Dennis P. Ward, Ph.D.
Tel. 1.919.226.7382
Fax 1.919.226.7462
dennis.ward@syngenta.com

Syngenta Biotechnology, Inc.
3054 E. Cornwallis Road
P.O. Box 12257
Research Triangle Park
North Carolina 27709 USA

August 26, 2013

Cynthia A. Eck
Document Control Officer
U.S. Department of Agriculture
Animal and Plant Health Inspection Service
Biotechnology Regulatory Services
4700 River Road, Unit 91
Riverdale, MD 20737

Subject: Supplemental information for Environmental Assessment of Herbicide Tolerant SYHT0H2 Soybean

Ref: Petition Number 12-215-01p

Dear Ms. Eck:

As a follow-up to a meeting between USDA BRS staff and petitioners on July 11, 2013, the attached supplemental information for the environmental assessment of Event SYHT0H2 soybean is being submitted. With this letter Petitioners are providing the following materials:

- Two paper copies of the Supplemental Information (dated August 26, 2103)
- One CD containing:
    - Supplemental information as a Word file
    - Supplemental information as a pdf file for internet posting.

Should you require additional information regarding this submittal don't hesitate to contact me. Thank you.

Sincerely,

Dennis P. Ward, Ph.D.
U.S. Lead, Seeds Regulatory Affairs

Encl.

cc: Michael Weeks / Bayer CropScience

Supplemental Information in Support of the Petition to Deregulate Herbicide-tolerant Event SYHT0H2 Soybean; Petition No. 12-215-01p

Date: August 26, 2013

Prepared by: Dennis Ward, Sydney Jarrett, and Brett Miller
Syngenta Seeds, Inc.

During a meeting held between USDA BRS staff and Petitioners on July 11, 2013 a request was made for more information on the expected adoption of SYHT0H2 soybean by growers and on how, when, and where herbicides will be used in conjunction with these soybeans. Chapter XII of the SYHT0H2 petition describes how herbicides will likely be used with the new soybean cultivar. We are providing herein an expanded description of the recommendations that will be given to growers on how to use the product as well as projections on product adoption.

A. Definitions and General Information Related to Application of Herbicides

1. Application Timing
    a. Preplant – application of a herbicide to the field in advance of soybean planting. Preplant applications can be made with a contact herbicide to clear a field of emerged weeds, often referred to as preplant burn down. Residual soil-applied herbicides can also be applied preplanting to control emerging seedling weeds.
    b. Preplant incorporated – application of a residual herbicide immediately prior to seedbed preparation in a conventionally tilled field. A practice that is most effective for herbicides that are volatile or require incorporation for activation. The herbicide is incorporated into the top 2-3 inches of soil which puts them in close proximity to the germinating weed seedlings to prevent them from emerging and competing with the crop.
    c. Preemergence – Application of selective herbicide(s) after crop planting but prior to emergence of both the crop or the weeds in order to control weeds before they emerge and compete with the crop. Generally, preemergent applications are most effective with soil residual herbicides. Herbicides applied preemergence are generally selective for certain weed types and do not harm the emerging crop.
    d. Early postemergence – Application of a herbicide shortly after the crop and/or weeds have emerged and are still small or in the early vegetative stages of growth. Smaller weeds are generally easier to control and are less competitive with the crop than larger weeds. Contact herbicides and herbicides with foliar activity are generally applied at this timing often in mixtures with soil residual herbicides which can provide an additional barrier to germinating weeds.
    e. Postemergence – Application of a herbicide after the crop and/or weeds have emerged. Contact herbicides and herbicides with foliar activity are generally applied at this timing to control escaped weeds.

