

# Corteva Agriscience's perspective and commitment to managing herbicide resistance

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## Abstract

Chemical weed control has been widely adopted and has led to increased efficiency and reduced crop production costs. With the increased use of herbicides and the introduction of herbicide-tolerant crops we have also seen an increase in herbicide resistant weeds which presents a challenge for farmers and land managers. It is incumbent upon the agriculture industry to be an indispensable partner in leading policy, research, education, and best management practices related to herbicide resistance. Corteva Agriscience is an active, engaged partner in herbicide resistance research, education, and communication globally to enable the long-term sustainable use of herbicide-tolerant crop traits and herbicides. Some of the key components of our commitment are highlighted in this Perspective paper and include memberships, partnerships, close involvement with CropLife International (and regional CropLife organizations), and Herbicide Resistance Action Committees at the Global, regional and country level, technical leadership and engagement in multiple scientific societies, and collaboration with universities and research institutes. Corteva is committed to advancing sustainable agriculture to enrich lives and our planet for generations to come and this drives our action through the entire product lifecycle and with our customers and consumers.

**Keywords:** Corteva™ Agriscience; herbicide resistance; sustainability; product stewardship

## 1 INTRODUCTION

Weeds are persistent, ubiquitous, and adaptive pests that pose significant financial and management costs to farmers year-in and year-out. The adoption and use of chemical weed control have largely replaced manual and mechanical weed control around the world and through increased efficiency has reduced the cost of crop production.<sup>1</sup> Herbicide resistance to at least one mode of action has been reported in more than 250 weed species globally.<sup>2</sup> These resistant species include grasses, broadleaves, and sedges in many different cropping systems, crops, environmental and ecological conditions. Simply put, crop and non-crop systems, and all of us by extension, will be impacted without a sustained, integrated and committed effort to manage herbicide resistance. Shaner and Beckie<sup>3</sup> concluded that we need a sustained international effort to develop and implement resistant weed management guidelines and best practices that are tailored to diverse 'agro-ecoregions'. In addition to the engagement and commitment by many players in the pesticide value chain, regulatory agencies are now more focused on requiring label language that provides resistance management guidelines or recommendations because they consider the label as the primary source of use instructions. The US Environmental Protection Agency (EPA) has noted that pesticide resistance is an adverse effect in that it can 'increase pesticide use and create unnecessary economic losses' and the lack of proper guidance on a label could strongly

influence their regulatory conclusions regarding the risks or benefits of a pesticide.<sup>4</sup>

Corteva Agrisciences' purpose statement, 'To enrich the lives of those who produce and those who consume, ensuring progress for generations to come', drives our perspective on herbicide resistant weeds and is central to our 2030 sustainability goals.<sup>5</sup> These sustainability goals include goals to benefit the farmer, the land, communities, and our company's operations. These goals and benefits are intertwined and are used to shape everything we do in the discovery, design, development, positioning and launch of new herbicide products and herbicide-tolerant crop traits and how we educate and communicate with our customers and practitioners in the field. Prospective new herbicide candidates must meet certain sustainability criteria in consideration for advancement in the product pipeline development process and it includes, among other things, assessing the ability to manage current resistant weeds and developing weed problems with the desire to minimize the potential for the development of new herbicide resistance.

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The increasing intricacy of our cropping systems, pest complexes, technology advancements, and farm management practices indicates the need for an approach to herbicide resistance management integrated with other management challenges faced today. Herbicide resistance management is at a critical crossroad – farmers are more aware of the issue and its potential impact on their enterprises, and they are looking to multiple sources for information including producer-oriented or trade publications, product literature and labels, growers' meetings, crop consultants, university extension programs and the internet. All of these sources in some way are connected to the crop protection industry (manufacturers, dealers, and retailers).<sup>6</sup> It has also been reported that in the United States, extension programming has been affected by the presence of herbicide-resistant weeds with agronomic crop specialists indicating their programs were twice as likely to be impacted when compared to horticultural crops.<sup>7</sup> This indicates that extension programs are being adjusted to help provide solutions to growers. In 2018, Schroeder *et al.* published a report of a listening tour with stakeholders and 'a major insight gained from the listening sessions was the fact that many of the participants felt they needed one or more new herbicides with unique mechanisms of action to address their weed management needs'.<sup>8</sup> While the authors pondered in that paper if they should have done more to lead the participants in the listening sessions away from the thought of a new herbicide active substance or mode of action as a solution, it is clear that to the stakeholders, herbicides will continue to be a very important part of their weed management programs. It is in the best interest of farmers to adopt management practices geared toward weed resistance because the practices of an individual farmer can impact the returns of their neighbors.<sup>9</sup> A US Department of Agriculture Economic Research Service report indicated that when a grower and neighbor both manage resistance the average percent increase in net returns relative to base case where neither managed resistance was 2.4, 7.2, and 19.7 when the neighbor alone managed resistance, grower alone managed resistance, and when both managed resistance, respectively (Fig. 1).<sup>9</sup> It is also in the best interest of the industry, as a whole, to preserve the utility and diversity of effective tools (including herbicides), as discovery of new modes of action has dramatically slowed<sup>10</sup> and the cost and regulatory hurdles for developing new herbicides continues to rise, now costing *ca.* \$300 million per product.<sup>11</sup> It will require much more work from university, industry, and other interested scientists to bring a community-wide, interdisciplinary

