The New Herbicide Mode of Action Classification System from Global HRAC

EWRS Online Training
2022 May 06

HERBICIDE RESISTANCE ACTION COMMITTEE

Global HRAC Member Companies

Our Members	Our Staff
BASF – Jens Lerchl **Bayer Crop Science –** Alberto Collavo **Corteva -** David Simpson **FMC –** Atul Puri **Gowan –** Laurent Cornette **Syngenta -** Gael Le Goupil **Sumitomo -** Yoshimi Fujino **UPL -** Giuvan Lenz	**Chair** Caio Vitagliano Santi Rossi - Corteva **Secretary/Treasurer** Roland Beffa – ext. consultant **Communications Lead** Gael Le Goupil - Syngenta

Global HRAC Initiatives and Activities

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- **Disseminate information on resistant weeds:**
  - HRAC Website (www.hracglobal.com)
  - International Herbicide-Resistant Weed Database, formerly The International Survey of Herbicide Resistant Weeds (weedscience.org)
  - Seminars and Symposia
- **Build recommendations:**
  - Working groups
  - Testing protocols
  - Best Manage Practices
  - Promoting Integrated Weed Management (IWM) / Combinations of agronomy and chemistry weed control / Weed Resistance Mitigation
- **Mode of Action Classification:**
  - Poster
  - Mobile tool
  - Coordination with other entities