2. Herbicidal Spectrum of Control
    a. Selective - The majority of herbicides on the market today are selective in that they only control certain species of plants or weeds but do not harm the crop. A classic example is a herbicide that predominantly controls broadleaf weeds but not grasses or vice versa. Mesotrione, which controls a broad-spectrum of broadleaf weeds but is safe to corn, is an example of a selective herbicide.
    b. Nonselective or broadspectrum - There are a few herbicides (e.g. glyphosate and glufosinate) that are broad-spectrum in that they have herbicidal activity against a broad range of plant species; they control both broadleaf and grassy weeds.
3. Herbicide Placement
    a. Contact herbicides - To be herbicidally effective some herbicides must come in contact with actively growing foliage; these are referred to as contact herbicides. They can be selective or broad spectrum in terms of the weeds they control.
    b. Soil-active residual herbicides - Herbicides that are applied to soil and can affect germinating or emerging weeds or the roots of young growing weeds. These herbicides typically remain active in the soil for days to weeks after application. The choice of which soil-residual herbicide to use is based on the weed species expected and their levels of infestation. Adequate soil moisture is critical for activating soil-applied herbicides because it facilitates their movement into the soil solution where it can become available for absorption into the germinating weed seedling. This approach to weed management is usually very effective because only tiny amounts of the herbicide are needed to control germinating or emerging weeds due to their small plant mass.
    c. Systemic herbicide – Herbicide active ingredient is absorbed by plant leaves or roots and circulates throughout the plant's vasculature and affecting its growing points.
4. Mechanism of Action
    a. Knowing the mechanism of herbicidal action for a given product and having more than one effective mode of action available for controlling the target weed species are key components of a weed resistance management program (i.e. Stewardship plan).
    b. The Weed Science Society of America has developed a numbering system for categorizing herbicides by known mechanism of action. The Group Number, identifying the category for mechanism of action, for a herbicide can be found on its label. The EPA label for a herbicide will also include recommendations on other herbicides the product of interest can be mixed with to optimize weed control and reduce weed resistance risk.
    c. Herbicide recommendations for many crops include application of mixtures. The reasons for advocating mixtures being to broaden the spectrum of weeds controlled in a grower's field and to deploy herbicides with multiple effective modes of action against the same set of weed species in order to reduce the risk of weed resistance.

B. Herbicides Used with SYHT0H2 Soybean

There will be a multitude of herbicide use options for soybean growers choosing to plant SYHT0H2 soybean. Understanding the herbicides to which tolerance has been engineered in SYHT0H2 soybean will be important to a grower in developing his weed control program. The best source of information about the herbicides is the EPA-approved label.

1. Mesotrione – A Group 27 Herbicide that inhibits the enzyme 4-hydroxyphenylpyruvate dioxygenase (HPPD), a critical enzyme in plant photosynthesis.
    a. Mesotrione has herbicidal activity against a number of broadleaf weeds, many of which are resistant to glyphosate, as well as ALS and PPO inhibitors, and triazines. Mesotrione is not effective for control of most grass weeds.
    b. Mesotrione is active as a preplant or preemergence herbicide when applied to the soil and retains activity in the soil for one to five weeks depending on the rate applied, soil moisture, and other soil characteristics such as pH, organic matter, etc.
    c. Mesotrione has contact herbicidal activity when applied post-emergence and is systemically active in target weeds.
    d. Mesotrione is formulated and offered to growers as Callisto® Herbicide (a 40% suspension concentrate). Callisto Herbicide is currently used primarily for weed control in corn. It is also registered for use in a small number of minor crops. An application to amend the Callisto label allowing for pre- and postemergence use in soybean is under review at EPA. See Table 1 for recommended use rates for mesotrione in corn and soybean. An entirely new formulation of mesotrione will be developed for use in soybeans whose label will contain herbicide mixtures tailored to control of weeds in SYHT0H2 soybean fields.

Table 1. Mesotrione use rates (g active ingredient/Ac) for corn and soybean.

Application timing	Corn Use Rate (g ai/Ac)	Proposed Soybean Use Rate (g ai/Ac)
Preplant, preplant incorporated, or preemergence	85.1 – 109.1	90.7
Early postemergence	42.5 – 85.1	42.5 – 90.7
Postemergence	42.5 – 85.1	42.5 – 51.0
Season maximum rate	85.1 – 109.1	141.6

Source: EPA label for Callisto Herbicide and amendment for addition of soybean to the label

    e. Mesotrione soybean use instructions (from EPA label):
        i. Mesotrione can be applied from 14 days prior to planting up through and including the R1 growth stage for control of weeds in soybeans.

