glyphosate-based herbicides coupled with glyphosate-tolerant crops simplified weed control by offering an easy to use, low toxicity, systemically acting active ingredient that reduced farm household labor requirements. Glyphosate-based herbicides also lowered barriers to the adoption of conservation tillage, helping to conserve soil resources, protect water quality and reduce carbon dioxide emissions. Following their widespread adoption, commodities produced from glyphosate-tolerant crops now comprise approximately $33 billion/year in US agricultural exports.

Distinct from the use of glyphosate in conjunction with glyphosate-tolerant crops, glyphosate-based herbicides also provide economical and effective weed control across many other agricultural and non-agricultural settings. It allows for simple and effective weed control in multiple crops, even when the crop itself is not glyphosate-tolerant. Glyphosate also simplifies adoption of cover crops by providing a simple, non-mechanical means to eliminate the cover crop prior to planting the cash crop. Outside of agriculture, glyphosate allows low cost weed control along highway, railroad and utility right of ways. In recreational settings, glyphosate provides cost-effective maintenance of landscape function and aesthetics. It is an indispensible option for land managers needing to control invasive weeds and as an aid in restoring native habitats. As an aquatic herbicide, glyphosate provides a non-mechanical option for removing weeds that can impede recreation and navigation.

Glyphosate-based herbicides are supported by one of the most extensive worldwide human health and environmental effects databases ever compiled for a pesticide product. Comprehensive toxicological and environmental fate studies conducted over the last 40 years have time and again demonstrated the strong safety profile of this widely used herbicide. Glyphosate works by inhibiting an enzyme present in plants that people and animals do not produce. Glyphosate exhibits low toxicity to humans and non-plant wildlife over both short- and long-term exposures. It does not cause cancer and it is not an endocrine disruptor. In the environment, glyphosate binds tightly to soil, degrades over time and does not accumulate in the food chain. Despite this strong safety profile, there is a great deal of misinformation about glyphosate; a careful examination of the various claims demonstrates that they are not supported by reproducible evidence.

Maintaining access to glyphosate will promote environmental and economic sustainability in agriculture. Its versatility has transformed weed control across a wide range of environments. Glyphosate’s ability to effectively control unwanted vegetation provides benefits that extend from individual farms to global trade to national parks to golf courses to local governments to gardeners. For all of these reasons, glyphosate earned the title of a “once in a century herbicide”. Continued access to this important technology is essential.
Anyone needing to control weeds, from farmers to land managers, understands the benefits that glyphosate provides, not only in terms of efficacy but also in terms of reduced labor and ease of use. Within agriculture, the advantages of glyphosate-tolerant cropping systems are well-documented, particularly at the farm level. Glyphosate-tolerant crops also underpin a significant amount of farm incomes and commodity export markets. The benefits of glyphosate also extend into systems that do not rely on glyphosate-tolerant crops by reducing the need for mechanical weed control and overall production costs. Outside of agriculture, glyphosate is a key tool for controlling weeds in rights of way alongside highways, near utility lines and near railroad tracks. It also plays a significant role in turf management and in stopping the spread of invasive or noxious weeds in terrestrial and aquatic settings.

Combining glyphosate with crops that could withstand applications of this herbicide transformed agriculture. Labor and machinery requirements declined and adoption of this technology is associated with increased off-farm income because of labor savings. Glyphosate-tolerant crop varieties greatly simplified weed control for corn, cotton and soybean farmers. It also allowed sugarbeet farmers to increase their yields by both eliminating weed competition and reliance on herbicides that can cause crop damage. Adoption of glyphosate-tolerant crops is also associated with an increased likelihood of adopting conservation tillage, which brings its own benefits in terms of reduced soil erosion, improved water quality and lower carbon dioxide (CO₂) emissions. Although glyphosate-resistant weeds have evolved, it is possible to manage this issue by developing and adopting diversified weed management plans. Today glyphosate-tolerant crops form the backbone of many major US row crops, accounting for over $33 billion of annual exports (calculated from GfK SeedService, 2016; USDA-FAS, 2016).

In agricultural systems where glyphosate-tolerant crops are not available, glyphosate still provides significant benefits by simplifying weed management and reducing the need for mechanical tillage. For orchards and vineyards, effective weed control is necessary to ensure productivity. In these settings, glyphosate is an essential tool for controlling vegetation beneath trees or vines. In wheat, glyphosate has allowed farmers to adopt no-till practices that help them to conserve soil moisture, thus enabling rotation with more profitable crops. In sugarcane, glyphosate improves harvest quality in addition to controlling weeds. Glyphosate also enables the adoption of cover crops by providing a simple and effective means to eliminate the cover crop just prior to planting a cash crop without raising concerns about plant back restrictions.

In non-agricultural settings, glyphosate provides cost-effective weed control along highways and other rights of way. In an economic analysis of highway median weed control, for example, glyphosate was 275% less expensive than alternative methods that included multiple mowing events and alternative herbicides (Tjosvold and Smith, 2010). For golf course managers, glyphosate applications to dormant turf allow undesirable species of weeds and grasses to be controlled without having to replace large sections of fairways. It also provides a simple means to eliminate turf in order to replace it with less water-intensive landscaping. Glyphosate has also delivered significant benefits for invasive weed management. National parks have relied on glyphosate to decisively manage non-native vegetation and in aquatic settings it has been used to replace mechanical weed removal to enable navigation and eliminate weeds that crowd out native wildlife.

Across a wide range of applications, glyphosate has become one of the most reliable and widely adopted herbicides in the US. Its benefits to agriculture in conjunction with glyphosate-tolerant crops as well as non-glyphosate-tolerant crops provide growers the flexibility they need to ensure ample harvests to satisfy global demand. In other applications, glyphosate provides simple, cost effective weed control to local governments, utilities, railroads and environmental managers. Continued access to this technology is essential for these benefits to be enjoyed in the future.
2.1 Benefits to agriculture in glyphosate-tolerant cropping systems

The most notable and economically significant impact of glyphosate has been its ability to transform agricultural practices in conjunction with glyphosate-tolerant crops. Combining a broad spectrum herbicide like glyphosate with crops tolerant to that herbicide enabled simplified and efficient weed control that reduced the need for alternative technologies such as tillage and hand labor. Following the introduction and adoption of glyphosate-tolerant crops (soybean, cotton, corn, canola, alfalfa and sugar beet), glyphosate replaced several other herbicides, lowered the cost of weed management and reduced the amount of labor needed to manage weeds in these crops. The combination of glyphosate and glyphosate-tolerant crops simplified conservation tillage practices, primarily for soybean, cotton and sugar beet farmers. Despite the development of glyphosate-resistant weed biotypes, glyphosate still has significant utility across agriculture. Today, glyphosate-tolerant crops are a foundation of US exports of corn, soybeans and canola, providing significant economic returns to US agriculture.

2.1.1 Expansion in agriculture and replacement of other herbicides

Glyphosate is currently used on a majority of corn, cotton, sugar beet, canola and soybean acres in the US and tends to be used in combination with other herbicides depending on the crop. Prior to the introduction of glyphosate-tolerant crops, soybean farmers had few postemergent herbicide options that would control broadleaf weeds while posing a lower risk of crop injury. While glyphosate is the most commonly used herbicide on these crops, it is often used in conjunction with other methods of weed control. According to USDA-ERS data, the use of glyphosate as the sole herbicide in soybeans peaked in 2006 at 89% of total US soybean acres. This figure declined to approximately 50% by 2012 (Livingston et al., 2015). In corn, where preemergent herbicides such as atrazine are commonly used, only a small minority of acres rely on glyphosate as the sole herbicide (Livingston et al., 2015). The overall trend since the mid-1990s, however, has been that applications of other herbicides have declined as applications of glyphosate have increased.

According to a US Geological Survey (USGS) analysis, the herbicides alachlor, cyanazine, fluazifop, metolachlor, metribuzin, MSMA and nicosulfuron have exhibited significant downward trends in total pounds applied since the early- to mid-1990s when glyphosate use began to increase (USGS-NAWQA, 2016). Atrazine is the only herbicide that was widely used prior to and during the mid-1990s whose use remained essentially unchanged following the introduction of glyphosate-tolerant crops. It is most commonly used as a preemergent herbicide in corn. The ability to include post-emergence applications of glyphosate allowed applications of most other herbicides to be adjusted while still controlling important weed species. Nolte and Young (2002a) listed the development of weed biotypes resistant to acetolactate synthase (ALS) (e.g., imidazolinones and sulfonylureas) and photosystem II inhibitors (triazines like atrazine) as a significant contributor to glyphosate’s growing adoption in the late 1990s. Kniss (2016) reported that two to three applications of glyphosate on glyphosate-tolerant sugar beets replaced four to six different herbicides applied between three to six times per year, at five to 10 day intervals, some of which could injure the sugar beets under certain environmental conditions. From the available data, it is clear that glyphosate’s simplicity and ability to complement other weed control tactics made significant contributions to its adoption.

2.1.2 Farm level benefits

During the first decade that glyphosate-tolerant crops were planted commercially, USDA researchers began examining the specific reasons why farmers chose to plant these crops. The researchers noted that adopters of this technology had higher off-farm incomes and hypothesized that reduced labor requirements for
farm management increased the amount of time available for off-farm work (Fernandez-Cornejo et al., 2005). Subsequent USDA research found that adoption of herbicide-tolerant soybeans was associated with increased off-farm household income, a finding the authors attributed to reduced labor requirements associated with glyphosate-tolerant soybeans (Fernandez-Cornejo et al., 2007). Gardner et al. (2009) demonstrated the reality of this relationship by examining USDA Agricultural Resource Management Survey data. They found that the average soybean farmer with 517 acres reduced labor requirements 14.5% by adopting herbicide tolerant soybeans. This reduction resulted in a total requirement of 94.5 hours of labor per growing season, allowing the extra time to be devoted elsewhere, including off-farm employment. Marra and Piggott (2006) documented that farmers who grow herbicide tolerant crops place a monetary value on the labor savings they experience. Studies from the first few years after the introduction of glyphosate-tolerant crops provide further understanding of why farmers quickly integrated glyphosate into their weed control tactics. In a study of corn, soybean and wheat rotations, Swanton et al. (2000) found that even in instances when glyphosate did not control weeds to the same extent as other herbicides (e.g., when used in a single application), the lower cost of weed control still allowed for a positive economic outcome. Johnson et al. (2002) calculated input costs for growers adopting glyphosate-tolerant corn and found that while input costs for this system were greater than for conventional corn, net economic returns were similar and glyphosate allowed more flexibility in application timing. Prior to the availability of glyphosate-tolerant sugarbeets, farmers typically relied on a complicated and intensive herbicide program and still had to incorporate hand weeding on approximately 40 to 60% of their fields. A survey of North Dakota and Minnesota sugarbeet growers shows that an average of 45% of farmers listed weeds as their most serious production challenge from year to year prior to the availability of glyphosate-tolerant sugarbeets. After the adoption of glyphosate-tolerant beets, that dropped to fewer than 15% (Kniss, 2016).