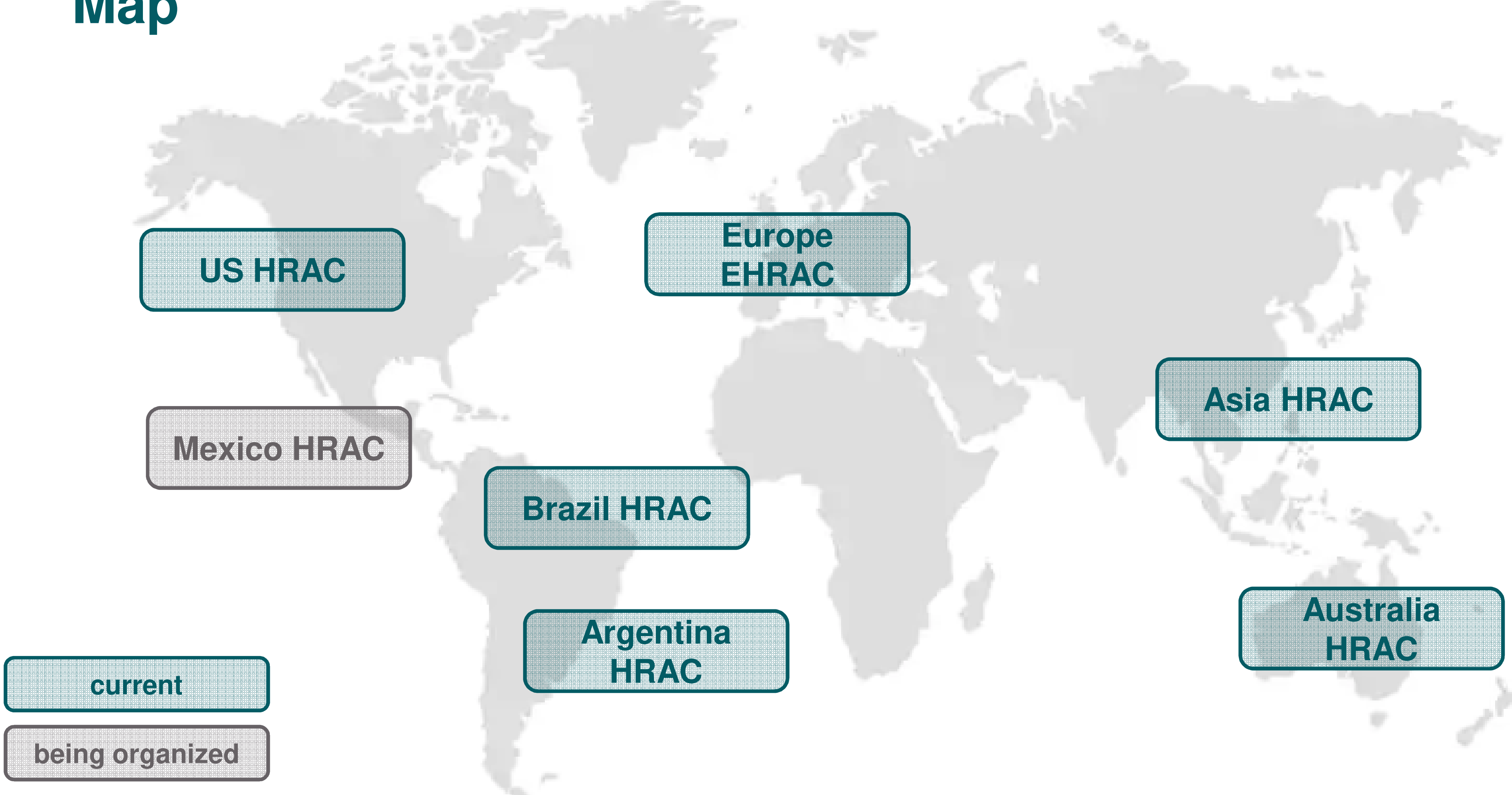
Working Groups

Key objectives for Working Groups

- Consolidate and communicate information for specific MOAs
- Monitor research
- Support intellectual dialogue
- Customize BMPs for a given MOA
- Address specific resistance topics (e.g. Monitoring)

Auxin	HPPD	Communications weedscienc.org hracglobal.com	Issues Engagement	MOA Classification	PPO	Group 15
Paul Schmizer	Roland Beffa	Gael le Goupil	Harry Strek	Jens Lerchl	John Pawlak	Laurent Cornette

Regional/Country HRAC's Map



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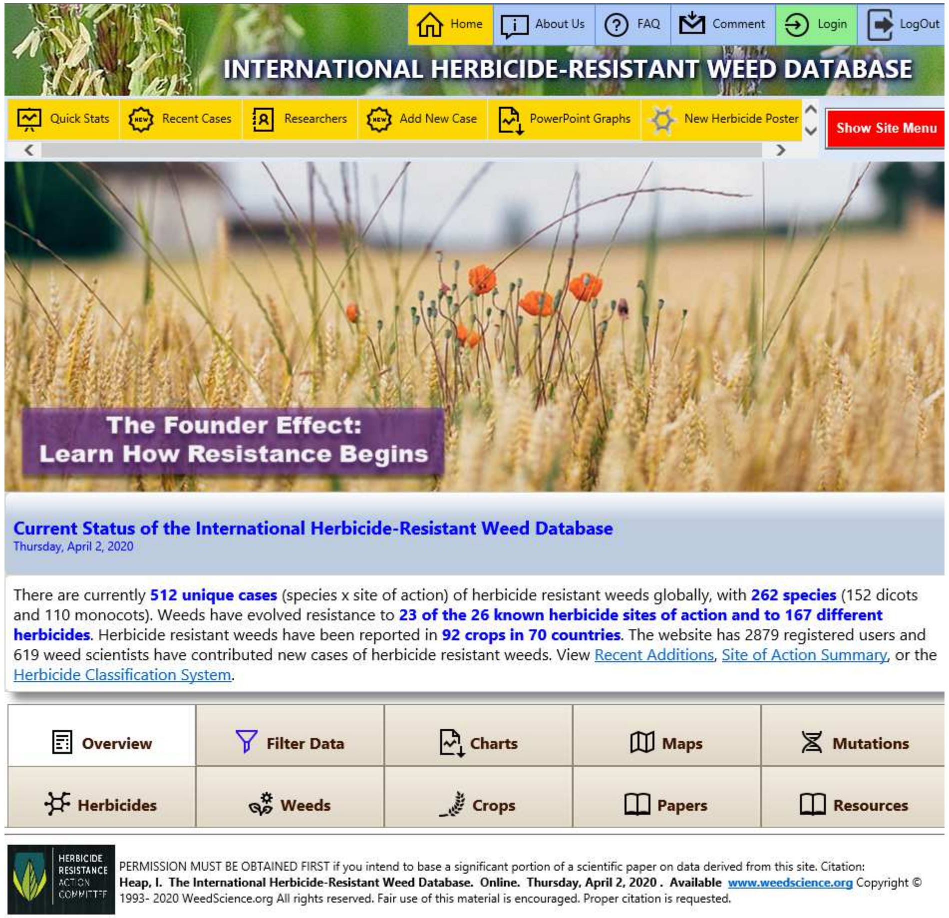
weedscience.org website

Link: weedscience.org

- Updated user interface
- Access to key features on the Home screen
- Customizable and downloadable searches
- GHRAC resistance confirmation criteria adopted by WSSA and worldwide recommended



Mode of Action Classification Update: Why it was done?