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ii. To prevent the risk of weeds developing resistance to mesotrione, always use full labeled rates. This helps prevent selection for, or population shifts toward, mariginally tolerant weed species and/or resistant species biotypes.

iii. It will be recommended to growers that mesotrione be applied in combination with other herbicides; for example, a preemergent grass herbicide such as s-metolachor. It could also be recommended that it be tank mixed with another preemergent broadleaf herbicide (other than another Group 27 herbicide), such as fomesafen or metribuzin, in order to broaden the weed spectrum and provide more than one effective mode of action for reducing weed resistance risk. Mesotrione could also be applied postemergence in a mixture with glufosinate. Specific mixture recommendations are under development and will be available for SYHT0H2 soybean commercialization. [**Note:** mesotrione will not be applied to SYHT0H2 soybean alone and would not be mixed with isoxaflutole. There would be no benefit to the grower since these herbicides control a similar weed spectrum and operate via a common mechanism of action.]

2. Isoxaflutole – A Group 27 Herbicide that inhibits the enzyme HPPD.
   a. Isoxaflutole (IFT) has herbicidal activity against a number of broadleaf and grass weeds, many of which are resistant to glyphosate as well as ALS and PPO inhibitors and triazines. IFT is active as a preemergent herbicide when applied to the soil and retains activity in the soil for six to eight weeks depending on the rate applied, soil moisture and other soil characteristics such as pH, organic matter, etc.
   b. IFT has contact herbicidal activity when applied post-emergence and is systemically active in target weeds.
   c. IFT is formulated and offered to growers as Balance® Pro Herbicide (a 40.5% suspension concentrate). Balance Pro Herbicide is currently used only for weed control in corn. An application for registration of this 40.5% suspension concentrate use in IFT-tolerant soybean is under review at EPA (product name – EXP32032A SC Herbicide). See Table 2 for use rates of IFT in corn and soybean.
   d. IFT soybean use instructions (from EPA label):
      i. May be applied in IFT tolerant soybean varieties either preplant, preplant incorporated (less than 2” deep), preemergence, or early postemergence (up to but not including first bloom).
      ii. To manage the selection and spread of resistant weed populations, it is important to use herbicides with different modes of action in tank mixture, rotation or in conjunction with alternate cultural practices.
      iii. To help prevent the development of resistance to IFT, always use the full labeled rates as shown on the label.

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Table 2. IFT use rates (g active ingredient/Ac) for corn and soybean.

Application timing	Corn Use Rate (g ai/Ac)	Soybean Use Rate (g ai/Ac)
Early preplant, preplant incorporated (8-30 days prior to planting)	21.3 – 42.6	35.5 – 42.6
Preplant , preplant incorporated (0-7 days prior to planting) or preemergence	21.3 – 42.6	28.4 – 42.6
Early postemergence	None	28.4 – 42.6
Season maximum rate	42.6	42.6

Source: EPA labels for Balance Pro Herbicide and EXP32032A SC Herbicide

e. Bayer CropScience (BCS) is actively pursuing registrations of IFT for corn and soybean in Minnesota, Michigan, and Wisconsin. These states represent the only major corn and soybean acreage in the US which have not registered IFT. At this time BCS is negotiating with each state on the conditions of registration for IFT. Currently IFT is registered for corn, and will be registered for use on soybean, in 28 states. These 28 states account for 81% of planted US field corn acreage in 2013 and 86% of planted US soybean acreage in 2013. Over the past ten years these same states have accounted for roughly the same percent of planted US acreage for these crops, 81% and 85% for corn and soybean, respectively (USDA-NASS QuickStats, 2013).