While many of the studies of glyphosate's role in effective weed control cite the importance of including multiple mechanisms of action to control resistance, the results of Reddy and Whitting (2000) provide an insight into why many soybean farmers began to rely on glyphosate as their sole mechanism of weed control following the introduction of glyphosate-tolerant soybeans. The authors found that a post-emergence application of glyphosate produced similar weed control as a preemergent herbicide combined with glyphosate post-emergence. Similarly, Kniss et al. (2004) reported that glyphosate-tolerant sugarbeets produced significantly greater economic returns than conventional varieties as a result of improved weed control with the greatest benefits being realized at three applications of glyphosate per growing season. Multiple glyphosate applications also produced the greatest economic benefit in a comparison of weed control tactics in soybean (Culpepper et al., 2000). These benefits were present when glyphosate was used alone or with a preemergent herbicide. In a comparison of weed control tactics in soybean, Nolte and Young (2002b) found the largest net economic returns were associated with a single application of glyphosate as a postemergent herbicide. In a related study of economics and efficacy of weed control tactics in corn, Nolte and Young (2002a) found the greatest net economic returns associated with the ability to use glyphosate as a postemergent herbicide. In both of the Nolte and Young studies alternative weed control programs were either associated with crop damage or reduced flexibility in application timing. Cotton growers also witnessed the advantages of combining glyphosate-based herbicides with glyphosate-tolerant crops early after this technology became commercially available. Cotton's slow growth makes it especially susceptible to early season weed competition. Consequently, conventional weed management programs rely heavily on preplant tillage and the use of a diverse suite of preplant, pre-emergence, post-emergence and post-directed herbicides to suppress weed emergence and growth (Givens et al., 2009a; Shaner, 2000; Young, 2006, Sosnoskie and Culpepper, 2015). Following the introduction of glyphosate-tolerant cotton, researchers examined how farmers could modify weed control programs to complement this new system. Askew et al. (1999) reported that glyphosate-tolerant cotton greatly simplified...
weed control in cotton, reduced variability in yield and economic returns and tended to result in greater profitability compared to alternative weed control programs. Similarly, Culpepper and York (1999) demonstrated that while glyphosate applications on glyphosate-tolerant cotton produced yields and economic returns that were similar to those from conventional weed control programs, glyphosate allowed the convenience of a postemergent application without risk of herbicide injury or carryover to subsequent crops. As farmers gained firsthand experience with the flexibility and relative simplicity that glyphosate-tolerant crops provide for weed management, adoption of this technology increased significantly. By 2013, 17 years after the introduction of glyphosate-tolerant crops, over 90% of soybean and over 80% of cotton and corn plantings were made with seed varieties tolerant to herbicides (Fernandez-Cornejo et al., 2014) with glyphosate-tolerant varieties predominating. Examinations of glyphosate’s benefits across multiple studies have concluded farmers see a direct economic benefit when glyphosate is used in conjunction with glyphosate-tolerant crops (Gianessi, 2008; NRC, 2010) with the precise magnitude of the economic benefit in any given year is determined largely by the price of glyphosate (Brookes and Barfoot, 2015). Combining data across multiple studies, Brooks and Barfoot (2015) estimated net annual benefits to farmers of $24/hectare for corn, $36/hectare for soybean $22/hectare for cotton and $52/hectare for other crops such as canola. Brookes and Barfoot (2016) subsequently calculated the amount of US farm income attributable to herbicide-tolerant crops, a category where glyphosate tolerance is the predominant option. In 2014, the most recent year of available data, $1.08 billion of farm income was attributable to herbicide-tolerant corn. Since the introduction of herbicide-tolerant corn, this technology has contributed $6.1 billion cumulatively to farm incomes. Herbicide-tolerant soybeans in 2014 accounted for $165.1 million of farm income. Since the introduction of herbicide-tolerant soybeans this technology has accounted for $12.93 billion in cumulative farm income. Herbicide-tolerant cotton varieties produced $47.5 million in farm income for 2014 and $1.07 billion in cumulative farm income since their introduction. Herbicide-tolerant sugarbeet produced $53.3 million in farm income in 2014 and has produced $348 million in farm income since its introduction in 2007.

USDA-NASS data confirm that US farmers continue to recognize benefits from using glyphosate-based herbicides even as glyphosate-resistant weeds have developed. Cotton and soybean farmers used glyphosate on 88% and 97% of their acres, respectively in 2015 while corn farmers used glyphosate on 77% of their acres (USDA-NASS, 2016). Rather than turning away from glyphosate, US farmers are incorporating other management practices to help manage weeds and improve crop performance. Corn and soybean growers are scouting for resistant weeds, rotating with other crops and incorporating additional herbicidal mechanisms of action (Livingston et al., 2015). In cotton, growers are relying on more diverse weed management systems that include chemical, cultural and mechanical controls while still including glyphosate as part of those systems (Sosnoskie and Culpepper, 2014).

2.1.3 Impacts on conservation tillage

Having crops that are tolerant to glyphosate or other herbicides is associated with the adoption of conservation tillage practices, including no-till production (Fernandez-Cornejo et al., 2014), because herbicide-tolerant crops simplify weed control and improve crop management flexibility. Klein and Wicks (1986) and Ramsel et al. (1987) described the herbicide regimes required for no-till production of a series of rotated crops in the era before glyphosate-tolerant crops became available. The authors describe the need to weigh herbicide selection with crop rotation plans to decide how best to balance weed management with crop production. Much of the complexity stemmed from having to control weeds with broad spectrum herbicides that left a residual that could harm subsequent crops. Glyphosate solved this problem because it could control the same weeds without leaving a residual.

A 2016 report from the National Academies of Sciences (NAS) on the impacts of genetically engineered crops stated that it is difficult to establish a cause and effect relationship between the adoption of herbicide-tolerant crops and conservation tillage in general (NAS, 2016). The report acknowledges, however, that multiple studies that found increases in conservation tillage and reduced tillage that followed the adoption of
herbicide-tolerant crops, particularly in soybeans, cotton and sugarbeet. The report also acknowledges that adopters of herbicide-tolerant crops are often more likely to also practice conservation tillage of one form or another. The report also notes that in areas where glyphosate-resistant weeds need to be managed, tillage has in some cases increased to control weeds directly or incorporate other herbicides into the soil. The association between conservation tillage and herbicide-tolerant crop adoption is strongest for soybean, cotton and sugarbeet. An analysis of the relationship between conservation tillage and glyphosate-tolerant soybean adoption found that adoption of glyphosate-tolerant soybean has a direct positive influence on the adoption of conservation tillage practices, with a 1% increase in glyphosate-tolerant soybean adoption leading to a 0.21% increase in conservation tillage (Fernandez-Cornejo et al., 2012). Subsequently, a 2012 USDA agricultural resource management survey found that approximately 97% of soybeans grown in the US were herbicide tolerant and 70% of US soybean growers practiced conservation tillage (USDA-NASS, 2014).

A 2004 report from the Conservation Technology Information Center (CTIC, Fawcett and Towery, 2004) examined the early years of glyphosate-tolerant soybean adoption (1996-2000). CTIC found that no-till practices increased in soybeans from 20.2 to 25.5 million acres and conservation tillage increased in soybeans from 26.9 to 32.2 million acres during this period. Conventional tillage in soybean declined slightly from 19.2 to 18.9 million acres. By 2000, 74.5% of no-till soybean acres, 63.9% of conservation tillage soybean acres and 52.9% of conventional tillage soybean acres were planted with glyphosate-tolerant soybeans. CTIC concluded that the availability of glyphosate-tolerant crops enabled both no-till and conservation tillage.

The use of glyphosate-tolerant crop technology greatly simplified cotton weed management by allowing growers to safely apply glyphosate over the top of the crop in order to control a broad spectrum of competitive species. This, in turn, complemented the ongoing transition of many growers to conservation tillage systems and postemergent-dominated weed management programs (Givens et al., 2009b). More recently, when glyphosate-tolerant sugarbeets became commercially available, over 50,000 acres of sugarbeet fields were converted to some form of reduced or conservation tillage practices in Nebraska, Colorado, and Wyoming. Conservation tillage simply wasn’t possible in sugarbeet before the introduction of glyphosate-tolerant varieties because intensive tillage was needed to obtain adequate weed control (Kniss, 2016).

Conservation tillage provides many well-documented benefits to farmers, the public and the environment overall, from savings in fuel and labor costs to reduced soil erosion, increased wildlife habitat, and improved water and air quality (CTIC, 2015). Conventional tillage practices require sometimes as many as five passes over the land with a plow; however, no-till requires just a single pass (to plant seeds). A Purdue University report calculated that a farmer implementing conservation tillage can save 225 hours of labor per year for a 500 acre farm; the equivalent of four 60-hour work weeks saved in a year (Staropoli, 2015). The utilization of crop residues in no-till farming drastically increases water infiltration and retention by the soil, meaning there is less runoff and more soil moisture available for the crop (Staropoli, 2015).

USDA’s National Resources Inventory found that farmers in the Upper Mississippi River basin have adopted conservation tillage on 91% of cropped acres. USDA also found that conservation practices such as these have reduced wind erosion by 64% and water erosion by 61% in the Upper Mississippi River basin (USDA-NRCS, 2012). Brookes and Barfoot (2016) calculated that herbicide-tolerant crops have reduced CO2 emissions in the US by 39.4 million metric tons (MMT) since their introduction in 1996 because of their ability to simplify conservation tillage. A report by ICF international and commissioned by Monsanto (ICF, 2016) estimated that the equivalent of 32 million metric tons of CO2 could be eliminated from 2016 to 2030 through greater adoption of conservation tillage enabled by herbicide-tolerant crops.

No-till or conservation tillage is extremely valuable on North Carolina farms. Glyphosate controls a broad spectrum of broadleaf and grassy weeds and cover crops in no-till and conventionally tilled fields. We need no-till on
the hills of the North Carolina piedmont to prevent erosion. In the east, no-till provides both a time and money value. Leaving a cover crop or crop residue on the soil surface helps prevent wind erosion on the flatter, sandier fields. Every time we pull a disk over a field for conventional weed control, it costs time and money and leaves the fields prone to wind erosion. Glyphosate controls many of the weeds in a no-till field and it offers more flexibility in application timing. Glyphosate does not leave residues in the soil that can prevent or delay planting. We would probably reduce our acres of no-till if glyphosate were no longer available and I believe we would increase our use of other herbicides.

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2.1.4 Value of US commodity exports of glyphosate-tolerant crops

Using export values of various crops, it is possible to estimate the value of US crop exports driven by glyphosate-tolerant crops. Assuming no channeling or identity preservation, the value created by glyphosate-tolerant crops for US commodity exports can be described as the product of the glyphosate-tolerant share of crop production and the value of exports. Table 1 shows the values for corn, soybeans, soybean meal, soybean oil and the rapeseed complex (canola-derived products) as annual averages for the years 2010–2014. Calculating these values as annual averages accounts for periods of high and low commodity prices.

From the data in the table it is readily apparent that glyphosate-tolerant soybeans drive most of the value created by US export markets. A 2010 report from the National Research Council (NRC) within the National Academies of Science (NAS) examined numerous reports and studies and noted that the availability of herbicide-tolerant soybean partially drove increases in soybean plantings in both the US and abroad, particularly Argentina and Brazil (NRC, 2010). NRC went on to observe that increased soybean availability reduced prices, making them a more affordable component of food and feed. According to NRC, reduced feed prices were a significant benefit for livestock producers around the world because feed can represent half the cost of livestock production.

<table>
<thead>
<tr>
<th>COMMODITY</th>
<th>VALUE (MILLIONS)¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corn</td>
<td>$8,321</td>
</tr>
<tr>
<td>Soybeans</td>
<td>$19,658</td>
</tr>
<tr>
<td>Soybean meal</td>
<td>$4,141</td>
</tr>
<tr>
<td>Soybean oil</td>
<td>$1,060</td>
</tr>
<tr>
<td>Rapeseed complex</td>
<td>$138</td>
</tr>
<tr>
<td>TOTAL</td>
<td>$33,317</td>
</tr>
</tbody>
</table>

¹Value of exports calculated from USDA – Foreign Agricultural Service Export Query Sales System. Market share of each glyphosate-tolerant crop obtained from GfK SeedService.

The impacts of the observations from NAS can be observed by examining the role that glyphosate-tolerant crops play in meeting global demands, particularly for soybeans, soybean meal and soybean oil. China, as the world’s largest importer of soybeans, accounts for 2/3 of the world’s traded soybeans, and relies on imported soybeans to meet over 85% of its demand. Of those, over 88% are cultivated using a glyphosate-enabled system (calculated from USDA-FAS and GfK SeedService data).