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- **Global HRAC mode[1] of action classification was last updated in 2010.** This update was needed to capture the new commercialized active ingredients as well as reflect the current state of knowledge for mode of action and chemical family classification.

- This update ensures stakeholders have the **latest information on mode of action** so they can develop effective herbicide rotation and mix strategies to manage resistance.

- With this update and revision, **Global HRAC will transition from letter to number mode of action codes**. Global HRAC believes a numerical code system is more globally relevant and sustainable compared to English/Latin letters. In geographies where the Latin alphabet is not used and/or where literacy rates are low, everyone understands Hindu-Arabic numerals (including China). Another concern about the English alphabet is that there are only 26 letters. Today we have 25 recognized modes of action including four new modes of actions since the last revision in 2010. Over the next 10 years we anticipate the addition of two to four new modes of action which will exceed the 26 letter maximum.

[1]Global HRAC considered alternatives to "mode" such as "site" recognizing the ongoing discussions and proposals to describe the interaction of an herbicide with its biochemical target, but decided to continue with "mode" given its global and historical acceptance and the fact that "mode" is preferred by the other resistance action committees in CropLife.

How it was done

HERBICIDE RESISTANCE ACTION COMMITTEE

- Global HRAC appointed a **Working Group (WG)** of herbicide technical experts (in herbicide chemistry, weed biology, plant physiology and biochemistry) from CLI member companies to prepare the update. Throughout the process, CLI member companies not represented on the Working Group were advised of and approved interim and final recommendations from the Working Group. Finally, input was solicited from Global HRAC, which included regional HRAC organizations, as well as the WSSA to ensure global consensus going forward.

- **Working Group members**:
  - **Rex Liebl**, BASF, RTP NC, USA
  - **Jeff Epp.** Corteva, Indianapolis, IN, USA
  - **Hubert Menne**, Bayer Crop Science, Frankfurt, Germany
  - **Bernd Laber,** Bayer Crop Science, Frankfurt, Germany
  - **James Morris**, Syngenta, Jealott's Hill, UK
  - **Matthias Witschel**, BASF, Ludwigshafen, Germany

What was done ?

HERBICIDE RESISTANCE ACTION COMMITTEE

The Global Herbicide Resistance Action Committee (HRAC) updated its herbicide mode of action classification system, specifically:

- Addition of new active ingredients
- Revise/update modes of action – new or category changes
- Revise/update chemical family classes
- Recommend changes to the MOA classification codes
- Harmonized the new HRAC system with the WSSA.

Changes since the last update in 2010 include:

- the addition of 14 new actives

ALS	PPO	HST	FAT	HPPD	DOXP	VLCFA	Auxin
Triafamone	Trifludimoxazin	Cyclopyrimorate	Methiozolin	Bicyclopyrone	Bixlozone	Ipfencarbazone	Halauxifen
Metazosulfuron	Tiafenacil			Fenquinotrione		Fenoxasulfone	Florpyrauxifen
				Tolpyralate			

- rationalization of chemical family names, and four new or updated modes of action:

- inhibition of fatty acid thioesterase (cinmethylin)
- inhibition of homogentisate solanesyltransferase (cyclopyrimorate),
- inhibition of solanesyl diphosphate synthase (aclonifen)
- inhibition of serine-threonine protein phosphatase (endothal).

Inhibition of Protoporphyrinogen Oxidase (Group 14)

HERBICIDE RESISTANCE ACTION COMMITTEE

The proposed classification reduces number of families and recognizes a common group (N-Phenyl) for many PPO herbicides separated by novel heterocycles.

- Oxadiazolone is aligned with IUPAC nomenclature rules.
- Fluthiacet-methyl is a prodrug with the (primary) active form an N-Phenyl imide.

