Summary  
Changes in the use of glyphosate with the introduction of Roundup Ready® crops in the mid-1990s have meant exposure of a whole new ‘genetic pool’ to the herbicide. Although weed population shifts and resistance have been observed before, following locally intense glyphosate use, the recent widespread adoption of homogeneous weed control methods, particularly in cotton and soybeans, has led to a burgeoning resistance problem. Despite the low frequency of resistance to glyphosate in natural weed populations, the characteristics of those weed species developing resistance are such that their spread is inevitable, unless appropriate management is undertaken. It has become apparent through our monitoring programs, surveys and experimental work that weed populations are changing. There is a pressing need for diversification of control methods to delay this onset and manage the development of glyphosate resistance. The use of integrated weed management techniques, such as alternating herbicidal modes of action will be necessary to ensure preservation of glyphosate and sustain its use in North American agriculture.

Keywords  
Glyphosate resistance, herbicides, resistance management.

THE USE OF GLYPHOSATE

Resistance development  
Towards the end of the last century, it was commonly believed that the development of resistance to glyphosate was improbable. In published opinions, for example, Bradshaw et al. 1997, it was proposed that the complex manipulations of the target, 5-enolpyruvylshikimate-3-phosphate synthase, enzyme required for the development of glyphosate-resistant crops were not expected to be duplicated in nature to evolve glyphosate-resistant weeds. However, at this time, there was already evidence for glyphosate resistance in rigid ryegrass (Lolium rigidum Gaudin) in Australia (Pratley et al. 1996, Powles et al. 1998).

In 1998, scientists at the University of California (UC) Davis reported resistance to glyphosate in rigid ryegrass populations in almond orchards in California (Di Tomaso and Lanini in Heap 2004). Up to 10-fold resistance was confirmed but there appears to have been little further work done until recent research on the inheritance of resistance in this population (Sima-mata et al. 2003). Recently, there have been reports of additional suspected-resistant populations which appear to be spreading (T. Lanini pers. comm.).

There has been prodigious adoption of Roundup Ready® soybeans in the United States of America (USA), since their introduction in 1996, with about 80% of the soybean area planted with them in 2003. Weeds, such as horseweed (Conyza canadensis (L.) Cronq.) that have considerable genetic diversity and a propensity to develop resistance to other herbicide modes of action, were exposed to intensive glyphosate use; it was almost inevitable that resistance would evolve. During 2000, a research program was initiated at the University of Delaware on horseweed that demonstrated 8–13 fold resistance to glyphosate compared with susceptible populations (VanGessel 2001). Resistant horseweed has become so widespread in the region, primarily through wind dispersal of the seeds, that all infestations are now assumed to be resistant.

There are now reports or publications indicating the presence of glyphosate-resistant horseweed populations in Arkansas, Indiana, Kentucky, Mississippi, New Jersey, North Carolina, Ohio, Tennessee (Mueller et al. 2003) and Virginia. Glyphosate resistance has also been reported in waterhemp species (Amaranthus spp.) in Iowa (Zelaya and Owen 2000) and creeping bentgrass (Agrostis stolonifera L.) in Ohio (Loux and Harrison 2002). Glyphosate resistance in L. multiflorum Lam. in Oregon was also recently reported.

Weeds that have higher inherent tolerance to glyphosate can become more prevalent (Norsworthy et al. 2001) and shifts in weed communities have been reported in glyphosate resistant crops (Wicks et al. 2001). The herbicide used has a significant effect on the diversity of the weed community and weed community shifts can occur as a result of natural tolerance to the herbicide or through avoidance related to weed cohort emergence (Hilgenfeld et al. 2001).

Shifts in weed populations are dependent upon the species present. Results from a study at the University of Wisconsin suggested that weed management and agronomic risks associated with glyphosate use in glyphosate-resistant corn and soybean were no greater
than those associated with conventional pre-emergence soil-residual herbicide programs (Stoltenberg and Jeschke 2003). However, the inherent tolerance of tropical spiderwort (*Commelina benghalensis* L.) to glyphosate has led to its dominance in Georgia cotton fields, spreading from five counties in 1999 to 52 counties in 2003. In the absence of tillage, enabled by glyphosate use, normally ephemeral species such as hophornbeam copper leaf (*Acalypha ostryifolia* Rid-dell) and star of Bethlehem (*Ornithogalum umbellatum* L.) are increasing in soybean and purple moonflower (*Ipomoea turbinata* Lag.) in cotton fields (S. Culpeper pers. comm.).