Following China, the European Union imports roughly 19 million metric tonnes (MMT) of soybean meal annually (USDA-FAS, 2016). Approximately 95% of the soybean meal imported by the EU is from the US, Brazil, Argentina, Canada, Paraguay and Uruguay - countries in which over 80% of the soybeans grown are glyphosate-tolerant (USDA-FAS, 2016, GfK Seed Service, 2016). Combined, these six countries export roughly 50 MMT of soybean meal annually (USDA-FAS, 2016). Even assuming that the country with lowest share of glyphosate-tolerant soybeans (Canada, 80%) applies across all six countries, it is clear that at least 40 MMT are
traded annually. Finally, China and India, the two most populous countries and the largest markets for soybean oil, are both heavily reliant (>85%) on imports of soybean oil crushed from glyphosate-tolerant soybeans (calculated from USDA-FAS and GfK SeedService data).

Over their first 20 years of cultivation, glyphosate-tolerant crops have grown from providing farmers with simplified weed management to becoming the foundation of trade between exporting and importing countries. Maintaining access to this vital technology is essential not only for farm level productivity but also for food security around the world. Reverting to pre-glyphosate tolerance agronomic practices would have significant effects on labor requirements, environmental impacts and the availability of commonly traded commodities. Notably, losing access to glyphosate would also complicate efforts to control weeds in other agronomic systems as well as non-agricultural settings.

2.2 Benefits to agriculture in non-glyphosate-tolerant crops

In agricultural systems where glyphosate-tolerant crops are not available, glyphosate still provides significant benefits by simplifying weed management and reducing the need for mechanical tillage. Labeled uses of glyphosate include hundreds of crops and crop groups that are not tolerant to glyphosate. Examples for a subset of these uses highlight the types of benefits glyphosate provides even when the crop in question is not glyphosate-tolerant. For orchards and vineyards, effective weed control is necessary to ensure productivity. In these settings, glyphosate provides a cost-effective replacement for alternative weed control tactics. In sugarcane production, glyphosate plays a central role in crop management. In wheat, glyphosate has allowed farmers to adopt no-till practices that allow them to conserve soil moisture, thus enabling rotation with more profitable crops. Glyphosate also simplifies efforts to incorporate cover crops across multiple cropping systems by providing a simple and effective means to eliminate the cover crop just prior to planting without imposing plant back restrictions that result from residual herbicide effects. While glyphosate is often associated with applications to crops engineered to tolerate it, growers across a wide spectrum of crop production systems recognize its benefits and rely on it to maintain their productivity.

2.2.1 Orchards and vineyards

A well maintained orchard floor is critical for ensuring year-round orchard success and a clean harvest operation. The orchard floor can be divided into two distinct areas: the area between the tree rows (generally planted with a permanent cover crop or grass) and the area directly beneath the tree. The permanent grass strip between tree rows helps to minimize erosion, increase soil aeration and permeability, and support the movement of equipment through the orchard during wet weather (Crassweller, 2016).

Weeds impact orchard and vineyard productivity and health by competing with trees and vines and by acting as hosts for a variety of pests (Mitchem, 2016; UCIPM, 2015). In the 2011 Chemical Use Survey for fruits conducted by USDA, respondents reported that 25 percent of apple acres and 16 percent of peach acres were treated with glyphosate (USDA-NASS, 2012). While glyphosate can cause damage if it contacts the trees and vines directly, it is a useful tool for orchard and vineyard floor management in a variety of situations. Orchards and vineyards are often planted into herbicide-killed perennial sod. Glyphosate can be used to eliminate the sod before planting and used to help maintain a weed-free area around the trees throughout the growing season (Gardner, 2011; UCIPM, 2015).

Connell et al. (2001) compared three methods for weed control in almonds. Two relied on herbicide programs that included glyphosate and the third was standard mowing. The herbicide programs that included glyphosate resulted in lower weed density and greater percent bare ground than mowing alone. The herbicide programs with glyphosate also resulted in lower labor
requirements and fewer passes of machinery through the orchard that could compact soil around the tree roots. In coffee plantations glyphosate is used to control vines that can interfere with crop productivity. According to the Kauai Coffee Company, glyphosate is an indispensable herbicide for their operations (Alexander and Baldwin, 2009). The versatility of glyphosate in orchard and vineyard management makes it an important tool for weed control management plans. When combined with other herbicides and management strategies, glyphosate offers a cost-effective and safe tool that growers can use to maximize weed control, and ultimately their yields.

2.2.2 Wheat

Wheat ranks third among US field crops in both planted acreage and gross farm receipts, behind corn and soybean. Wheat grown in the US is classified as winter wheat or spring wheat depending on the season in which they are planted. Weeds can reduce wheat yields by competing with the crop for moisture, light, space, and nutrients. Weeds can also interfere with harvest and may result in dockage and lower quality grain, which adds to the total economic impact of weeds in wheat.

Winter annual grasses like cheatgrass and jointed goatgrass are some of the most troublesome weeds in wheat because of their competitiveness and difficulty to control. In Colorado, winter wheat yields decreased by 28 percent when jointed goatgrass emerged with wheat in the fall. When jointed goatgrass emerged at the same density in early spring, wheat yields only declined by 8 percent (Lyon and Klein, 1997). To successfully control jointed goatgrass and other problem weeds requires a multifaceted approach. The use of glyphosate for initial weed control in the spring is an important management practice. Glyphosate is very effective at killing jointed goatgrass and other grass weeds and is often used prior to planting wheat or after wheat is harvested to control unwanted growth in wheat stubble (Schmale et al., 2008).

The practice of no-till and conservation tillage is an effective tool for reducing erosion in wheat. Crop residue helps shield the soil surface from erosion due to heavy rains and helps allow more water to soak into the soil. The conserved soil moisture can be used to produce a more lucrative second crop such as corn. In the past, wheat growers relied on a winter wheat - fallow rotation that left their fields unproductive for more than 12 months at a time. The percentage of wheat acres managed as no-till with an additional rotation crop has increased from less than 5% to more than 20% of total acres in both the Northern and Central Great Plains since 1989 (Hansen et al., 2012). No-till planting of wheat reduced erosion by 90 to 95 percent (Shroyer et al., 1997). The percentage of no-till acres in wheat has increased by over 15 percent in the last 26 years in the Great Plains region (National Wheat Foundation, 2015). Glyphosate is most often applied to no-till wheat fields before planting, at planting, or after planting but before the wheat emerges to help ensure minimal weed competition with the wheat. Fallow applications are also made after harvest to help keep weeds from utilizing soil moisture. In 2015, 14 percent of planted winter wheat acres received an application of glyphosate (USDA-NASS, 2016).

2.2.3 Sugarcane

While there are no glyphosate-tolerant varieties of sugarcane being grown commercially, glyphosate still plays an important role in the cultivation and harvest of this crop. In the US, sugarcane is produced in Florida, Louisiana, Texas, and Hawaii. Sugarcane accounts for about 45% of the total sugar produced domestically with Florida and Louisiana responsible for 90% of that amount (USDA-ERS, 2016). The value of sugarcane is determined by the amount of recoverable sugar per weight of cane and is the basis on which sugarcane growers are paid. This is estimated by the theoretical recoverable sugar (TRS). Sugarcane varieties with high sugar content are more economical for mills to process. Growing seasons in Florida and Louisiana are short compared with most other locations where sugarcane is grown, meaning that TRS is typically lower. Sugarcane ripening is induced by various stresses and shorter day length. Applying herbicides such as
2.2.4 Cover crops

Cover crops can provide numerous benefits including reduced soil erosion, increased soil organic matter content, improved air and water filtration through soil and reduced soil compaction (Kladivko, 2011). Additionally, a 2016 report from ICF International and commissioned by Monsanto (ICF, 2016) indicates that cover crops have the potential to reduce greenhouse gas emissions by the equivalent of 117 million metric tons of CO₂ by 2030 if they are more widely adopted. Cover crops are unique in that most are planted for agronomic benefits and are not harvested for seed, fruit, or forage. Instead, cover crops are terminated before planting production crops. Cover crops are increasing in popularity. Results from a 2013-2014 Conservation Technology Information Center survey found that cover crop acreage among survey respondents increased 30 percent per year from 2010 to 2013 (CTIC, 2014).

If not terminated properly, cover crops have the potential to become weeds and can slow soil drying and warming in spring. Farmers must terminate their cover crop prior to cash crop emergence in order to obtain federal crop insurance (USDA-RMA, 2015). It is essential, therefore, that termination methods are reliable and provide complete control. Nearly half of the respondents to the SARE-CTIC cover crops survey applied a herbicide for cover crop termination (CTIC, 2014). Glyphosate is the standard herbicide for cover crop termination. Annual ryegrass, cereal rye, and oats are all popular grass species used as cover crops. Glyphosate can be used to effectively control all of these species. Crimson clover and Austrian winter peas are popular legume species that require a spring termination. Glyphosate alone or mixed with 2,4-D also provides acceptable termination of these species. In addition, glyphosate does not have a planting restriction, so crops can be seeded into cover crop stubble without the risk of herbicide injury (Hartzler, 2014; Legleiter et al., 2012).

2.3 Benefits outside of agriculture

Outside of agriculture glyphosate has many applications that promote transportation safety, utility reliability, environmental restoration and recreation. Federal and state laws require weed control along transportation rights of way and mandate specific practices for the control of noxious and invasive weeds. Glyphosate is an essential tool to satisfy these requirements along highways and railroads.

In an economic analysis of highway median weed control, for example, glyphosate was 275% less expensive than alternative methods that included...
multiple mowing events and alternative herbicides. In utility rights of way, glyphosate provides a simple and effective method to control vegetation that can interfere with reliable delivery of electrical power. Glyphosate also delivers significant benefits for noxious or invasive weed control. National parks, for example, rely on glyphosate to decisively control invasive vegetation and restore native habitats. In aquatic settings glyphosate replaces mechanical control of emerged aquatic weeds to enable navigation and maintain wildlife habitat. In recreational environments that include managed turf grass, glyphosate applications to dormant turf allow undesirable species of weeds and grasses to be controlled. This allows golf course managers to cost-effectively renovate fairways without the need for total replacement. Glyphosate’s versatility across these settings makes it an essential tool for weed control beyond its more widely known uses in agriculture.

2.3.1 Highway, railroad and utility right of ways
State and local governments, utilities and railroads all must control unwanted vegetation within their right of ways. Along roadways, uncontrolled vegetation can block views of other motorists, roadway signs, animals and obstructions. Water and snow can also build up on the roadway if vegetation prohibits proper drainage. Excessive vegetation can also be a fire hazard (Eck and McGee 2007; Green et al., 1996). Vegetation on railroad right of ways must be managed to maintain proper visibility for train operators as well as motorists approaching a railway. In addition, vegetation can create fire hazards or come in contact with overhead electrical lines, block visual and electronic monitoring of the railway and reduce braking efficiency when crushed between the train wheels and track, thus hindering acceleration and braking (Progressive Railroading 2008; Amec Foster Wheeler, Inc. 2015). Federal track safety regulations mandate the control of vegetation on railroad property that is immediately adjacent to the roadbed (49 CFR 213 § 37). For utility right of ways, fire hazards associated with dried vegetation pose a threat to reliability. Utilities also need access to equipment and lines, necessitating vegetation control.

Weed control in right of ways can involve mechanical controls, herbicides or controlled burning. In many areas, the terrain prevents the use of mechanical methods for vegetation control and burning poses safety and environmental concerns. Non-selective herbicides such as glyphosate can be used in areas where all vegetation requires control or used as a spot treatment to control individual or clumps of weedy vegetation. In addition, glyphosate is a systemic herbicide allowing complete control, including roots.