Active ingredients	Previous classification	New classification
acifluorfen, bifenox, chlomethoxyfen, chlornitrofen, fluorodifen, fluoroglycofen-ethyl, fluoronitrofen, fomesafen, lactofen, nitrofen, oxyfluorfen	Diphenyl ethers	No change
pyraflufen-ethyl	Phenylpyrazoles	No change
oxadiargyl, oxadiazon	Oxadiazoles	N-Phenyl-oxadiazolones
azafenidin, carfentrazone-ethyl, sulfentrazone	Triazolinones	N-Phenyl-triazolinones
fluthiacet-methyl	Thiadiazoles	N-Phenyl-imides (procide)
butafenacil, saflufenacil	Pyrimidinediones	N-Phenyl-imides
pentoxazone	Oxazolidinediones	N-Phenyl-imides
chlorphthalim, cinidon-ethyl, flumiclorac-pentyl, flumioxazin, flumipropyn	N-Phenyl-phthalimides	N-Phenyl-imides
trifludimoxazin, tiafenacil	New	N-Phenyl-imides
pyraclonil	Other	No change

Inhibition of Very Long Chain Fatty Acids (Group 15)

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- **Reclassify the acetamides**: diphenamid, naproanilide, and napropamide as unknown since recent evidence demonstrates these a.i.s are not VLCFA inhibitors,
- **Reclassify the thiocarbamates and benzofurans** (previously classified as "Lipid Synthesis Inhibition – not ACCase") to "Inhibition of VLCFA" since reports point to this as the MOA for thiocarbamates and benzofurans.

Active ingredients	Previous classification	New classification
cafenstrole, fentrazamide, ipfencarbazone	Other and tetrazolinone	Azolyl-carboxamides
anilofos, piperophos	Other	α-Thioacetamides
pyroxasulfone, fenoxasulfone	Others	Isoxazolines
indanofan, tridiphane	Unknown, other	Oxiranes
acetochlor, alachlor, allidochlor=CDAA, butachlor, butenachlor, delachlor, diethatyl-ethyl, dimethachlor, dimethenamid, metazachlor, metolachlor, pethoxamid, pretilachlor, propachlor, propisochlor, prynachlor, thenylchlor	Chloroacetamides	α-Chloroacetamides
mefenacet, flufenacet	Oxyacetamides	α-Oxyacetamides
butylate, cycloate, dimepiperate, EPTC, esprocarb, molinate, orbencarb, pebulate, prosulfocarb, thiobencarb=benthiocarb tiocarbazil, tri-allate, vernolate	Thiocarbamates	No change
benfuresate, ethofumesate	benzofurans	No change

Inhibition of Very Long Chain Fatty Acids (Group 15)

A GHRAC Working Group published common advices regarding the combination or sequence of actives ingredients belonging to group 15.

In January 2020, HRAC updated the mode of action classification scheme, adding new mode of action classes and reviewing the correct positioning of each active ingredient. For legacy HRAC group N it turned out that most of its active ingredients needed to be moved into HRAC group 15 (legacy group K3) and class N was deleted.

Combinations or sequences of products containing active ingredients from different HRAC groups are part of resistance management recommendations. In line with this advice, it is common practice for European farmers to tank-mix or sequence products of the former HRAC groups N and K3 to control grasses like Alopecurus spp or Lolium spp.

Based on this experience and the fact that HRAC group 15 (K3) covers a multi-enzyme mode of action with a complex pattern of substrate specificity, **combinations or sequences of products containing active ingredients from the former HRAC Groups N and K3 (new Group 15) are still supported by HRAC.**

Download here the GHRAC group 15 Working Group recommendation Le

GHRAC Group 15 Working Group recommendation letter
Download File (0.29MB)