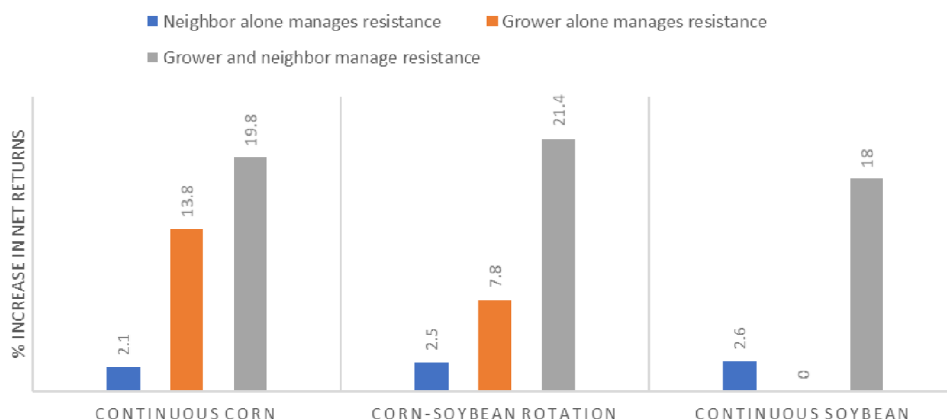
approach to understand the complexity of managing weeds within the context of the whole farm operation and to effectively communicate strategies for mitigation.<sup>12,13</sup> It is therefore incumbent on industry members to be an indispensable partner at the forefront of the effort leading research, education and management related to herbicide resistance. Unfortunately, perception could become reality as it relates to the adage 'if you are not part of the solution, you are a part of the problem'.

There has been a steady and significant increase in the area of herbicide-tolerant (HT) crops planted globally since commercialization of glyphosate tolerant soybean and corn in 1996 and 1997, respectively. In the United States, based on US Department of Agriculture survey data, soybean, corn, and cotton acres planted to HT-crops averaged greater than 90% in 2020.<sup>14</sup> There have been many benefits and challenges of HT-crops to the environment since their commercialization. Vencill *et al.*, Duke and Reddy and Nandula have provided excellent reviews and perspectives on this topic.<sup>15–17</sup> The benefits gained through the introduction of this technology have led to the expansion of its use, despite the challenges that exist. First generation HT-crops generally provided tolerance to and enabled selective in-crop use of a single, broad-spectrum herbicide, (e.g. glyphosate).<sup>10</sup> Next generation HT-crops have sought to enable use of multiple broad spectrum herbicide modes of action, enabling farmers the flexibility to use effective herbicide mixtures, even on weeds resistant to current herbicides.<sup>18</sup> Many of the primary suppliers of HT-crop technology are themselves producers of herbicides used in these systems. To enable the long-term sustainable use of these HT-crop traits and herbicides, Corteva Agriscience is committed to being an active partner in herbicide resistance research, education, and communication globally. We employ a company-wide, integrated and cross disciplinary approach to achieving this goal.

The key components of this broad-based, sustainable resistance management approach within Corteva Agriscience include but are not limited to the following.

## 2 HERBICIDE RESISTANCE ACTION COMMITTEE (HRAC) AND CROPLIFE ENGAGEMENT

Corteva is highly engaged regionally and globally with CroPLife and the Herbicide Resistance Action Committee (HRAC). We share the common commitment of ensuring that our products and



**Figure 1.** Increase in returns for corn–soybean grower given the grower's glyphosate management decisions and those of the grower's neighbor compared to a base case in which neither the grower nor neighbor manages resistance.<sup>9</sup>

technologies are properly used and stewarded to help support healthy food, healthy people and a healthy planet. The strategic and technical expertise of our colleagues are leveraged in support of our industry in everything from promoting best management practices (BMPs) to providing input on significant policies that could affect producers, consumers, and land managers. HRAC supports the highly valued and cited International Herbicide Resistant Weed Survey website used by thousands to understand the scope and frequency of herbicide resistance globally, over time.<sup>2</sup> Corteva colleagues are actively engaged and many have held various leadership roles within these organizations in their respective countries or on the Global HRAC.