Studies in several states and counties detail the economic benefits of relying on glyphosate. Washington State Department of Transportation recognized in the 1970s that glyphosate could be an integral part of highway right of way management because of its efficacy and cost-effectiveness (Ryan et al., 1978). Subsequently, in 2003, the same agency reported that right of way weed control with the use of herbicides in was $979,217 while the cost without herbicides would be $2,151,422 (WSDOT, 2003). An analysis of weed control costs across the 6500 miles of roadways in Hillsborough County, Ohio found that using a combination of herbicides that featured glyphosate to replace mowing saved over $1,000,000 per year (Gallagher, 2013). A study from Santa Cruz County, California found that excluding glyphosate from weed control operations in favor of mowing alone would result 275% increase in highway management costs (Tjosvold & Smith, 2010).

A 2010 study conducted for an Arkansas electric cooperative observed that mechanical methods allowed for the re-growth of vegetation and increased the stem count of undesirable vegetation. The study also noted that herbicides applied to targeted plants can control the entire plant including roots and reduce the stem count by 35 – 50%. With adequate initial herbicidal control, the amount of herbicides used over time
can decrease as more desirable vegetation takes the place of the undesirable vegetation. This study found that long term costs over a six year cycle of right of way maintenance were $50 to $70 million lower than mowing alone (Finley Engineering, 2010).

The value of herbicides such as glyphosate for trackside weed control was highlighted when the Alaska Railroad Corporation attempted to control unwanted right of way vegetation from 1983-2010 with mechanical brush-cutting, manual labor, steam, and burning. Those efforts could not adequately control vegetation and the railroad was fined for failing to maintain its lines. Those fines led to the adoption of an integrated vegetation management plan that includes glyphosate (ARRC, 2016; Bluemink, 2010). A similar effort to limit railroad herbicide use in Montpelier, Vermont was initiated specifically to end glyphosate applications on a two mile section of track. Montpelier has agreed to fund manual weed control at a cost of $3,000 per control event (Tron, 2016).

2.3.2 Recreational settings

Golf courses, parks, picnic grounds, fair grounds, sports fields, shorelines and other recreational areas that include managed landscapes rely on various weed control methods to maintain their function and aesthetics. Glyphosate’s ability to control a wide spectrum of weeds, including perennials, makes it a valuable tool in these settings to support their intended purpose. Its lack of residual activity allows new vegetation to be seeded or planted shortly after application. Its low cost compared to other alternatives makes it an affordable option for renovating existing vegetation.

One primary use for glyphosate is in the renovation of turf grass stands on golf courses. Patton et al. (2004) noted that glyphosate can be applied to dormant turf in fairways to eliminate undesirable species, thus maintaining the desired turf quality without the cost of replacement. Glyphosate’s lack of residual activity makes it a strong choice compared to alternative herbicides that can control grasses. Bermudagrass, zoysiagrass, creeping bentgrass, and quackgrass are a few of the golf course grasses that can be controlled with glyphosate formulations. Additionally, when existing grass needs to be removed, new turf can be seeded within days of application. Glyphosate products can also be used to spot treat weeds in sand bunkers, native, and no-mow areas (Throssell, 2009).

A 1996 Arizona Cactus and Pine Golf Course Superintendents Association survey points to the significant value of glyphosate for golf course management. In terms of weed problems, survey respondents ranked annual bluegrass as the greatest problem, followed by bermudagrass, nutgrass, and crabgrass/cupgrass. Glyphosate products were the most commonly used postemergence products. Glyphosate products were applied an average of 3.7 times per season on 529.2 acres with an average effectiveness rating of 3.4 out of 4 (Merrigan et al., 1996).

In recent years glyphosate has emerged as an essential tool for land managers to convert some of their landscaping to less water intensive options. Cupit (2015) noted the positive role of glyphosate in removing turf from selected areas of the Ironwood Country Club in Palm Desert, California. Cupit (2015) credited glyphosate will saving billions of gallons of water while also posing low risks to human health and the environment. The Conejo Recreation & Park District (CPRD) in Thousand Oaks, California determined the use of glyphosate was a favorable option to convert turf to woodchips and mulch in order to save water. CPRD noted that glyphosate’s lack of residual activity would also allow it to plant drought-tolerant trees and other plants within 48 hours of application once the herbicide reached the turf roots. Glyphosate was selected over other methods including mechanical sod removal, torching, smothering with tarps and an acetic acid/salt mixture. These other methods would either pose significant costs, unacceptable safety hazards, insurmountable logistical challenges or long term soil damage, respectively. Notably, removing turf with glyphosate and replacing it with drought friendly landscaping would allow CPRD to participate in a “Cash for Grass” rebate program (CPRD, 2015).

Farther north in California, the city of Petaluma has launched an experiment to evaluate the effectiveness of various glyphosate alternatives, including “organic” herbicides for weed control in public parks. Park officials have expressed concern over the cost of alternatives, their increased frequency of applications and need for additional protective equipment during application. With respect to cost, a 140-gallon
mix of glyphosate and water costs $62 compared to the cost of two alternatives at $1,136 and $1,001, respectively. The alternatives do not offer the same control benefits of glyphosate, which kills the roots; therefore, treatments need to be repeated to maintain desired weed control. The alternatives have proven to be extremely pungent during application resulting in several workers complaining of eye irritation and one experiencing respiratory difficulties; therefore, additional protective equipment is required, which was not need with the glyphosate formulations (Gneckow, 2016).

2.3.3 Invasive and noxious weeds

The Federal Noxious Weed Act of 1974 provided for the control and management of non-native and native weeds that are designated as noxious or injurious in some manner to agriculture, humans, or the environment. The act was superseded in 2000 by the Plant Protection Act. Several states have their own noxious, invasive, or nuisance weed laws. Kansas, for example, requires every person, company, organization, or agency to control and eradicate noxious weeds. The persistence of perennial weeds necessitates herbicides such as glyphosate that can control roots in addition to aboveground portions (Kansas Department of Agriculture, 2016). Herbicides are often the most cost-effective option to control invasive weeds because of their known performance and lower labor requirement (Beck, 2013). The expense of control increases as the size of the infestation increases; therefore, it is important to find and remove invasive weeds early rather than waiting. Costs of manual or mechanical control can exceed the cost of using herbicides by 800 to 1500% (Beck, 2013).

Saguaro National Park in Arizona relied on glyphosate to control invasive Buffelgrass. The Park chose glyphosate based on it is the only herbicide effective against Buffelgrass, its low potential for adverse impacts on non-target species, and low potential for leaching (SNP, 2015). In Oregon, the Mary’s Peak Resource Area (MPRA), Salem District Bureau of Land Management, conducted an environmental assessment for plans to control noxious weeds and identified glyphosate as the only acceptable herbicidal control (Wilson, 2010). Glyphosate is often recommended in prairie restoration because of its ability to degrade rapidly and lack of soil residual qualities. This allows for planting of desired species the next day (Shooting Star Native Seeds, 2016). Nyami et al. (2011) reported that for prairie restoration, glyphosate in combination with a selective herbicide such as imazapic is more effective for reducing weed populations and increasing native species.

Controlling noxious weeds in rangeland is difficult because the expense to control is rarely cost effective because of relatively low revenues per unit area (Sheley et al., 2007). Glyphosate formulations provided substantial short-term control of an invasive rangeland grass with few effects on native grasses (Simmons et al., 2007; Sheley 2007). In a study of Canada thistle control in Medicine Lake National Wildlife Area, Montana, targeted glyphosate applications effectively controlled Canada thistle while allowing biomass of shrubs, forbs, and other desired species to increase and expand waterfowl habitat (Krueger-Mangold et al., 2002; Sheley et al., 2007).

In the Pacific Northwest, Himalayan blackberry is a troublesome invasive weed that spreads aggressively, displacing native vegetation and limiting access to food for large herbivores such as deer (Soll, 2004). Glyphosate and glyphosate-containing mixtures are the recommended control method for this weed because of their efficacy. Additionally, only glyphosate has approval from the National Oceanic and Atmospheric Administration – Fisheries (NOAA-Fisheries) for use in 100 year flood plains of rivers that host salmon and related species (Soll, 2004). Herbicidal controls are more cost effective for eliminating Himalayan blackberry, with broadcast applications costing as little as 25% of mechanical or manual methods (Soll, 2004). In Washington State, glyphosate is the herbicide of choice to control reed canarygrass on the Hoh, Quinault, and Queets Rivers. The reed grows in creeks, slowing water flow and raising water temperatures past the point where native fish can survive. The restoration team chose glyphosate because of its efficacy, low potential for adverse impacts and ability to reduce labor requirements (Dudley, 2016).

Poison ivy and poison oak both pose a hazard to humans through direct contact. Every year in the US there are approximately 2 million cases of skin poisoning caused by these plants and their relatives. In California, poison oak is the most hazardous plant in the state as measured by the number of lost work hours (UCIPM, 2009). For the
Midwest and northeast region of the US, poison ivy is one of the most common causes of blistering dermatitis (Calhoun, 2010). Physical or mechanical control of these weeds can lead to direct exposure and subsequent skin rashes, making herbicides a preferred option for control (Williamson et al, 2015). These plants grow quickly and may be spread either through seeds or by underground rhizomes (Williamson et al., 2015). Equipment such as bulldozers or brushrakes often leave pieces of roots behind that subsequently resprout and mowing must be repeated several times during the season to achieve any control (UCIPM, 2009). Glyphosate’s ability to act systemically kills both the above and below ground potions of poison ivy and poison oak and it is recognized as one of the most effective herbicides for controlling these species (UCIPM, 2009). It may be applied as a spray or directly to stumps after cutting the plants. Glyphosate-based herbicides labeled for use on these species may include glyphosate as the sole active ingredient or, more often, may include additional herbicides to provide rapid control (Williamson et al., 2015).

Kudzu, an invasive species that some refer to as "the plant that ate the south" is a woody-stemmed vine that can grow rapidly, outcompeting native vegetation, including trees (Nespeca, 2007). It is able to fix nitrogen, similar to soybean or clover and eventually reaches heights of 100 feet and a spread of 50 to 60 feet (FIPRC, undated). Originally from Japan, kudzu was introduced to the US in 1876 as an ornamental. In the 1920s and 1930s it was widely planted as either a forage or groundcover. Once its invasive properties became well known, USDA banned it as a cover crop in 1953 (FIPRC, undated). It is now present in states from Florida to the Great Lakes as well as from the coastal Atlantic states to Nebraska, Kansas, Oklahoma and Texas. It is also present in Oregon, Washington and Hawaii (FIPRC, undated). In addition to the damage kudzu causes by smothering other plants, it is also the host to the kudzu bug that is now becoming a devastating pest in southern US soybean fields. Controlling kudzu itself can help limit the damage these bugs cause for soybean growers and the need for associated insecticide applications (Reisig and Bachelet, 2013). While small patches of kudzu may be controlled manually, mechanically or through livestock grazing (Miller, 2008), herbicides are the most practical treatment for large patches (Nespeca, 2007). In residential and environmentally sensitive settings, glyphosate-based herbicides are the preferred method of herbicidal control because of their strong safety profile (Miller, 2008). Glyphosate’s systemic activity means it can be effective when applied either as a foliar spray or to stumps after vines are cut (Nespeca, 2007).

2.3.4 Aquatic weeds

Aquatic weeds can potentially impact water quality, fisheries, water control structures, electrical generation equipment, irrigation equipment, recreational activities, and the health of humans, livestock, and wildlife. The presence of certain aquatic weeds can cause water to have foul odors and/or taste, deplete oxygen resulting in fish kills, plug water intakes, disrupt recreational activities and limit navigation. Some aquatic weeds can serve as breeding grounds for mosquitoes that act as disease vectors (Getsinger et al., 2014). Control options include both mechanical and herbicidal options with herbicides typically being less expensive. Glyphosate is often the herbicide of choice for aquatic weed control because of its low cost and low toxicity to other aquatic organisms. Glyphosate formulations for aquatic settings do not contain surfactants because they can cause toxicity to aquatic organisms.