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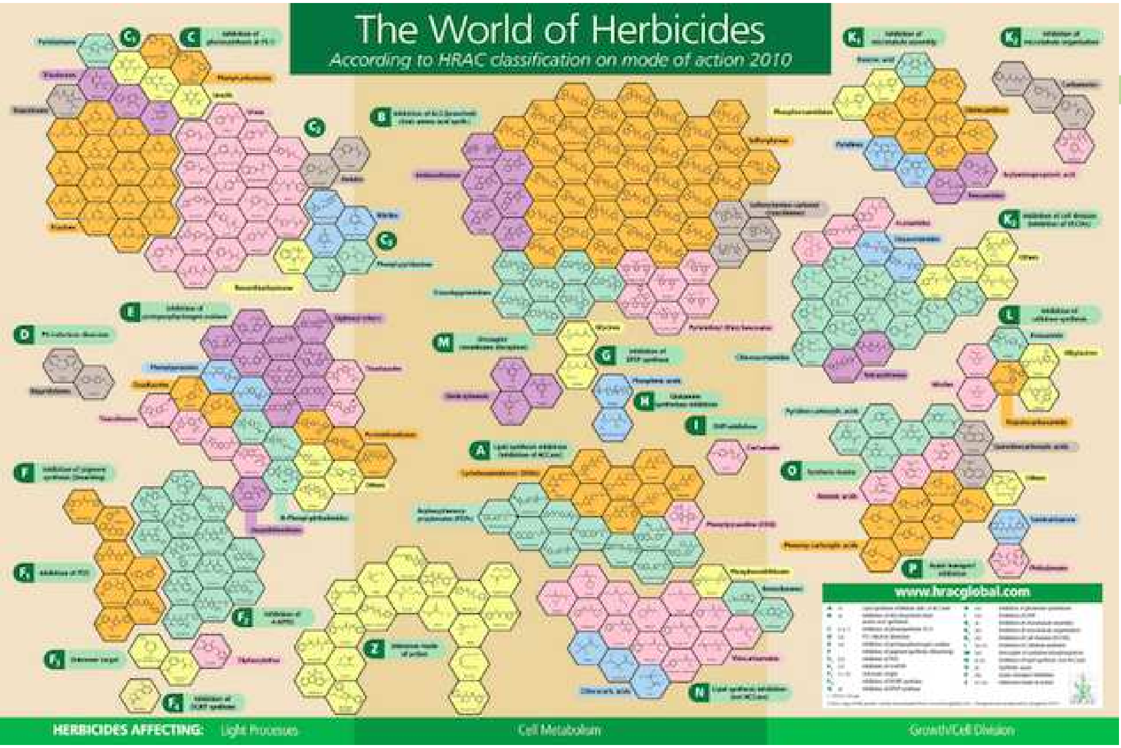
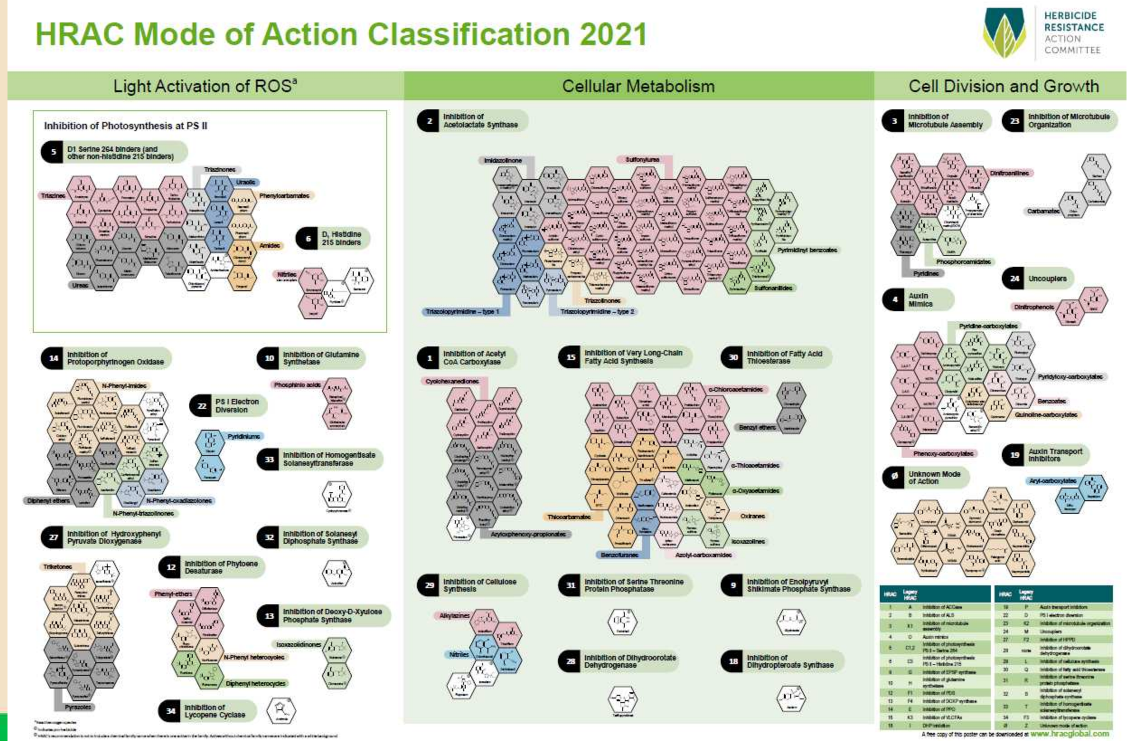
HRAC MoA Classification Poster Update