3. Glufosinate – A Group 10 herbicide that interferes with the normal functioning of the nitrogen assimilation pathway in plants.
    a. Glufosinate is a broad-spectrum contact herbicide. It is herbicidally active against a large number of broadleaf and grass weeds. It must be applied to actively growing green tissue to be effective. It has no residual or preemergent activity when applied to soil.
    b. Glufosinate can be used as a preplant burn down agent to clear a field of emerged weeds prior to planting the soybean crop. It can also be applied from crop emergence up to but not including the bloom growth stage.
    c. Glufosinate is formulated and offered to growers as Liberty® 280 SL Herbicide (a 24.5% suspension concentrate). Liberty 280 SL is labeled for use as a preplant burn down agent in many crops and is labeled for postemergent applications to the following Liberty-tolerant crops: cotton, corn, canola and soybean. See Table 3 for recommended use rates for glufosinate in corn and soybean.

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Table 3. Glufosinate use rates (g active ingredient/Ac) for corn and soybean.

Application timing	Corn Use Rate (g ai/Ac)	Soybean Use Rate (g ai/Ac)
Preplant burn down	240 - 298	240 – 298
Postemergence	182	182 - 298
Season maximum rate	365	538

Source: EPA label for Liberty 280 SL Herbicide.

d. Integrated weed resistance management recommendations on the Liberty 280 SL label include:
    i. Rotate crops.
    ii. Rotate herbicide modes of action by using multiple modes of action during the growing season and apply no more than two applications of a single herbicide mode of action to the same field in a two year period.
    iii. Rotate herbicide tolerant trait systems.
    iv. Although timely postemergent applications of Liberty 280 SL can provide complete weed control, residual herbicides at burn down, planting, or tank mixed with Liberty 280 SL help ensure optimal weed management particularly if environmental conditions delay timely postemergent applications. Residual herbicides can also reduce early season weed competition and are a key element of good weed resistance management practices.

4. Application rates – All three product labels direct growers to apply the herbicides at labeled rates. Applying less than the recommended rate reduces herbicidal efficacy and creates selection pressure for evolution of resistant weeds. Applying more than the highest recommended label rate is wasting product (and money) and is illegal. As can be seen from the information in Tables 1, 2, and 3 herbicide use rates in soybean will be very similar to the rates currently used in corn.

C. Product Use Recommendations

Commercialization of SYHT0H2 soybean is still a few years away because of the need to obtain regulatory approvals in key export markets. Both companies are conducting field research to develop the best herbicide product use recommendations for growers adopting SYHT0H2 soybean. However, it is known what some of these use recommendations will be. Three examples are presented here:

1. Preplant burn down with glufosinate, paraquat or glyphosate to clear a field of weeds along with application of residual herbicides, mesotrione or IFT, plus a residual grass and/or additional broadleaf herbicide (i.e. s-metolachlor or metribuzin). If needed, an early postemergent application of glufosinate (with or without mesotrione/IFT or other soybean selective herbicide); or
2. Soil-incorporated mesotrione or IFT with a residual grass and / or additional broadleaf herbicide (i.e. s--metolachlor or metribuzin) at time of planting. This could be followed by

one or two postemergent applications of glufosinate alone or mixed other soybean selective herbicides (i.e. s-metolachlor or fomesafen); or

3. Use of glyphosate, paraquat, glufosinate, or tillage to clear a field of weeds prior to planting. Early postemergent applications of residual herbicides, mesotrione or IFT, tank mixed with other soybean selective residual herbicides recommended on the label (i.e. s-metolachlor or fomesafen).

D. Current Herbicide Use on Soybean

Soybean is grown to some extent in most farming regions of the U.S. but production is concentrated in the Heartland region (see Figure 1 and Table 4). The Heartland region is also where the largest amount of corn is grown. The data in Table 4 shows that the vast majority soybean and corn grown in the U.S. receives one or more herbicide applications. Glyphosate is the most broadly used herbicide in soybean production today, but the use of other herbicides is increasing. Based on 2012 USDA survey data glyphosate was applied 98% of the soybean area planted in USDA Program States; substantially the same as the 96% of soybean area treated in 2006 (see Table 5). The widespread use of glyphosate throughout U.S. agriculture has led to the development of weeds that are resistant to the herbicide, thus reducing its utility for growers.