In California’s Sacramento-San Joaquin Delta, for example, California’s Department of Boating and Waterways relies on glyphosate as part of its water hyacinth control efforts to improve navigation and ensure a reliable water supply (CADBW, 2016). Glyphosate formulations are less expensive than mechanical or manual removal. Glyphosate applications cost approximately $250/acre while costs for 2,4-D or mechanical control may cost two to four times as much. Disposal following mechanical removal adds additional cost (WSDE, 2001; SFEI, 2003; Gibbons et al., 1999). In Southern California, invasive arundo/giant reed and tamarisk/salt cedar are aggressive and environmentally damaging plants in Los Angeles and Ventura counties. Mechanical, biological, and cultural methods are options, but do not provide long-term control. Glyphosate is a primary herbicide for these control efforts because of its ability to act systemically and reduce labor requirements (VCRCD, 2003).

In Michigan and several other states, Phragmites, a semi-aquatic invasive reed can overwhelm areas
alongside ponds and marshes, forcing out native wildlife, particularly waterfowl. It spreads either through seeds or underground rhizomes, making it particularly difficult to control with herbicides that do not act systemically. Glyphosate applied either as a spray or a direct wiper application is effective at controlling this aggressive plant. Michigan’s Department of Environmental Quality notes that glyphosate is one of two commercially available herbicides that can control Phragmites (MDEQ, 2014).

In Florida, where all public waters are known to host at least one non-native aquatic plant (Mossler and Langeland, 2013), controlling invasives is of paramount importance. Of the 11 most common invasive aquatic weeds in Florida, six can be controlled with glyphosate. Most are grasses that invade shorelines and crowd out native wildlife. At a cost of $120 per acre, glyphosate has significant cost advantages over several alternative herbicides that can cost as much as $600 per acre (Mossler and Langeland, 2013).

2.4 Managing herbicide resistant weed biotypes

Reliance on a single mechanism of action, whether chemical or non-chemical selects for herbicide resistant biotypes of certain weed species and additional management tools are necessary to maintain an effective weed control system (Ashworth et al., 2016; Culpepper, et al. 2011; Lanini et al., 1994; NRC 2010; Livingston et al., 2015). These types of adaptations in resistance management strategies are not new, as weed resistance to multiple herbicides has occurred for decades. The first report of a resistant weed population was made in 1957 (Delye, 2013).

Worldwide, 416 herbicide-resistant weed biotypes have been reported to be resistant to 21 different herbicide mechanisms-of-action (Heap, 2015). Glyphosate-resistant weeds, which occur in certain areas of the US, account for approximately 6% of US herbicide-resistant biotypes. As a point of comparison, weeds resistant to herbicides that inhibit acetolactate synthase (ALS) and photosystem (PSII) account for 33% and 17% of the herbicide-resistant biotypes, respectively (Heap 2014).

In order to determine how best to manage resistant weeds, it is essential to scout fields to identify suspect populations. Norsworthy et al. (2012) listed three key criteria to identify resistant weeds:

1. failure to control a weed species normally controlled by the herbicide at the dose applied, especially if control is achieved on adjacent weeds;
2. a spreading patch of noncontrolled plants of a particular weed species;
3. surviving plants mixed with controlled individuals of the same species.

Subsequent to Norsworthy et al. (2013), Shaw et al. (2013) provided a comprehensive set of best management practices (BMPs) that can be used to control resistant weeds and slow the development of future resistant weeds. Their BMPs are comprised of 12 elements as follows:

“Understand the biology of the weeds present; Use a diversified approach toward weed management focused on preventing weed seed production and reducing the number of weed seeds in the soil seedbank; Plant into weed-free fields and then keep fields as weed free as possible; Plant weed-free crop seed; Scout fields routinely; Use multiple herbicide MOAs that are effective against the most troublesome weeds or those most prone to herbicide resistance; Apply the labeled herbicide rate at recommended weed sizes; Emphasize cultural practices that suppress weeds by using crop competitiveness; Use mechanical and biological management practices where appropriate; Prevent field-to-field and within-field movement of weed seed or vegetative propagules; Manage weed seed at harvest and after harvest to prevent buildup of the weed seedbank; and Prevent an influx of weeds into the field by managing field borders.”

Following on that work, Gibson et al. (2015), reporting ongoing results of the Benchmark Study on Glyphosate Resistant Weeds, observed that the seed bank of weeds remaining in the soil is slow to respond to BMPs. The authors cautioned that farmers need to keep the seed bank of weeds in mind when developing BMPs for their fields.

As noted by Shaw et al. (2013) and Evans et al. (2015), herbicide combinations with multiple mechanisms of action applied at the same time, as part of a diversified weed management plan, are the best option for controlling herbicide resistant weeds. Controlling the existing biotypes and preventing the development of new ones is of
paramount importance for maintaining glyphosate’s benefits.

To that end, Monsanto has developed the Roundup Ready PLUS® Crop Management Solutions program to provide weed management options and economic incentives for soybean, corn and cotton farmers to incorporate additional mechanisms of action into their weed control strategy. As a next step in this effort, Monsanto is also developing a new platform that will add dicamba as an additional post-emergence mechanism of action for certain Roundup Ready® crops.

Controlling current glyphosate-resistant weed biotypes and slowing or preventing the development of new resistant biotypes would increase farm productivity and avoid the need for additional land to be cultivated. According to Livingston et al. (2015) corn and soybean yields are approximately 7% and 2.5% greater, respectively, on farms that report no glyphosate-resistant weeds. Greater productivity on existing acres will spare other lands that could either remain unchanged or put to other uses.

There are thousands of publications from land grant universities showing the advantages of continuing to use glyphosate in weed management plans for the major crops. In addition to controlling weeds in the crop, glyphosate is still the number one burndown herbicide. Controlling cover crops, especially grain cover crops such as wheat and rye, would be extremely problematic without glyphosate as a burndown herbicide. Without glyphosate it would be more challenging to convince a grower to plant cover crops. Growers are not going to use a herbicide if it’s not effective. It’s obvious that growers are convinced that glyphosate offers a good return on their investment. Glyphosate is still a critical tool in our weed management plans.

2.5 Potential impacts of losing access to glyphosate

Without access to glyphosate farmers would either convert to other herbicides with corresponding crops tolerant to those herbicides or revert to previous weed control methods, both mechanical and chemical. A collection of analyses provide insights about the types of impacts they would face.

In terms of ease of use, farmers would have to again consider whether available herbicides will leave residues that can harm subsequent crops, whether available herbicides are efficacious against the weeds present in the field, and whether available herbicides are compatible with their specific crop. To the extent that other weed control tactics result in additional herbicide applications or increased reliance on mechanical weed control, losing access to glyphosate would likely increase labor requirements and potentially decrease off-farm income. An analysis of USDA data demonstrated that farmers who adopt glyphosate-tolerant soybeans have been able to reduce household labor requirements by 14.5% (Gardner et al., 2009). This reduction in labor requirements makes it possible to earn extra income off the farm. Consistent with this observation, USDA also found that adoption of herbicide-tolerant soybean was associated with increased off-farm household income Fernandez-Cornejo et al., 2007). Glyphosate also improves harvest quality by eliminating seeds from hundreds of weeds species prior to harvest, thus reducing dockage for foreign matter in grain shipments.

Without herbicides like glyphosate, growers would likely struggle to incorporate no-till and other conservation tillage production practices, which in turn would increase soil erosion. Gianesi and Reigner (2006) estimated that reverting back to tillage practices that predominated prior to the use of glyphosate-tolerant crops in agriculture would release 356 billion pounds of sediments into streams and rivers and result in an estimated $1.4 billion in downstream damage associated with water treatment costs and possible dredging.
Tillage causes widespread soil disturbance that can lead to erosion and top soil loss, impacting the sedimentation and turbidity of streams. In fact, EPA has identified sediment as the second most important cause of impairments of assessed rivers and streams (EPA, 2015a). Additionally, the US National Research Council (NRC) examined the impacts of herbicide-tolerant crops on farm sustainability and specifically considered the role of conservation tillage. NRC noted that conservation tillage reduces soil erosion, increases soil water retention and reduces soil degradation while decreasing runoff (NRC, 2010).

NRC also concluded that conservation tillage reduces CO₂ emissions from agriculture (NRC, 2010). In a review of environmental impacts, Brookes and Barfoot (2016) calculated a fuel savings of 1,836 million liters enabled by glyphosate-tolerant corn and soybean between 1996 and 2014. This fuel savings equates to 4,901 million kg reduction in CO₂ emissions during that same period. Additionally, the authors calculated that the adoption of conservation tillage enabled by glyphosate-tolerant corn and soybean allowed 39,398 million kg of carbon to be sequestered in soil. In 2014 alone, this was equivalent to removing 4,592 million kg of CO₂ from the atmosphere or equal to removing 1.9 million cars from the road for one year.

European economists and agricultural scientists have already pondered what the loss of glyphosate would mean for farmers on that continent. The projected impacts are apparent at the farm level, to the environment and to the broader economy. In the UK, losing access to glyphosate would likely increase the occurrence of weeds resistant to other herbicides because eliminating glyphosate would reduce in the available mechanisms of action (Cook et al., 2010). Losing access to glyphosate would also increase weed control costs, tillage and CO₂ emissions in the UK, Germany and France (Cook et al., 2010; Garvert et al., 2013; Wynn et al., 2012). Without glyphosate farmers in France would experience an estimated 10% yield loss (Wynn et al., 2012) and farmers in coastal Germany would have no herbicides to control one of their most important species of weed (Garvert et al., 2013). More land would also be needed to produce the same amounts of various commodities with France alone requiring 670,000 additional hectares of land to produce the same amount of food and feed (Wynn et al., 2012). Importantly, reduced productivity would force the EU as whole to change from a net wheat exporter to a net wheat importer (Garvert et al., 2013).

Economic losses for Germany alone would range from €79 – 202 million (Steinmann et al., 2012). Across the EU, economic losses would range from €1.4 – 42 billion (Garvert et al., 2013). Notably, farmers in the EU do not have the choice of growing glyphosate-tolerant crops; all of these losses occur in agricultural systems where glyphosate is used only with conventional crops.

Glyphosate still has value in a weed management plan, even in the presence of glyphosate-resistant weeds. The whole world seems to revolve around glyphosate-resistant pigweed control. But there are a whole lot of other weeds in the field that are not resistant. As soon as you leave Roundup® agricultural herbicide off, you see them. Without glyphosate, weed management in the major crops becomes more complicated and more expensive. In cotton, the only herbicide we have for over the top use, other than glyphosate, is an ALS inhibitor, and we have weed resistance to ALS herbicides. There is no good option for post broadleaf weed control in cotton until we get dicamba or 2,4-D registered for use on cotton.

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2.6 Policy considerations

EPA has stated that it will require weed resistance management to be part of registrations for all new and existing herbicides used on herbicide tolerant crops (EPA, 2014a). The Agency has also issued a proposed rule that would add herbicide label
requirements for resistance management based on the potential for resistance to develop to the active ingredient (EPA, 2016). In general, this type of approach is preferable to other options that could, in fact, be counterproductive. Put simply, the Agency could 1) reduce maximum application rates; 2) limit glyphosate use on crops to alternate years; or 3) require a weed resistance management (WRM) plan. Household uses as well as those for land management and environmental restoration have not been associated with the development of glyphosate resistant weeds and these uses would not have to be changed to address this issue. An analysis of these options demonstrates that the first two would be counterproductive and WRM plan is the only feasible and sustainable choice.

Reducing maximum allowable rates would necessitate adding additional weed control mechanisms to glyphosate and this would result in similar socioeconomic impacts to what many farmers are currently experiencing as they revisit weed management practices. Livingston et al. (2015), for example, calculated that corn and soybean farmers reporting glyphosate-resistant weeds had increased costs of $19.88 per hectare attributable to increased management requirements. Most importantly, reducing application rates would run counter to best management practices developed by the Weed Science Society of America (WSSA) (Norsworthy et al., 2012). WSSA advises that herbicides should be used at full labeled rate to prevent the development of herbicide resistance. It can therefore be expected that reducing application rates will eventually result in more biotypes of glyphosate-resistant weeds and glyphosate would become obsolete.