It is interesting to note that, since the introduction of Roundup Ready technology in 1996, there has been a significant increase (up to 200% for foxtails – *Setaria* spp.) in labelled rates for control of some common weed species, such as barnyard grass (*Echinochloa crus-galli* (L.) P.Beauv.), waterhemp (*Amaranthus rudis* Sauer) and lambquarters (*Chenopodium album* L.). The need to increase rates may reflect both the development of resistance and the inherent variability in sensitivity of individuals in a population. The latter was demonstrated for waterhemp (*A. rudis* and *A. tuberculatus* (Moq.) J.D.Sauer) populations in Illinois, where there was considerable variation in response to glyphosate at lower than recommended rates (Padzoldt et al. 2002). This also demonstrates why full labelled rates are necessary to prevent survival and proliferation of less sensitive individuals.

**Loss of diversity** An analysis of the extent of use of different modes of action in soybeans, corn and cotton in the USA illustrates the trend towards a loss in diversity in herbicide use. In 1996, glyphosate was applied to 21% of soybean acres, while eight alternative modes of action were applied to 228% (Figure 1. Percentages above 100 indicated multiple applications to the same area. Mode of action groups are defined by Herbicide Resistance Action Committee, HRAC or Weed Science Society of America, WSSA). In contrast, in 2002 glyphosate was applied to 121% of the soybean area and alternative herbicides to 62%.

Similarly, in cotton in 1996, 16% was treated with glyphosate compared with 150% in 2002. At the same time, alternative modes of action in cotton accounted for 269% in 1996 and 131% in 2002 (Figure 2).

In contrast, before the introduction of Roundup Ready corn, there was still a diversity of modes of action available, and rotating between corn and soybean ensured rotation of mode of action (Figure 3).

With the increasing adoption of Roundup Ready corn (estimated at 14% of the crop or 5 million hectares in 2003, Doane 2003) and concomitant use of glyphosate, the opportunity for rotation of mode of action could be lost.

**Preserving the technology** The use of glyphosate continues to grow, accounting for 32% (2003, $1.39 billion) of all herbicide sales in the USA (Doane 2003) and 22% (2003, $3.2 billion) of all global crop protection product sales. There are a number of drivers
for this growth including: favourable price; growth in conservation tillage, driven by economic benefits and the USA’s Farm Bill conservation incentives; increase in glyphosate-resistant crops; industry crop loss and weed control insurance programs; and simple low management inputs.

The benefits of glyphosate to society are clear. It has been a key to the adoption of no-till and conservation-till farming, leading to reductions in erosion and off-target movement of nutrients. For example, it is estimated that there has been a decline in soil erosion from 20 to 10 t ha\(^{-1}\) in some areas of Tennessee (T. Mueller pers. comm.) since the adoption of no-till farming.

There are differing opinions as to the threat of resistance to glyphosate and the strategies for dealing with it. There is a strong drive, particularly where resistance is not yet apparent, to use (or abuse) the technology and apply as often as desired. Resistance is thought unlikely to occur or will evolve very slowly and, by then, there will be other modes of action available to deal with the problem. However, it is apparent that the introduction of new active ingredients with novel modes of action has declined significantly in the past 10 years. There are higher hurdle rates in terms of the cost of active ingredients, a need for lower effective use rates, efficacy spectrum challenges, strict environmental impact standards, increasing development costs (estimated at approximately $180 million per herbicide) and duration of development (currently about nine years), and less investment in new active ingredients.

The maintenance of alternative active ingredients is also becoming more costly with re-registration estimated to cost up to $5 million and their loss will severely limit the opportunities to manage glyphosate resistance once it evolves. Research trials and farmer applications have demonstrated excellent control of glyphosate-resistant \textit{C. canadensis} biotypes with alternative active ingredients, such as paraquat plus dicamba, 2,4-D, prometryn or metribuzin, applied before planting.

In 30 year simulations of resistance evolution in \textit{L. rigidum} in Australian no-till cropping, use of preplant, sequential applications of full rates of glyphosate and paraquat reduced the risks of resistance to these herbicides to <2% and no resistance was predicted to either at year 30 (Neve et al. 2003). In contrast, when annual glyphosate (alone) use was simulated, there was a 20% probability of resistance evolving after 30 years in early-sown crops and in 90% of populations after 30 years when sowing was delayed. Where in-crop applications were also used, resistance was predicted in a small number of populations after seven years and almost 100% of populations by year 20. Although \textit{Lolium} spp., particularly in Australian cropping systems, can be considered exceptional in their ability to develop resistance to many herbicides, there are other very common genera across the USA, such as \textit{Amaranthus} and \textit{Conyza}, that are showing a similar propensity for resistance development (Heap 2004).