Table 4. Soybean and corn production in 2012 by Farm Resource Region and acres treated with one or more herbicides (Syngenta proprietary data, 2013).

Farm Resource Region	Soybean Acres Grown	Soybean Acres Treated	Corn Acres Grown	Corn Acres Treated
Basin and Range	N/A	N/A	125,501	125,501
Eastern Uplands	N/A	N/A	1,837,304	1,793,830
Fruitful Rim	97,577	97,577	1,531,145	1,480,995
Heartland	42,030,248	41,715,218	53,568,987	53,113,673
Mississippi Portal	7,193,144	6,901,535	2,646,821	2,646,309
Northern Crescent	6,861,631	6,766,057	12,243,546	11,775,563
Northern Great Plains	8,606,158	8,563,844	8,510,961	8,372,566
Prairie Gateway	6,034,096	5,959,018	12,684,494	12,618,977
Southern Seaboard	3,366,955	3,358,379	2,516,280	2,494,515

N/A – Data not collected in survey.

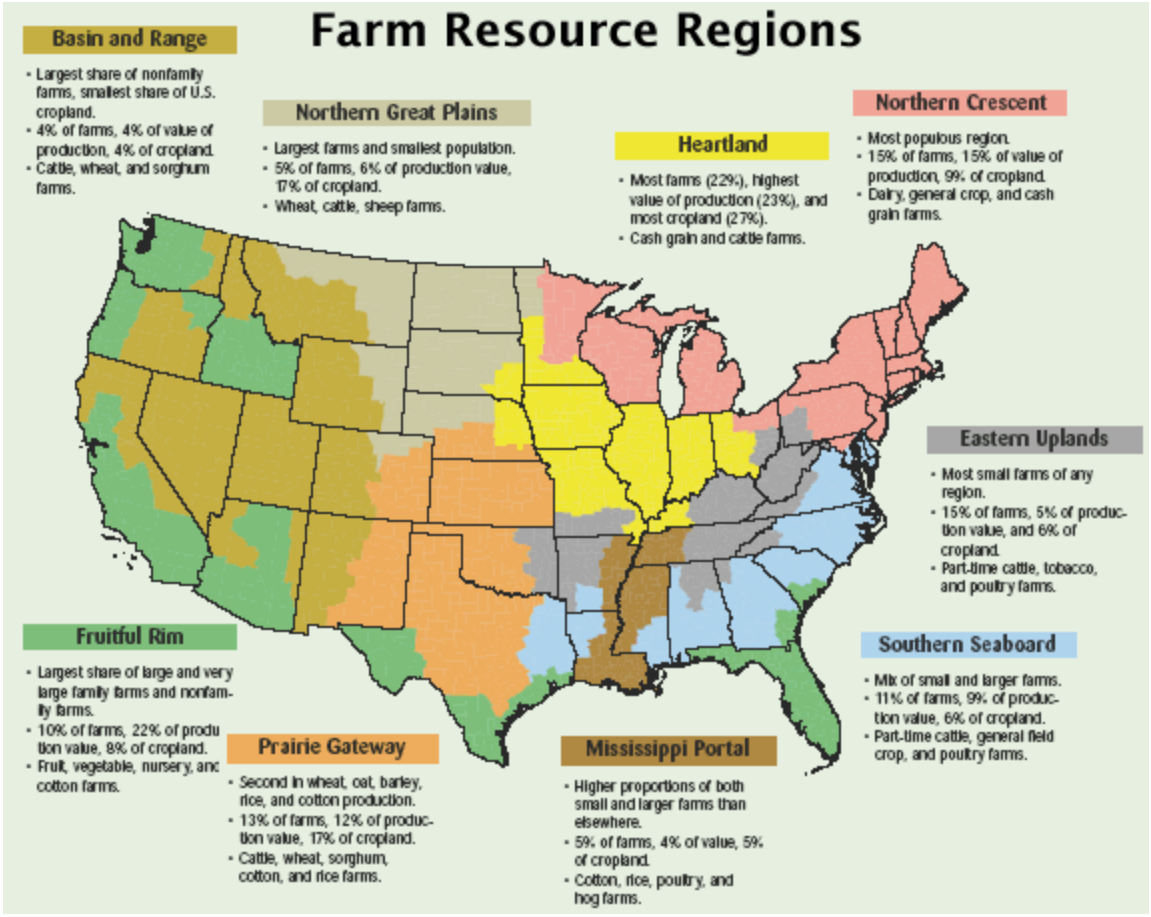

Figure 1. Farm resource regions as defined by USDA. (http://webarchives.cdlib.org/wayback.public/UERS_ag_1/20111128195215/http:/www.ers.usda.gov/Briefing/ARMS/resourceregions/resourceregions.htm)

Table 5. Corn and soybean acres treated (as a % of acres planted) with glufosinate, glyphosate, isoxaflutole, or mesotrione.

	Corn % Acres Treated			Soybean % Acres Treated		
Herbicide	**2010**	**2005**	**2003**	**2012**	**2006**	**2005**
Glyphosate (all salts)	76	33	19	98	96	91
Glufosinate	2	5	3	3	0	0
Isoxaflutole	7	6	8	0	0	0
Mesotrione	17	20	13	0	0	0

Source: USDA-NASS QuickStats (2013)

Glufosinate was applied to 3% of the soybean arces planted in 2012 and 2% of the corn area planted in 2010, the years for which USDA data are available (Table 5). Mesotrione and IFT are not currently used in soybean production. In 2010 mesotrione was applied to 17% of the corn arces planted and IFT was applied to 7% of the corn arces planted in program states.

E. Product Adoption

SYHT0H2 soybean is expected to be attractive to growers with infestations of glyphosate resistant and other resistant weed biotypes on their farms. Grower survey results in 2012 indicate that 61.2 million acres of U.S. cropland are infested with glyphosate resistant weeds, almost double the acreage reported for 2010 (see Figure 2).[1] Results of this survey indicate that resistance is very problematic in the South. Survey results also revealed that an increasing number of farms have at least two or more resistant species on them.