Limiting glyphosate use on crops to alternate years would require farmers to either adopt a new weed management system for non-glyphosate years or move away from glyphosate use entirely in favor of an alternative weed control platform. Rotating glyphosate with other herbicides on a year-by-year basis contradicts published studies that have consistently found rotating herbicides to be counterproductive. It can therefore be expected that mandatory rotation would eventually result in more biotypes of glyphosate-resistant weeds and glyphosate would become obsolete. Evans et al. (2015) examined the effect of rotating herbicide mechanisms of action (MOAs) on herbicide resistance. The authors reported that while rotation reduces exposure to an herbicide, resistance alleles will decrease in frequency only if they carry a high fitness cost. According to the authors, glyphosate resistance in *Amaranthus palmeri* and *A. tuberculatus*, two of the more common glyphosate resistant weeds in US agriculture, carries a low fitness cost and the authors concluded that rotating MOAs would in fact lead to more resistance.

In both of the above scenarios, it is likely that glyphosate-resistant weeds would become more prevalent and glyphosate’s utility in agriculture would be significantly reduced or eliminated. The impacts of such an outcome would likely include increased complexity of weed management, increased farm labor requirements and reduced farm household income, reductions in conservation tillage, increased soil erosion, additional CO₂ emissions and additional water quality impairments.

In contrast with reduced application rates or mandating use only in alternate years a WRM plan will enable many of the benefits associated with glyphosate use in agriculture to continue. It is expected that under this alternative conservation tillage would be able to continue on much of the same acres it is practiced on today, preventing soil erosion, reducing CO₂ emissions and retaining soil moisture.

Additional herbicide use would also be expected as additional mechanisms of action are included alongside glyphosate. The Agency is reviewing a combination of glyphosate and 2,4-dichlorophenoxyacetic acid (2,4-D) to be used on crops tolerant to both of these herbicides and is considering a registration for dicamba that would expand its uses to include soybean and cotton. Other herbicides could be used separately from glyphosate as is currently the case for preemergent applications of atrazine in corn and acetochlor in soybean. Post-emergence applications of herbicides such as glufosinate could also be part of weed control strategies in conjunction with glyphosate. Regardless of the herbicide, all labeled uses will have to meet FIFRA requirements (i.e., no unreasonable adverse effects on the environment and reasonable certainty of no harm to humans) prior to commercialization.
A comprehensive WRM plan necessitates increased costs associated with weed scouting and additional weed control mechanisms whether they are cultural, mechanical or chemical. Building on the work of Norsworthy et al. (2012) and Shaw et al. (2013), Edwards et al. (2014) calculated the input cost per hectare and net returns per hectare for BMPs developed on a site-specific basis by academic advisors and compared those costs and returns to what they termed “standard practices”. Standard practices were whatever weed control methods were used on each farm prior to the study and typically included glyphosate as a primary herbicide. The authors reported that for corn, cotton and soybean the cost differential between BMPs and standard practices ranged from $17/ha to $54/ha with BMP costs always being greater. Net returns, however, tended to favor BMPs.

Consistent with Edwards et al. (2014), Livingston et al. (2015) reported that corn and soybean farmers who relied on at least one herbicide in addition to glyphosate had greater production costs (approximately $20/acre for corn and $12/acre for soybean). These same farmers, however, produced greater yields (approximately 6 bu/acre for corn and 4 bu/acre for soybean) and had greater operating returns (approximately $21/acre for corn and $49/acre for soybean) when they used other herbicides in addition to glyphosate.

Monsanto’s WRM plan for glyphosate builds upon WSSA expertise in how to detect and prevent herbicide resistance and adds monitoring and reporting requirements as well as an education component to ensure glyphosate users are able to take appropriate actions. The WRM plan makes it clear that Monsanto takes resistant weeds seriously and establishes a clear set of expectations and actions to address resistance. Glyphosate’s many benefits and advantages have made it central to weed control over recent decades. Establishing a robust WRM plan, as Monsanto has done, will ensure glyphosate’s continued role in decades to come.
3. SAFETY OF GLYPHOSATE

Over more than four decades, glyphosate has undergone extensive testing and assessment to evaluate its safety for a wide range of herbicidal uses. Six complete data sets exist to support government reviews alongside thousands of publications in the peer-reviewed literature. Much of the information addressing short term and long term toxicity, carcinogenicity, effects on wildlife and environmental fate has been summarized in a collection of publications. Taken together, the data support a conclusion that glyphosate exhibits low toxicity, is not a carcinogen and does not accumulate in the environment. Additionally, widely circulated claims that glyphosate is the cause of a host of adverse effects are not supported by reliable science and in many cases are directly refuted by the large body of knowledge about this herbicide. This robust safety profile is a primary reason why glyphosate has become one of the most widely used herbicides in the US and around the world.

Saltmiras et al. (2015) compiled the existing data addressing glyphosate’s physiochemical properties, environmental fate and uptake by plants. The document also reviews glyphosate’s metabolism in mammals, acute toxicity, repeated dose toxicity, genotoxicity, carcinogenicity, developmental and reproductive toxicity, effects on the endocrine system and neurotoxicity. The authors then combine all of this information with a human dietary exposure assessment to produce a human health risk assessment. Taken together, the data and information support a conclusion that glyphosate exhibits low toxicity, is not a reproductive toxicant or a selective developmental toxicant, is non-genotoxic, non-carcinogenic, non-immunotoxic and is not an endocrine disruptor. Furthermore, glyphosate’s physiochemical properties, environmental fate and pharmacokinetics contribute to very low human exposures. This combination of low hazard and low exposure indicate that glyphosate presents negligible human health risk to farmers, pesticide applicators and consumers.

Giesy et al. (2000) summarized the body of environmental effect studies conducted on glyphosate as well as some glyphosate-containing products to conduct an ecotoxicological risk assessment. The data included published literature as well as Monsanto’s studies conducted in support of product registration globally. The risk assessment was conducted using a conservative hazard quotient method, in which a hazard quotient less than 1 indicates minimal risk of adverse effects. The no effect level for the most sensitive species was used as the toxicity endpoint for aquatic and terrestrial organisms potentially exposed to glyphosate or glyphosate-based herbicides. Exposure levels were derived from environmental monitoring data or dissipation models. The predicted maximum acute and chronic hazard quotients were less than 1 for aquatic and terrestrial organisms following terrestrial glyphosate uses, confirming a minimal risk of adverse effects. This assessment indicates that application of glyphosate in terrestrial and aquatic sites, including agriculture, forestry, residential, right of ways and habitat restoration, poses minimal risk to non-target species. Since Giesy et al. (2000) was published, two additional publications that add further support to the conclusions of Giesy et al. (2000) on honey bees (Thomson et al., 2014) and soil-dwelling organisms (von Merey et al., 2016) have become available and are also included.

Along with the abundant data demonstrating the low human health and environmental risks associated with glyphosate, it is important to consider reports about adverse effects associated with exposure to glyphosate or glyphosate-containing herbicides. Allegations about purported harms caused by glyphosate surface from time to time and they sometimes receive more attention than the studies indicating a low risk to human health and the environment. Reports that glyphosate is an endocrine disruptor, accumulates in milk, causes kidney disease, disrupts intestinal bacteria, irreversibly binds soil minerals, causes a host of disorders and diseases and disrupts honey bee learning have all been
circulated through traditional and social media in recent years. There are also claims that the surfactants used in glyphosate-based herbicides are more harmful than originally believed. By carefully considering each of these claims it is possible to understand that none of these reports is based on reliable science. There are also claims that glyphosate use is a major driver of declining monarch butterfly populations. Monsanto has taken special interest in this assertion and is engaging with researchers and conservation groups to restore monarch butterfly habitat. Most concerning among all the allegations about glyphosate, the International Agency for Research on Cancer (IARC) classified glyphosate as a probable carcinogen in 2015. This conclusion is in stark contrast to the conclusions of every regulatory agency or authoritative body that has reviewed glyphosate. A closer look at how IARC chose its classification reveals why it was incorrect.

Glyphosate’s exceptional safety profile makes it one of the most versatile tools for weed control both within and outside of agriculture. Its low toxicity to humans and wildlife along with its low potential for adverse environmental effects permit a range of uses and reduces the need for special precautions. Glyphosate’s central role within agricultural systems that rely on crops genetically engineered to tolerate its use, however, sometimes place this herbicide at the center of controversy. It is essential to give claims of adverse effects sufficient scrutiny to assess their validity and understand how they relate to the overall body of knowledge. Across multiple reviews over more than four decades, the consistent conclusion has been that glyphosate can be used safely for many applications without causing significant risks to human health or the environment.

3.1 Glyphosate environmental fate and toxicology

This section was originally published as a chapter in “Amino Acids in Higher Plants”. A copy of this publication is available from the publisher at http://www.cabi.org/cabebooks/ebook/20153121434.


3.2 Glyphosate ecotoxicology

This section was originally published as a peer-reviewed article in “Reviews in Environmental Contamination and Toxicology”. It is available from the lead author at http://www.usask.ca/toxicology/jgiesy/pdf/publications/JA-228.pdf.


3.3 Glyphosate and honey bees

This section was originally published as a peer-reviewed article in “Integrated Environmental Assessment and Management”. It is available from the publisher at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4285224/.

3.4 Glyphosate and soil biota

This section was originally published as a peer-reviewed article in "Environmental Toxicology and Chemistry". It is available from the publisher at http://onlinelibrary.wiley.com/doi/10.1002/etc.3438/epdf.


3.5 Common claims about glyphosate

From time to time allegations surface that glyphosate use is associated with adverse impacts. While many are readily contradicted by the large body of safety data in the published literature, it is important to consider each on its own merits. The most concerning claim is that glyphosate is a probable carcinogen (IARC, 2015). Other common allegations include endocrine disruption (e.g., Richard et al., 2005; Gasnier et al., 2009; Young et al., 2015), accumulation in human milk (Honeycutt and Rowlands, 2014), widespread presence in food (e.g., Rubio et al., 2014) or urine (e.g., Mesnage et al., 2012; Adams et al., 2016), kidney damage (Jayasumana et al., 2013), toxicity to intestinal microflora through action as an antibiotic (Samsel and Seneff, 2013), correlations with Autism spectrum disorder or other disorders and diseases (e.g., Swanson et al., 2014), unexpected toxicity of the surfactants in glyphosate-based herbicides (e.g., Defarge et al., 2016), damage to crop nutrition through action as a mineral chelator (e.g., Huber, 2007; Johal and Huber, 2009), harm to honey bees (Balbuena et al., 2015; Herbert et al., 2014), declining milkweed and monarch butterfly populations (Pleasants and Oberhauser, 2013) and high toxicity to larval amphibians (e.g., Relyea et al., 2005a; Relyea et al., 2005b; Meza-Joya et al., 2013). While these examples encompass the most common claims, information about other claims is available from www.gmoanswers.com.

3.5.1 Glyphosate does not cause cancer

In 2015 IARC convened a panel to review glyphosate. Based on its partial review of the published literature, IARC classified glyphosate as a probable human carcinogen, class 2A (IARC, 2015). This finding was in stark contrast with regulatory reviews of glyphosate and raised concerns that those reviews had misclassified glyphosate’s hazard. IARC’s monograph does not present new research or data and it is not a ‘study’. It does not contain or consider new data on the hazard, exposure or risk of glyphosate. All the key studies considered by IARC in their monograph have been previously reviewed and considered by regulatory agencies. Subsequent to IARC’s announcement, regulators in the EU (EFSA, 2015), Canada (PMRA, 2015) and Japan (FSCJ, 2016) have concluded that glyphosate is not a carcinogen. The European Chemicals Agency (ECHA) issued its proposed listing and classification of glyphosate in 2016, concluding no cancer classification was warranted because the weight of the evidence did not provide an indication of carcinogenicity (ECHA, 2016).