Poster 2010



Poster 2020



HRAC/WSSA Codes vs Legacy HRAC Codes

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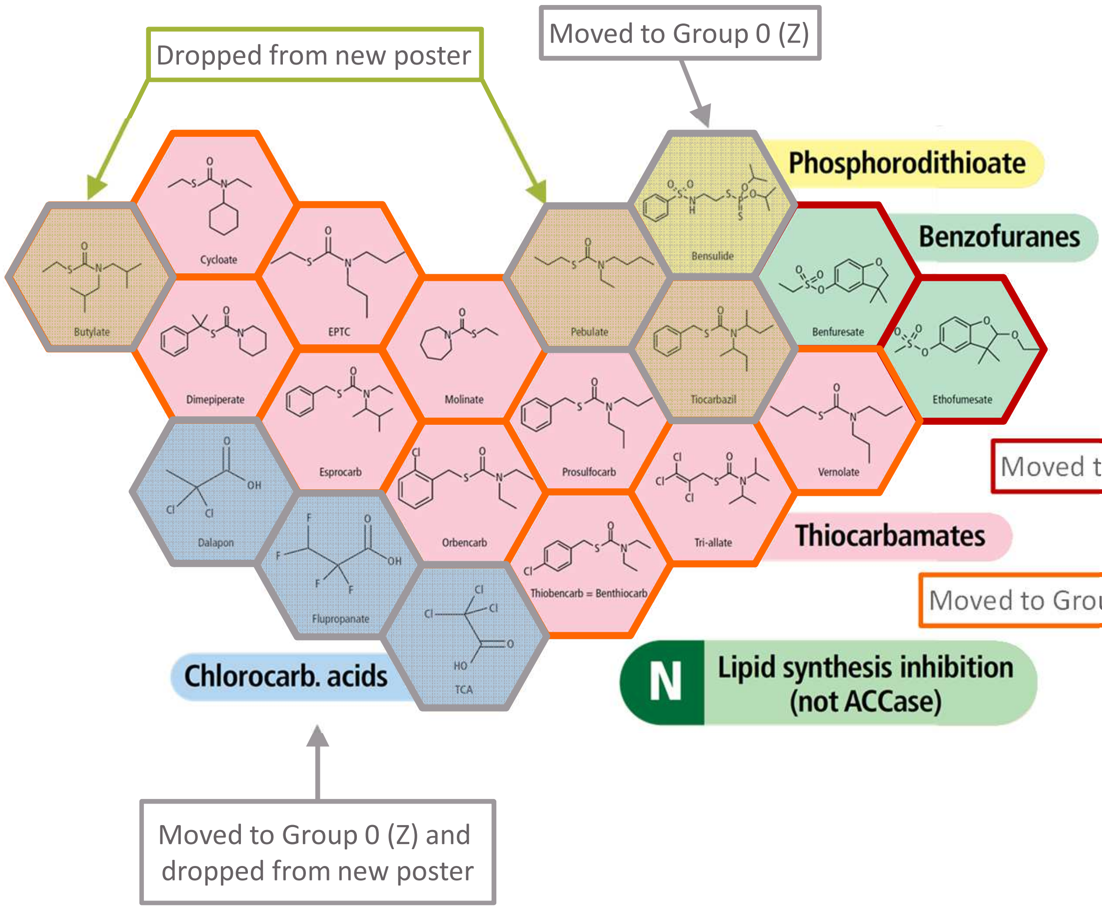
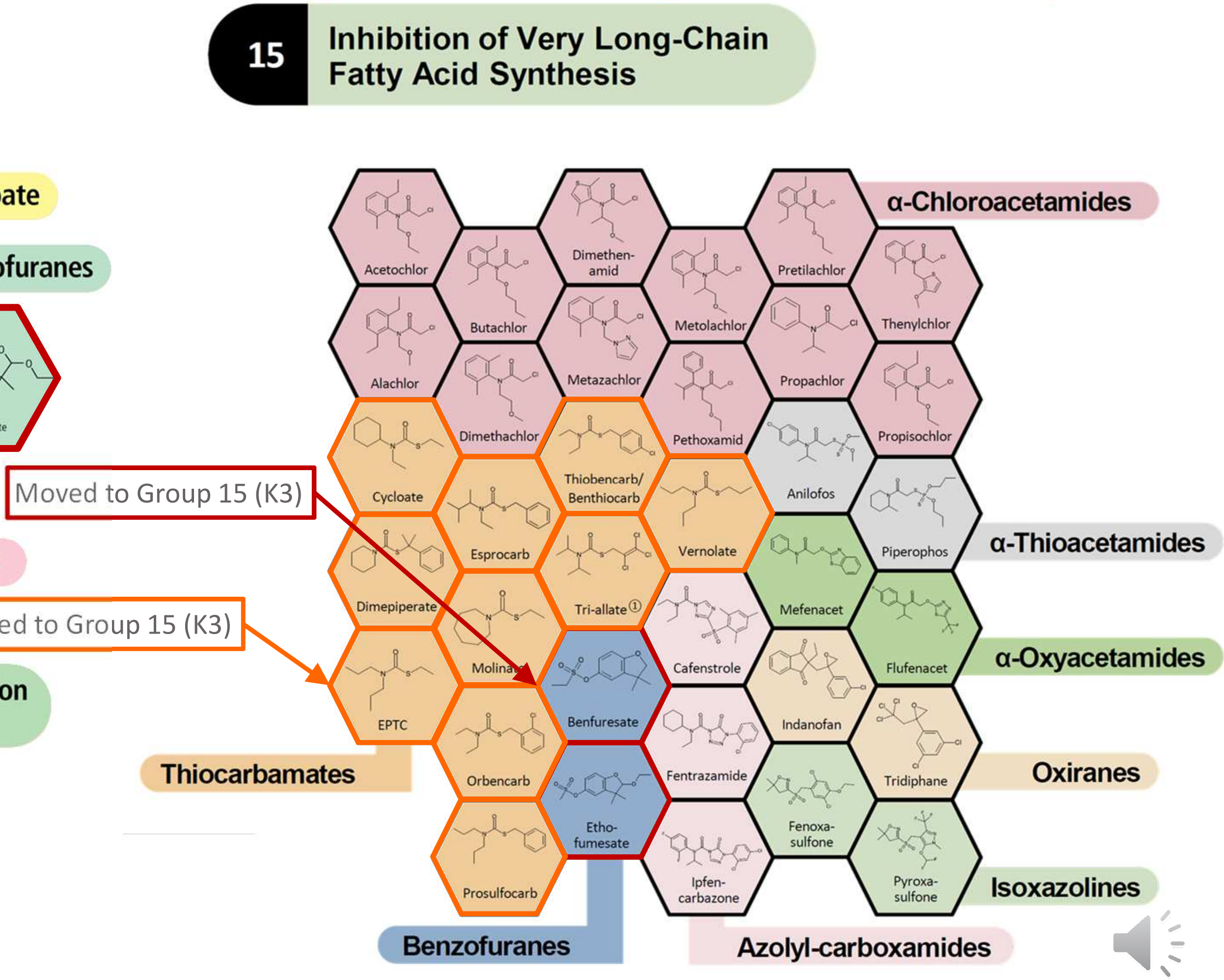
HRAC	Legacy HRAC	
1	A	Inhibition of ACCase
2	B	Inhibition of ALS
3	K1	Inhibition of microtubule assembly
4	O	Auxin mimics
5	C1,2	Inhibition of photosynthesis PS II – Serine 264
6	C3	Inhibition of photosynthesis PS II – Histidine 215
9	G	Inhibition of EPSP synthase
10	H	Inhibition of glutamine synthetase
12	F1	Inhibition of PDS
13	F4	Inhibition of DOXP synthase
14	E	Inhibition of PPO
15	K3	Inhibition of VLCFAs
18	I	DHP inhibition