### 3 TECHNICAL LEADERSHIP AND ENGAGEMENT

Through its many technical experts locally, regionally, and globally, Corteva contributes significantly to the body of knowledge related to weed resistance management. One good example is the 2nd Global Herbicide Resistance Challenge Symposium that was held in May 2017 that resulted in the frequently cited article on weed resistance to synthetic auxin herbicides.<sup>19</sup> The symposium (and the resulting article) provided an overview of the current state of knowledge of synthetic auxin herbicide resistance mechanisms and included case studies and perspectives mitigating resistance. The symposium featured a presentation by Richard Napier of the University of Warwick with whom Corteva has collaborated to gain a greater understanding of the differential binding of different auxin mimic herbicide classes to different F-box receptors.<sup>18</sup> Another important example of Corteva Agriscience's commitment and leadership can be seen in the development of the Resistance Management Symposium for the International Weed Science Congress 2021 in Bangkok, Thailand, that will bring together leading experts from around the globe to address the topic generally and with some focus on weed resistance management in rice crops. For these types of workshops, seminars, or symposia Corteva colleagues have often played a leading role in proposing, developing, planning, facilitating, presenting, and securing speakers or presenters.

In addition to these larger more formal settings, Corteva personnel also participate in and contribute by speaking at local and regional meetings or in classes at colleges and universities in the vicinity of where we operate. Corteva scientists also frequently publish their research related to weed resistance in refereed publications around the world.<sup>19–21</sup> Amongst articles published between January 2017 and December 2018, Busi *et al.*<sup>19</sup> was one of the most downloaded articles in the 12 months following online publication in Pest Management Science. Since publication in January 2002, Tranel and Wright<sup>21</sup> has been the second most cited Weed Science article with 410 citations as of October 4, 2020. All these activities are possible because of our committed, active involvement with professional and scientific societies, institutions of higher learning, and research institutes and agencies.

### 4 INTERNATIONAL WEED GENOME CONSORTIUM

Corteva seeks to advance the knowledge and tools available to address weed resistance management using the latest genomic tools available to science. The International Weed Genomics Consortium (IWGC)<sup>22</sup> represents a community of scientists from over 20 academic institutions and several industry sponsors with

interests in the genomics of weedy species. As a founding and sponsoring member of the IWGC, Corteva Agriscience is leveraging its capability and expertise in plant genomics and investment in genome sequencing and genome assembly (developed for crop breeding) to support insightful weed genomics data for the weed science community. The vision of the IWGC is to coordinate and efficiently (i) obtain reference genomes for some of the most important weed species worldwide, (ii) provide user-friendly genome analytical tools and training through web-based databases and resources, and (iii) facilitate discussion and collaborations within the field of weed genomics.

Corteva and several other major crop protection industry companies are supporting the establishment of the IWGC through financial and technical capability contributions. Corteva is committing to improve the speed, quality, and cost of sequencing and assembly reference genomes of the prioritized weed species identified by the consortium's board. The IWGC will then annotate and publish these reference genomes for the benefit of the wider weed science community.<sup>22</sup> Ultimately, the vision is to link genomics tools and information and websites at the Global HRAC-supported International Herbicide Resistant weed database.<sup>2</sup> Collectively, the industry and university partners strongly value the benefits of providing training workshops, tools, and expertise to fledgling genomicists to help advance science while guiding the next generation weed scientists on the power and limitations of these new tools to understanding and managing weed resistance mechanisms.

### 5 RESISTANCE BASELINE AND BEST MANAGEMENT PRACTICE STUDIES

In order to responsibly manage and maintain the utility of our plant protection products, Corteva recommends and promotes BMP strategies including herbicide programs, and suggested cultural practices as appropriate to local agricultural conditions.<sup>23</sup> One of the most common management strategies recommended to farmers to combat herbicide resistance is to apply mixtures, sequences (within the same growing season), or rotations (over multiple growing seasons) of herbicides with different modes of action in their fields. Such diversity in herbicide use reduces the intensity of selection for resistance to any one herbicide. To demonstrate the value of the use of effective BMPs to manage herbicide resistance, Corteva provided financial support for a multi-year field experiment established in collaboration with the University of Lleida in Spain to be conducted over a period of 4 years from 2018 to 2021. This study examines the risk of herbicide resistance development through combinations of herbicides with different modes of action in conjunction with agricultural practices that impact resistance risk. For example, a continuous corn cropping system represents a high-risk herbicide resistance management strategy, while a corn–soybean rotation is a medium-risk resistance management strategy. The findings so far suggest that only a combination of multiple diverse management practices, such as crop rotation in combination with herbicide rotation with different modes of action can manage resistance in a sustainable manner, even reducing the selection pressure exerted against a resistant population when it is already established in a field.