Unlike regulatory agencies, IARC did not consider the total weight of scientific evidence available for glyphosate (APVMA, 2016). It is clear from the limited 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 done by regulators globally, overwhelmingly supports the conclusions of safety and lack of carcinogenic potential of glyphosate.

IARC selectively cited data and made very basic errors in data interpretation within each of the four areas of evidence they considered (animal carcinogenicity, exposure, genotoxicity, and epidemiology). The most striking highlights are given below.

Animal carcinogenicity: In reaching their conclusion of “sufficient evidence” of carcinogenicity in animals, the IARC panel interpreted isolated findings of tumor incidences in particular studies, 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 all the isolated tumors discussed by IARC were
spontaneous and not related to glyphosate treatment. Table 2 compares IARC's conclusions with those of 14 previous and six subsequent reviews. Moreover, multiple long-term toxicology studies conducted according to international standards were not reviewed by IARC but clearly corroborate the lack of carcinogenic potential of glyphosate.

Exposure: The IARC monograph considered an incomplete literature review, citing old references where more recent ones exist, and appears to selectively use references and data. IARC cites detections of glyphosate in different matrices (urine, serum, soil, air, water, and food) without putting the levels and potential exposures into the proper context. In reality, regulatory authorities and WHO/FAO’s Joint Meeting on Pesticide Residues (JMPR) establish acceptable daily intakes (ADIs) and/or acceptable operator exposure limits to account for potential human exposures and establish safe exposure levels. When exposure is put into the proper context it is consistently concluded that there are no health concerns with exposure to glyphosate.

Genotoxicity: In reaching their 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 not conducted according to international guidelines. Furthermore, IARC disregarded a plethora of more relevant data, peer reviewed literature reviews, and opinions of numerous other scientists who have carefully considered all the available data and concluded glyphosate is not genotoxic.

Epidemiology: In reaching their conclusion of “limited evidence” in humans for the carcinogenicity of glyphosate, IARC used relatively small case-control studies with design limitations and little to no estimation of glyphosate exposure. 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 (De Roos et al., 2005). IARC’s classifications are not based on the potential overall cancer hazard indicated by all cancer-related studies, but can be the result of one or more studies in which there is a statistically significant difference between control and one or more treated groups or even an examination of data trends that is prone to false positives. Weight of evidence from the full set of studies and exposure are not at all taken into account.

Further, IARC is only 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 JMPR and the International Programme on Chemical Safety) previously concluded glyphosate is not carcinogenic (IPCS, 1994; JMPR, 2004). WHO also assessed glyphosate based on exposures through drinking water and concluded it does not represent a hazard to human health through that route of exposure (WHO, 2011). Most recently, JMPR completed an ‘extraordinary review’ of glyphosate in May 2016 and stated, “In view of the absence of carcinogenic potential in rodents at human-relevant doses and the absence of genotoxicity by the oral route in mammals, and considering the epidemiological evidence from occupational exposures, the Meeting concluded that glyphosate is unlikely to pose a carcinogenic risk to humans from exposure through the diet” (JMPR, 2016). It is expected that other key pesticide regulatory agencies globally will evaluate the evidence presented in the IARC monograph over the coming months and years to determine whether its conclusions in any way impact the existing risk assessment and whether additional risk management measures may be needed.

All allegations about the safety and environmental impacts of glyphosate deserve attention and careful evaluation. Such findings must be evaluated based on their methods, the strength of their conclusions and in light of the existing body of knowledge. Given the extensive scrutiny that glyphosate has undergone since its initial registrations, it is not surprising that many claims about purported adverse effects do not stand up to close scrutiny. Across multiple reviews over more than four decades, the consistent conclusion has been that glyphosate can be used safely for many applications without causing significant risks to human health or the environment.
### TABLE 2. Comparison of conclusions regarding the four rodent cancer bioassays IARC relied on to support its classification of glyphosate.

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<tr>
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<sup>1</sup>A 'No' indicates the agency or organization concluded the assay did not support a finding of carcinogenicity while a 'Yes' indicates it did.
3.5.2 Glyphosate is not an endocrine disruptor
As part of requirements set forth in the 1996 Food Quality Protection Act, EPA initiated the endocrine disruptor screening program (EDSP) in 1998 (EPA, 1998). Through the EDSP, EPA issues lists of chemicals to be tested based in part on the potential for human exposures. Glyphosate met that criterion and was included in the first round of testing. Importantly, EPA has stated the list of chemicals to be tested “should not be construed as a list of known or likely endocrine disruptors. Nothing in the approach for generating the initial list provides a basis to infer that by simply being on the list these chemicals are suspected to interfere with the endocrine systems of human or other species, and it would be inappropriate to do so” (EPA, 2015b). Through the EDSP analysis of glyphosate, EPA reviewed ten EPA-mandated studies as well as data from the scientific literature. In 2015 EPA concluded that “glyphosate demonstrates no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways in mammals or wildlife” (EPA, 2015c). In vitro assays included estrogen receptor (ER) binding, ERα transcriptional activation, androgen receptor binding, steroidogenesis and aromatase activity. In vivo assays included the uterotrophic assay in rats to assess the estrogenic pathway, the Herberger assay in castrate immature male rats to assess the androgenic activity, pubertal assays in male and female rats to assess estrogenic, androgenic and thyroid pathways and steroidogenesis, a fish short-term reproduction assay to assess estrogenic and androgenic and thyroid pathways and steroidogenesis and a frog metamorphosis assay to assay the thyroid pathway. The collection of assays along with data from the scientific literature informed conclusions about the potential of glyphosate to affect the hypothalamic-pituitary-gonadal axis (estrogen and androgen pathways) and the hypothalamic-pituitary-thyroidal axis. The weight of evidence provides a strong demonstration that glyphosate does not adversely affect estrogen, androgen and thyroid pathways system function.

3.5.3 Detectable glyphosate residues do not indicate a health concern
As Saltmiras et al. (2016) described, glyphosate may be detected in various matrices including foods and urine. This fact has been exploited by groups opposed to glyphosate and glyphosate-tolerant crops in an attempt to raise concerns about human or animal exposures (e.g., Mesnage et al., 2012; Kruger et al., 2014). When evaluating such reports, it is important to consider whether glyphosate was measured using a reliable method, whether the samples were handled and stored correctly and whether the measured amounts equate to a health concern. Reports of glyphosate in honey, soy products and other foods (Rubio et al., 2014), for example, were generated by relying on an assay that has not been validated for use in these matrices (Abraxis, 2016). Rather, the method is validated for use only in water samples and it is not possible to rule out false positives or other errors. Adams et al. (2016) reported that glyphosate was present at detectable levels (i.e., greater than 0.2 ppb) in the urine of 121 non-randomly selected people who voluntarily submitted urine samples. The analytical method was similar to other validated methods but details of any validation were not provided. Sample collection and storage were also not reported. Importantly, the levels were in the low ppb range (approximately 3 ppb), a level consistent with low exposures through the diet as well as previous investigations of urinary glyphosate levels (Acquavella et al., 2004). Based on the well-established understanding of glyphosate’s absorption and excretion, it is expected that glyphosate would be excreted in urine (Saltmiras et al., 2016). The mere presence of a chemical in urine or food does not equate to a health concern, rather it is the amount of exposure that matters for human health. Specific to this question, EPA calculated an upper estimate of exposures to glyphosate through the diet, drinking water and home uses in 2013. They reported that these sources equate to 13% of the amount the Agency considers safe for humans, indicating it is unlikely that current dietary, drinking water and home uses of glyphosate pose a risk to human health (EPA, 2013).

3.5.4 Glyphosate does not accumulate in milk
Regarding allegations that glyphosate is present at detectable levels in human milk (Honeycutt and Rowlands, 2014), the original reports were posted on a web site that did not supply basic information about the validation of the assay or how samples were collected and handled. The assay was a commercial kit that was only validated for water samples. Milk, however, is a complex matrix that would require separate method validation to avoid false positives or otherwise inaccurate results. EPA and Germany’s BfR have questioned the biological plausibility of glyphosate appearing in milk, the validity of the enzyme-linked
immunosorbent assay (ELISA) used to detect glyphosate by Honeycutt and Rowlands (2014) and the methods used for sample collection and documentation (EPA, 2014b; BfR, 2015). Bus (2015) provides a detailed discussion of the physiochemical and biological reasons why glyphosate would be unlikely to be present in milk or otherwise bioaccumulate. Direct affirmation of these doubts comes from a series of studies conducted in Germany (Steinborn et al. 2016; Von Soosten et al., 2016), the U.S (McGuire et al., 2016; Ehling and Reddy, 2015) and New Zealand (NZMPI, 2012). Steinborn et al. (2016) developed a liquid chromatography-tandem mass spectrometry (LC/MS-MS) method and a gas chromatography-tandem mass spectrometry (GC/MS-MS) to quantify glyphosate in human milk samples. Samples were collected as part of a German government program to conduct voluntary screening of human milk samples for pesticides using the two different methods. None of the 114 samples contained levels of glyphosate above the limits of detection (LOD, 0.5 μg/L, parts per billion, ppb or 1 μg/L, ppb depending on the assay). McGuire et al. (2016) relied on LC/MS-MS analysis to analyze milk samples from 41 women. Urine was also collected from 40 of the same women. None of the milk samples contained glyphosate above the LOD (1 μg/L, ppb) even when it was present at detectable levels in the urine of the same individuals (McGuire et al., 2016). Additional reports have shown that glyphosate was not detectable in retail cows’ milk, cows’ milk powder, or pooled human milk (NZMPI, 2012; Ehling and Reddy, 2015). Von Soosten et al. (2016) fed dairy cows a diet containing various levels of glyphosate that reflected levels in commercially available feed for 26 days. No glyphosate was present in milk at levels greater than the limit of quantitation (3 μg/kg, ppb) even though it was detectable in urine and feces. There has never been detectable glyphosate in any sample analyzed by a validated assay and these results agree with what is known about glyphosate’s pharmacokinetics as described by Bus (2015).

3.5.5 Glyphosate does not cause kidney disease

Jayasumana et al. (2014) speculated that glyphosate interacts with another factor in the environment to propose that a combination of glyphosate with arsenic, other heavy metals, or some unknown material results, by some unknown means, in kidney injury among certain populations within Sri Lanka. Chronic kidney disease of unknown cause (CKDu) has been a significant health issue in parts of Sri Lanka for many years. The reasons for this have been explored at length by World Health Organization (WHO) and by other experts and organizations in Sri Lanka and in other locations but no clear cause has emerged. There are no indications of kidney damage from short or long term animal studies at relevant doses (Williams et al., 2000). Other risk factors have been proposed for CKDu, including exposure to metals or to fluoride, snake bite, dehydration, non-prescription analgesics and genetic predisposition. The National Academies of Sciences of Sri Lanka (NASSL) has stated that “...the scientific data is lacking to support the contention that glyphosate is the cause of CKDu....” NASSL further notes that they “are not aware of any scientific evidence from studies in Sri Lanka or abroad showing that CKDu is caused by glyphosate. The very limited information available on glyphosate in Sri Lanka do not show that levels of glyphosate in drinking water in CKDu affected areas (North Central Province) are above the international standards set for safety. Further, CKDu is rarely reported among farmers in neighbouring areas such as Ampare, Puttalam and Jaffna or even the wet zone, where glyphosate is used to similar extent. It has also not been reported in tea growing areas where glyphosate is far more intensively used” (NASSL, 2015).