At product maturity (defined here as five years post-launch) Syngenta and BCS estimate that SYHT0H2 could be planted on 12 to 15% of US soybean acres. These adoption rates include having the trait in most Syngenta branded soybean lines as well as licensing the trait to other seed companies. By the time SYHT0H2 soybean is commercialized there are expected to be multiple herbicide-tolerant soybean events that seed companies and growers can choose from. Glyphosate tolerance is expected to still be a prevalent trait in the soybean market but competition provided by other weed control systems will drive its use down.

There are not region-specific adoption targets for SYHT0H2 soybean. The trait and associated herbicides will be of potential benefit to any grower that has a problem with glyphosate or other herbicide resistant weeds. Adoption of SYHT0H2 soybean is expected to be greatest in the Heartland, Northern Great Plains, Mississippi Portal, and Northern Crescent regions that account for more than 85% of soybean acreage in 2012 (Table 4). Over the past 12 years there have been 68 reported incidents of glyphosate resistant weeds in these regions.[2] Ten of the 11 weed species in these regions with documented resistance to glyphosate are controlled by at least one of the three herbicides to which SYHT0H2 is tolerant based on EPA labels (see Table 6). Only one species, Italian rye grass, is not listed on product labels as being controlled by any of these herbicides. Only two of the 68 glyphosate resistance incidents involved this weed. Incidents of glyphosate resistant weeds roughly track those regions where corn and soybean are heavily planted, with the exception of California (see Figure 3).

It is assumed that growers planting SYHT0H2 soybean will make at least one herbicide application containing mesotrione or IFT, and/or glufosinate. A conservative assumption is that increased regional use of the mesotrione or IFT will be 0.5X the number of acres planted with SYHT0H2 soybean (assuming equal market share for the two herbicides). A conservative assumption regarding use of glufosinate is that it will increase in direct proportion (i.e. 1X) to the acres of SYHT0H2 soybean planted.