Corteva Agriscience's weed management businesses employ recommendations of program approaches for resistance management. We also establish resistance baselines and may actively monitor sensitivity shifts either directly or through our many collaborators globally. For example, as a part of our

responsible care approach to product design and development, the Enlist™ weed control system was intended to be a programmatic approach to weed management in labeled crops. Enlist crops contain either *aad-12* gene for 2,4-dichlorophenoxyacetic acid (2,4-D) tolerance or *aad-1* gene for 2,4-D plus quizalofop tolerance. Currently, the Enlist trait is combined with various other herbicide tolerant traits which enable the selective use of glyphosate, glufosinate, 2,4-D choline, and quizalofop (or haloxyfop in Latin America). The recommended herbicide program with the Enlist weed control system includes the use of pre-emergence or residual herbicides followed post-emergence application of 2,4-D choline plus glyphosate or glufosinate. The Enlist 360 technical training<sup>24</sup> is a key component of the Enlist stewardship program<sup>25</sup> and was developed and deployed to provide wide ranging, readily accessible, and easily understood information related to the responsible use of Enlist products. This approach is critical to preserving and extending the utility of glyphosate in these cropping systems for weeds on which it is still an effective option for control, as well as extending the utility of 2,4-D-choline and glufosinate.<sup>26,27</sup>

## 6 RESISTANCE MANAGEMENT MODELS

The development of resistance management models to generate use recommendations and build a body of knowledge around new or existing technology is best done with cross-functional collaborative teams as well as internal and external experts and stakeholders. These models account for aspects of the weed biology, farmer practices, environment, and herbicide characteristics that influence evolution of resistance or control of the weed population. Corteva Agriscience is fully committed to this collaborative team approach for creating durability models, exemplified by the Enlist weed control system mentioned earlier, as well as the Inzen™ herbicide-tolerant sorghum trait. Inzen herbicide-tolerant sorghum trait is a non-transgenic herbicide tolerance trait that provides tolerance to applications of the herbicide nicosulfuron that inhibits branched chain amino acid synthesis by inhibition of acetolactase synthase (ALS). This trait allows post-emergence control of traditionally hard-to-control grasses with an application of nicosulfuron without harming the sorghum. Corteva scientists provided technical input to university researchers who were developing a major simulation model to assess management options to mitigate risks of ALS-resistance evolution in shattercane (*Sorghum bicolor* (L.) Moench ssp. *drummondii* (Nees ex Steud.) de Wet ex Davidse) populations in US sorghum (*Sorghum bicolor* (L.) Moench ssp. *bicolor*) production areas. The models predicted that resistance would evolve rapidly if Inzen sorghum was planted continuously due to high selection pressure and crop-to-weed gene flow. The authors stated that 'Inzen technology is going to last only if sorghum growers adopt a proactive and diversified management approach'.<sup>28</sup> It is this kind of management approach that Corteva embraces, supports and promotes – not only for this technology to last, but all the technologies that enable modern crop production systems globally.

## 7 COMPREHENSIVE AND TRANSPARENT APPROACH TO PRODUCT STEWARDSHIP

Corteva Agriscience embraces a comprehensive and transparent approach to product stewardship including educational/outreach

activities with internal and external stakeholders, highlighting the need for resistance management and a program approach to weed management. Examples of this include the following.

### 7.1 Enlist™ weed control system

In North America, *Conyza*, *Amaranthus* and *Ambrosia* species have evolved resistance to glyphosate- and ALS-inhibiting herbicides across the corn-, soybean- and cotton-producing regions. *Amaranthus* spp. have also developed widespread resistance to protoporphyrinogen oxidase (PPO)-inhibiting herbicides and limited resistance to 4-hydroxyphenylpyruvate dioxygenase (HPPD) inhibitors and photosystem-II (PSII)-inhibiting herbicides.<sup>2</sup> Enlist herbicides, containing 2,4-D choline, provide effective post-emergence control of these resistant species. However, without a clearly defined strategy for an integrated weed control program, over-reliance on Enlist herbicides would result in high selection pressure for 2,4-D resistance. Thus, Corteva developed the Enlist weed control system to ensure producers utilized multiple effective herbicides within a season and layered residual herbicides (e.g. cloransulam-methyl + sulfentrazone, cloransulam + flumioxazin, or chlorimuron ethyl + flumioxazin + thifensulfuron methyl) with post-emergence herbicides (e.g. glyphosate + 2,4-D choline, glufosinate, and 2,4-D choline).<sup>29</sup> From 2012 through 2019, Corteva hosted or trained thousands (>55 000) of producers, retailers and applicators to participate in an interactive Enlist Ahead field, classroom, or online training programs in the United States, Brazil and Argentina. During the training program, audiences were educated on growing herbicide resistance issues and BMPs that include starting with a clean seedbed, use of residual herbicides followed by an in-season application of 2,4-D choline plus glyphosate or glufosinate. In collaboration with the weed extension scientists, research trials at universities have focused on the total weed control program to demonstrate the importance of the program rather than efficacy of a single product.