3.5.6 Glyphosate does not harm digestive system microorganisms

Claims about adverse effects on digestive system microorganisms (e.g., Samsel and Seneff, 2013) were considered as part of the recently completed scientific review of glyphosate in the EU. After reviewing the available data, EFSA concluded that there were no effects at realistic doses and any effects on digestive function were the result of pH alterations associated with high doses and not the result of altered intestinal microorganisms (EFSA, 2015). There are three studies that have examined effects on gut microbiology and microbial function that use mixed populations of digestive microbes. The first study relied on a simulated in vitro rumen1 to monitor microbial populations under controlled conditions for a long period.

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1 A rumen is the part of the stomach in animals such as cows and sheep where microbes ferment feed materials to complete an initial step in digestion. Healthy microbe populations are necessary for proper rumen function.
(Riede et al., 2014). No adverse changes in rumen parameters attributable to glyphosate or a glyphosate-based herbicide were detected, including increased populations of pathogenic bacteria. The second study specifically looked for effects on Clostridium botulinum in response to claims that farms in Germany were suspected of having a rare form of visceral botulism. Although this is often cited, a team of veterinarians investigated the situation and found no evidence in these herds that indicated the presence of botulinum toxin (Seyboldt et al., 2015). The third study was conducted with sheep fed diets containing formulated glyphosate-based herbicides added at concentrations reflecting the highest glyphosate residues measured in grass three to eight days after application (Huther et al., 2005). There was no indication that glyphosate caused adverse effects on rumen microbes. Part of the claim that glyphosate adversely effects digestive system microflora rests on a patent obtained by Monsanto Company for the use of glyphosate to inhibit the 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) enzyme present in certain pathogenic microbes (Abraham, 2010). EPSPS is the same enzyme glyphosate inhibits in plants to act as a herbicide. While the patent describes glyphosate’s ability to inhibit EPSPS activity, it is important to note that the patent demonstrated these results through in vitro testing of isolated EPSPS enzymes and required the concurrent addition of oxalic acid or its derivatives to be effective. The patent is specific to members of the protozoan parasite phylum, Apicomplexa, including organisms such as Toxoplasmum sp., Plasmodium sp. and Cryptosporidium sp. To date, there have been no in vivo tests of glyphosate’s ability to act as an antibiotic for Apicomplexa infections and there is no indication that consumption of glyphosate as a residue on certain foods or feeds results in adverse effects on digestive system microorganisms.

3.5.7 Glyphosate does not cause various disorders and diseases

Several publications rely on comparisons of glyphosate use and the incidence of various disorders and diseases over time to hypothesize that glyphosate causes these disorders and diseases. Swanson et al. (2014) provide some of the more widely circulated claims, including allegations that glyphosate causes Autism spectrum disorder, Alzheimer’s, obesity, anorexia nervosa, liver disease, reproductive and developmental disorders and cancer. Rather than providing experimental evidence that describes a causal association, the publication and others like it rely on correlations to imply causation. Typically glyphosate use data from USDA are correlated with disorder and disease incidence data from various sources and then placed against the backdrop of a range of hypothesized mechanisms that the available scientific evidence directly contradicts. No new experiments or data are provided to support the purported associations. Similar claims based on these correlations have received little to no scientific support and have been strongly criticized for their methodology and assumptions (Novella, 2014; Katirae, 2015).

3.5.8 Surfactants from glyphosate herbicides are often mischaracterized

Formulated herbicides such as Roundup® branded products contain surfactants (an inert) along with glyphosate (the active ingredient). Surfactants are a class of chemical used to increase the water solubility of other materials, reduce the surface tension of water and, in the case of herbicides, allow active ingredients to pass through the outer layer of a weed’s leaves. Unprotected cells are susceptible to damage by surfactants because they can disrupt cell membranes. Consistent with this expectation, scientific publications relying on in vitro test systems with unprotected cells will show that formulated pesticides are more toxic than would be expected from the active ingredient alone (e.g., Defarge et al., 2016). In vitro test-systems commonly expose unprotected cells being grown in culture to a mixture of glyphosate and surfactant at concentrations that are often hundreds or thousands of times greater than concentrations observed in the body following environmental or dietary exposures. Unprotected cells are susceptible to membrane damage by surfactants and this does not necessarily indicate a true toxic effect to intact organisms. A 2007 study described the effects of Roundup® branded herbicide, the surfactant from Roundup® branded herbicide and several other common surfactants on cultured cells (Levine et al., 2007). The authors demonstrated that 1) some of the adverse effects attributed to formulated herbicides based on in vitro studies are actually a reflection of the fact that cellular processes dependant upon intact membranes are disrupted by multiple surfactant
classes at supraphysiological concentrations, 2) surfactants present in consumer products and used every day can disrupt membranes more effectively than Roundup® branded herbicide or the surfactant it contains. Williams et al. (2000) reviewed toxicological data for polyethoxylated tallow amine (POEA), one of the primary surfactants used in Roundup® branded herbicide, concluding it poses a low hazard for acute or sub-chronic exposures. Giesy et al. (2000) conducted an ecotoxicological risk assessment of glyphosate-containing herbicides as well as the surfactants they contain, including POEA and concluded that POEA does not pose a significant risk to wildlife outside of aquatic habitats.

3.5.9 Glyphosate does not injure crops by chelating metals

Glyphosate’s ability to chelate certain metals forms the basis of claims that its use as a herbicide damages plant health by making needed minerals unavailable to crops (e.g., Huber, 2007; Johal et al., 2009). Duke et al. (2012) examined these and similar claims in detail. The authors examined the available literature on crop nutrition, crop disease and crop yield from studies that compared glyphosate-tolerant crops to their conventional counterparts. They concluded that while the data on crop nutrition vary depending on experimental conditions, the majority of scientific evidence indicates glyphosate does not adversely affect crop nutritional status. Likewise, they found that most of the available data support a conclusion that glyphosate does not alter crop susceptibility to disease. Finally and most notably, the authors found that yield data from glyphosate-tolerant crops do not support a conclusion that glyphosate use adversely impacts yield. Additional support for these claims is often obtained from a patent issued to Stauffer Chemical in 1964 for the use of aminomethyleneephosphinic acids as pipe descalers (Toy and Ewing, 1964). While the patent demonstrates the ability of a class of chemicals, to which glyphosate belongs, to chelate metals, it provides no demonstration that glyphosate itself is an unusually strong chelator compared to many others present naturally in the environment or produced commercially. Duke et al. (2012) reviewed the available literature about glyphosate and its ability to chelate minerals in agricultural settings. They concluded that significant effects of glyphosate on mineral availability are unlikely because soil mineral concentrations are several orders of magnitude greater than the concentrations of glyphosate even with the highest concentrations of glyphosate that could be expected.

3.5.10 Glyphosate does not pose health risks to honey bees

A pair of recent studies purports to demonstrate that glyphosate causes deleterious but sublethal effects in honey bees (Balbuena et al., 2015; Herbert et al., 2015). Balbuena et al. (2015) suffered from low sample numbers that limit the ability to draw reliable conclusions while Herbert et al. (2015) obtained conflicting results using individual bees vs. whole hives, indicating problems with the reliability of the underlying study methods. In contrast, Thompson et al. (2014) described a method for determining hive level glyphosate exposures to bees and used those exposure data to select doses for a follow up brood (larval bee) study. In phase one, bees from four colonies were allowed to collect nectar and pollen on glyphosate treated Phacelia tanacetifolia (purple tansy) a highly attractive crop to bees for seven days. Glyphosate levels were measured in nectar and pollen collected by the bees as well as in the hive. These concentrations were then used in set doses for phase two of the study that assessed toxicity to brood by feeding hives glyphosate in a sucrose solution over five consecutive days. Thompson et al. (2014) considered survival of eggs, young larvae and old larvae as well as pupae weight. No adverse effects on adult bees or bee brood survival or development were observed in any of the glyphosate-treated colonies. These results are consistent with EPA’s previous conclusions that found glyphosate to be “practically nontoxic” to honey bees (EPA, 1993).

3.5.11 Collaborations are underway to support monarch butterflies

Glyphosate’s broad adoption and its ability to control weeds while killing their roots also meant it could eliminate many difficult to control weeds, including members of the genus Asclepias (milkweeds). Milkweed species are the host plants for monarch butterfly larvae and there are reports of declining milkweed populations in the US that attribute these declines to glyphosate use (Pleasants and Oberhauser, 2012). Consequently, researchers have attributed declining monarch butterfly populations to glyphosate use but others have also cited illegal logging in the butterfly’s overwintering habitat (Vidal et al., 2014), climate
change (Guerra and Reppert, 2013) and a lack of floral resources during autumn (Inamine et al., 2016). There are now concerted efforts in the US to restore milkweed populations outside of cultivated fields to help sustainably restore monarch populations, including the Monarch Butterfly Conservation Fund established by the National Fish and Wildlife Fund. Monsanto has made significant commitments in support of those efforts (NFWF, 2015) and is actively engaged in establishing more habitat for monarchs within the US.

3.5.12 Glyphosate is not toxic to larval amphibians

Reports of glyphosate-based herbicides on larval amphibians, particularly frog larvae, have circulated for several years (e.g., Relyea, 2005; Relyea et al. 2005; Meza-Joya et al., 2013). Such studies typically rely on applying a formulated herbicide product that contains surfactants to aquatic systems containing larval amphibians, often well in excess of the amount allowed by the product label for terrestrial uses. The researchers then report various measures of survival or other toxicity. Glyphosate itself has undergone testing on amphibians and the results consistently demonstrate low levels of toxicity (EPA, 1993; Giesy et al, 2000). Giesy et al. (2000) reviewed the available data on the toxicity of glyphosate and glyphosate-based herbicides to amphibians and noted the glyphosate-based herbicides exhibited more toxicity than glyphosate alone. They attributed this difference to the presence of surfactants in the formulated product. Surfactants disrupt cell membranes, resulting in the loss of cell function (Lucy 1970; Dimitrijevic et al, 2000). Killing cells with surfactants in an aquatic organism’s gills or elsewhere in its body would by definition lead to death or other indications of injury. For this reason, glyphosate-based herbicides intended for aquatic use do not contain surfactants and products for terrestrial use that do contain surfactants have label instructions that direct applicators not to apply the product to waterways or allow the product to run off into waterways. When used according to label instructions, glyphosate-based herbicides can be applied without harming amphibians.
 Glyphosate combines a unique set of attributes that make its continued registration in the public interest. From its broad activity spectrum, systemic mechanism of action, lack of residual activity and ease of use to its strong safety profile for humans, animals and the environment, coupled with the benefits it provides by simplifying weed management and enabling widespread conservation tillage, glyphosate is well-deserving of its characterization by Duke and Powles (2008) as a “once-in-a-century herbicide”.

In combination with glyphosate-tolerant crops, this herbicide has transformed agriculture by reducing costs and labor requirements for weed control. It has also lowered the technical barriers to conservation tillage, helping to foster less environmentally impactful farming practices. Its value in agriculture extends from the individual farm level to export markets for US commodities. In order to maintain these benefits in the future it will be necessary to include other management tactics to control resistant weeds.

Glyphosate also enables simple and effective weed management even in crops that are not tolerant. It also provides cost-effective weed control in rights of way and recreational settings. Glyphosate is commonly used to control invasive and aquatic weeds because of its wide activity spectrum, ease of use, low cost, and low potential for adverse impacts.

Glyphosate’s strong safety profile has been well known since it was first registered. In short term and long term studies glyphosate exhibits low toxicity and does not disrupt endocrine system signaling. Glyphosate is not mutagenic or carcinogenic in studies at the cellular level, whole animals or human populations. Glyphosate does not persist in the environment and it does not bioaccumulate.

Now entering its fifth decade of use, glyphosate is central to weed control in the US and around the world. Maintaining access to this important tool will promote environmental and economic sustainability in agricultural and any other setting where weed control is needed. While it is clear that any weed management tactic used repeatedly on its own will lead to resistant biotypes, it is equally clear that glyphosate provides significant benefits today and will continue to do so in the future.
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