[1] Stratus Agri-Marketing Inc. (2013). http://www.farmchemicalsinternational.com/article/32880/glyphosate-resistance-spreads-in-the-u-s; accessed August 5, 2013.
[2] (International Survey of Herbicide Resistant Weeds. http://www.weedscience.org/summary/home.aspx; accessed August 2, 2013

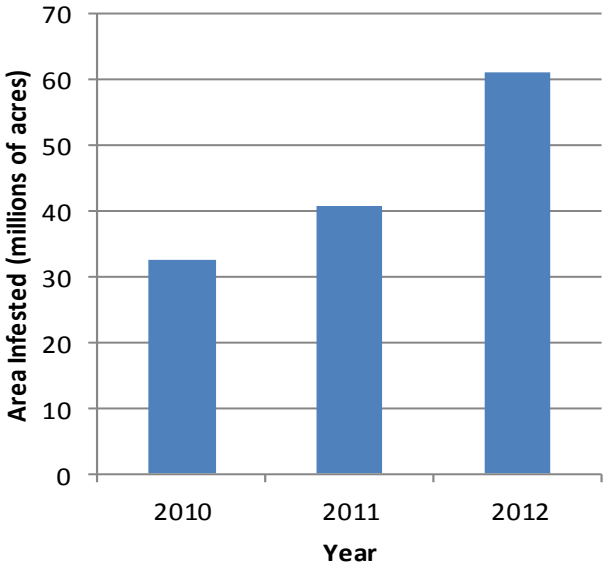

Figure 2. Crop area infested with glyphosate resistant weeds, grower survey results for years 2010-2012 (Stratus Agri-Marketing Inc., 2013).

Adoption of SYHT0H2 soybean will reduce the use of glyphosate for weed control in soybean because postemergence applications will not be possible (unless SYHT0H2 soybean is combined with a glyphosate-tolerant trait at a future date). Use of glyphosate for preplant burn down of weeds will still be an option for growers planting SYHT0H2 soybean. Grower adoption of other herbicide tolerant traits in coming years will also reduce the selection pressure on glyphosate.

F. Impacts on Agricultural Practices Related to Weed Control

The introduction and adoption of SYHT0H2 soybean will not impact current agronomic practices except by reducing risk for development of glyphosate-resistant weeds in soybean production. Providing growers with alternative weed control options through planting SYHT0H2 soybean will reduce the use of glyphosate for weed control in soybean and thus reduce selection pressure for development of resistant weeds. Selection pressure will also be reduced for other herbicides currently used for weed control in soybean, including PPO-inhibiting herbicides such as fomesafen. Although glyphosate will remain a key product for weed control in soybean the ability that growers will have to mix it with mesotrione or IFT and/or glufosinate further reduces resistance risk for glyphosate as well as the other herbicides.

Table 6. List of weed biotypes that have been confirmed resistant to glyphosate in the four major soybean growing regions of the U.S. and whether they are controlled by mesotrione, IFT, or glufosinate.

Farm Resource Region	Weed Species	Control by Mesotrione	Control by Isoxaflutole	Control by Glufosinate
Heartland	Annual Bluegrass			x
	Common Ragweed	x	x	x
	Common Waterhemp	x	x	x
	Giant Ragweed	x	x	x
	Horseweed	x	x	x
	Kochia	x	x	x
	Palmer Amaranth	x	x	x
Northern Great Plains	Common Ragweed	x	x	x
	Common Waterhemp	x	x	x
	Giant Ragweed	x	x	x
	Horseweed	x	x	x
	Kochia	x	x	x
Mississippi Portal	Annual Bluegrass			x
	Common Ragweed	x	x	x
	Common Waterhemp	x	x	x
	Giant Ragweed	x	x	x
	Goosegrass		x	x
	Horseweed	x	x	x
	Italian Ryegrass			
	Johnsongrass		x^	x^
	Palmer Amaranth	x	x	x
	Spiny Amaranth	x		
Northern Crescent	Common Ragweed	x	x	x
	Common Waterhemp	x	x	x
	Giant Ragweed	x	x	x
	Horseweed	x	x	x
	Palmer Amaranth	x	x	x