### 7.2 Italy – Florpyrauxifen-benzyl (Rinskor™ active) use only as part of a herbicide program

Florpyrauxifen-benzyl (Rinskor active) and halauxifen methyl (Arylex™ active) are new herbicide active ingredients from Corteva Agriscience and are members of a unique synthetic auxin chemotype, the arylpicolinates (HRAC/WSSA Group 4). Members of the arylpicolinate family demonstrate novel and differentiated characteristics in terms of use rate, spectrum, weed symptoms, environmental fate, toxicology profile, and molecular interaction as compared to other auxin chemotypes.<sup>30,31</sup> Florpyrauxifen-benzyl formulated products are recommended for broad spectrum weed control in rice production in Italy, where weed pressure is high, and weed resistance is a growing issue among farmers. Due to the special and challenging conditions for weed management in Italy, and after several years of development and characterization, Corteva designed a program, under which florpyrauxifen-benzyl products are recommended and only allowed to be used as part of pre-defined herbicide programs, which involve florpyrauxifen-benzyl formulated products (straight and pre-mixtures) and also other modes of action in pre-emergence and in post-emergence applications.<sup>32</sup> This approach is designed to ensure the sustainability of a new and differentiated herbicidal tool, while helping growers combat weeds efficiently, delay resistance and improve yields.

### 7.3 Asia Pacific program approach demonstration by technical education activities

Asia Pacific is the largest rice producing region in the world, and as in every rice region, weed resistance is a growing issue. Rice farmers need efficient herbicide solutions, so Corteva recently introduced florpyrauxifen-benzyl as a new herbicidal tool for the control of a broad spectrum of weeds in the region. Understanding the potential of resistance development and growers' need for effective and durable tools for managing weeds, a comprehensive regional initiative to educate our internal partners and our customers in the best practices for use of this new herbicide as part of a program approach was launched. This initiative highlights the use of different modes of action in pre- and post-emergence, formulated herbicides pre-mixtures and tank mixtures, in one-shot and/or sequential applications, in order to achieve the best possible weed control.

Corteva Agriscience research and development (R&D), sales and marketing teams collaborated with external partners (Universities, Research Institutions) to conduct several training sessions across the region with field demonstration or education plots that illustrated the proper use of the new herbicide to maximize weed control and ensure better yield for farmers. This activity represents even higher relevance in a geography like Asia, where an effective practice such as crop rotation is not frequently practiced in rice production.

### 7.4 Halauxifen-methyl (Arylex active) cereal herbicides

The registration of Corteva Agriscience's newest cereal herbicide Arylex (halauxifen-methyl) provided the opportunity to offer wheat and barley growers herbicide products formulated with multiple actives containing different modes of action. A deliberate effort was employed to offer products containing halauxifen-methyl for weed control in small grain cereals only in commercial formulations with other herbicidal actives. This approach provides overlap of weed control options in the same product as well as an increased spectrum of weed control. The benefit of Arylex herbicide mixtures to wheat growers has been notable in Europe for the control of *Papaver* resistant to ALS herbicides (Group 2) as well as 2,4-D.

Careful consideration has been given to the product labels of each halauxifen-methyl-containing herbicide mixture. Use restrictions provided to growers on these labels provide limitations for the number of applications of halauxifen-methyl in a crop during a growing season as well as in consecutive seasons. These restrictions are employed to limit the selection pressure of Arylex on susceptible weed populations in wheat and barley fields. All labels recommend rotation with other effective herbicides for control of weeds.

All of these approaches are intended to ultimately impact or influence grower and land manager mindset and practices to effectively and sustainably manage productive cropping systems or maintain resilient natural areas to deliver their maximum ecosystem services. Corteva is committed to advancing sustainable agriculture to enrich lives and our planet for generations to come.<sup>5</sup>

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