**Proactive stewardship** The prevention of resistance development is crucial to the sustainability of glyphosate in United States agriculture. In the absence of glyphosate resistance, but with the anticipation of excessive use of glyphosate, there have been efforts made by university cooperative extension personnel to consider the impact and risks associated with resistance. Dr. Chris Boerboom at the University of Wisconsin brought together representatives from agri-business in Wisconsin, such as commodity groups, universities and industry to develop a series of stewardship practices for glyphosate (http://ipcm.wisc.edu/uw_weeds/).

The key points that arose from their discussions were that:

1. glyphosate and Roundup Ready crops are valuable tools for Wisconsin farmers;
2. the risk of glyphosate-resistant weeds will increase with improper use of glyphosate;
3. glyphosate-resistant weeds will reduce the value of this technology; and
4. new herbicides are not being developed to replace glyphosate.

Wisconsin farmers should be proactive leaders and practise glyphosate stewardship.

The following glyphosate stewardship practices were therefore promoted.

1. Rotate between Roundup Ready and conventional crops, or crops with other types of herbicide resistance. Use Roundup Ready crops in your rotation where they have the greatest economic and management value.
2. Rotate glyphosate with other herbicide modes of action. Rotate non-glyphosate herbicides over time as well.
3. Apply glyphosate at labelled rates at the correct stage of growth.
4. If glyphosate is used as a burn-down treatment and in-crop, tank mix the glyphosate applied in the burn-down treatment with another mode of action.
5. Use cultivation after in-crop applications of glyphosate when possible.
6. Scout fields regularly and identify weeds present.
7. Respond quickly to changes in weed population.
Funding for resistance research by commodity groups, such as the Soybean Promotion Board, in different states is increasing as a result of the greater awareness of glyphosate resistance.

The cost to the farmer of glyphosate resistance in the USA has not yet been determined. However, the presence of glyphosate-tolerant, tropical spiderwort increased herbicide costs by 33% in heavily infested fields in Georgia (S. Culpepper pers. comm.). Controlling large infestations of glyphosate-resistant horseweed has been estimated to cost $100 acre⁻¹ in the first year of discovery. The cost of resistance to the farmer is scenario-dependent and a definition of the cropping systems/practices and herbicide strategies that prevent its development is difficult. However, it was apparent from studies done on resistant blackgrass (Alopecurus myosuroides Huds.) that a strategy of prevention can cost significantly less than dealing with resistance once it develops (Orson 1999).

CONCLUSIONS
Syngenta is concerned for the sustainability of glyphosate and other herbicides. This is demonstrated by our determination to include both mode of action symbols and specific resistance management statements on Touchdown® (glyphosate) product labels. These statements are as follows.

Diversify glyphosate-dependent weed control programs with alternative herbicides or cultural practices.

1. In Roundup Ready (RR™) corn and RR soybean systems do not use more than two applications of a glyphosate-based herbicide over a two-year period. Diversify with alternative herbicides/cultural practices.

2. In RR cotton up to three glyphosate applications may be used in crop per year if employing in-crop cultivation/residual herbicide.

3. Use alternative burn-down and/or residual herbicides for RR crops likely to require more than one application of glyphosate.

4. To manage RR resistant volunteers rotate RR crops with conventional crops.

5. Use full label rates of glyphosate and tank mix partners. Minimise weed escapes.

6. Monitor treated weed populations for any loss of field efficacy.

7. Contact your local extension specialist, certified crop advisor, and/or manufacturer for herbicide resistance management and/or integrated weed management recommendations for specific crops and resistant weed biotypes.

The inclusion of these statements is part of a proactive, realistic, but diversified, approach to weed management that is designed to reduce the pressure on glyphosate. Based on farmer surveys, awareness of glyphosate-resistance is increasing, but the risks and consequences involved are not well understood.

The consequences of loss of this technology due to widespread resistance are far-reaching, with the economic viability of rural communities and even the vulnerability of the nation’s food supply at issue.

ACKNOWLEDGMENTS
The authors would like to thank their colleagues, Jerry Wells and Dirk Drost, for information contributed to this paper.

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