^ - labeled for control of seedlings

Source: International Survey of Herbicide Resistant Weeds.
http://www.weedscience.org/summary/home.aspx; accessed August 2, 2013
EPA labels

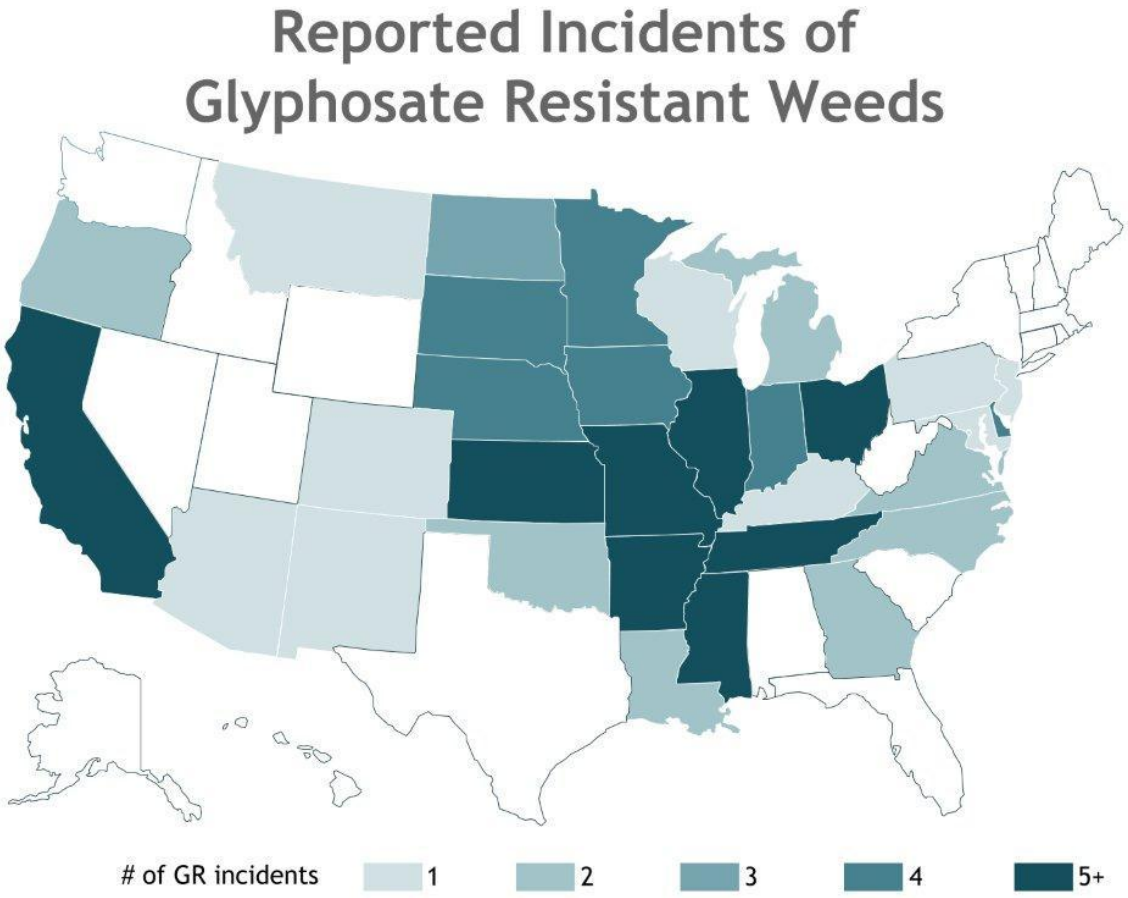

Figure 3. Reported incidents of confirmed glyphosate resistant weeds by state. (International Survey of Herbicide Resistant Weeds. http://www.weedscience.org/summary/home.aspx; accessed August 2, 2013).