HRAC	Legacy HRAC	
19	P	Auxin transport inhibitors
22	D	PS I electron diversion
23	K2	Inhibition of microtubule organization
24	M	Uncouplers
27	F2	Inhibition of HPPD
28	none	Inhibition of dihydroorotate dehydrogenase
29	L	Inhibition of cellulose synthesis
30	Q	Inhibition of fatty acid thioesterase
31	R	Inhibition of serine threonine protein phosphatase
32	S	Inhibition of solanesyl diphosphate synthase
33	T	Inhibition of homogentisate solanesyltransferase
34	F3	Inhibition of lycopene cyclase
Ø	Z	Unknown mode of action

HRAC Herbicide Mode of Action Classification 2020

Some chemical classes from eliminated Group N have migrated to Group 15

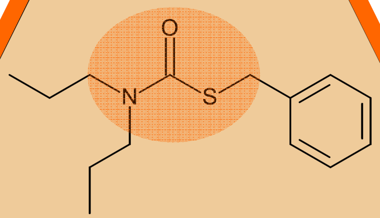




HRAC Herbicide Mode of Action Classification 2020

Updates, unified globally, and change to numeric system – hracglobal.com/tools/

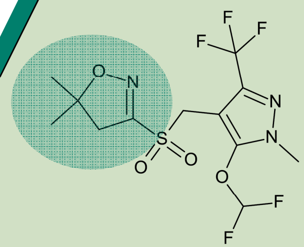
15 **Inhibition of Very Long-Chain Fatty Acid Synthesis**



Prosulfocarb

Boxer®

Thiocarbamate



Pyroxa-sulfone

Sakura®

Isoxazoline

TARGET SITE RESISTANCE

- naturally occurring **mutations**
- theoretical risk **higher**
- practical risk **low**

METABOLIC RESISTANCE

- **metabolizes** herbicide faster
- theoretical risk **higher**
- practical risk **lower**

sequence

mixture

mixture + IWM

HERBICIDE RESISTANCE ACTION COMMITTEE

Global HRAC supports combination or sequence of active ingredients belonging to former Groups N and K3 (new Group 15)

R. Beffa (Bayer Crop Science), **L. Cornette** (Gowan Crop Protection), **G. Le Goupil** (Syngenta), **C.V.S. Rossi** (Corteva Agriscience) and **B. Sievernich** (BASF).

*Written in cooperation with Europe HRAC.

Weed control is an important method of safeguarding the yield and quality of crops. Herbicides provide farmers with an effective and economic weed control tool, which can be integrated with different cultural techniques in a flexible and sustainable way to ensure crop production is optimized. Maintaining the effectiveness of herbicides and reducing the risk of selecting for herbicide resistance requires the implementation of certain strategic elements. One of the most important of these is the careful rotation of herbicides with different modes of action (MoA) against the targeted weeds.

To enable farmers to identify a herbicide's mode of action easily and quickly, HRAC developed a letter-based classification system back in the 1980s. Since then, many new active ingredients, some with new modes of action, have entered the market. Additionally, new research methods have helped to further clarify the precise modes of action of herbicides already on the market. In order to capture all these new developments, in January 2020, following consideration of the latest scientific findings, HRAC updated the mode of action classification scheme, adding new mode of action classes and reviewing the correct positioning of each active ingredient.

Moreover, a transition from the former letter-based system to a new numeric based system was implemented to bypass the limitation in the number of classes set by the letter-based system and to foster use in geographical areas in which the Latin alphabet is not commonly used.

For HRAC group N – "Inhibition of lipid synthesis (not ACCase)" - it turned out that most of its active ingredients needed to be moved into HRAC group 15 (K3; Inhibition of Very Long-Chain Fatty Acid synthesis - VLCFAs) – and class N was deleted. However, in contrast to many other HRAC groups (e.g., 1 (A) – ACCase, 2 (B) – ALS, 9 (G) – EPSPs, 27 (F2) – HPPD, etc.), the inhibition of VLCFAs takes place in a multi-enzyme system, which shows a complex pattern of substrate specificity to individual active ingredients. Specific target sites have not yet been identified (4).

Indeed, it is believed that **herbicides in HRAC group 15 (K3) might exhibit a multi-site or at least a multi-enzyme mode of action, with several elongases being involved**, and that there could be significant differences between the herbicides. Further investigations are required to identify the specific target sites of the different members of group 15 (K3) in more detail. So far, weed resistance to inhibitors of VLCFAs has only rarely been observed and, in most cases, no cross-resistance was reported.

Combinations or sequences of products containing active ingredients from different HRAC groups are part of resistance management recommendations. In line with this advice, it is common practice for European farmers to tank-mix or sequence products of the former HRAC groups N and K3 to control grasses like *Alopecurus spp* or *Lolium spp*. A similar approach to broadleaves weeds (e.g. *Amaranthus* spp) applies to other regions of the World. Such an approach has been in use for years with only few cases of resistance evolving against group 15 inhibitors active on grasses (1, 2 & 3).

Based on this experience and the fact that HRAC group 15 (K3) covers a multi-enzyme mode of action with a complex pattern of substrate specificity, **combinations or sequences of products containing active ingredients from the former HRAC Groups N and K3 (new Group 15) are still supported by HRAC.**

Based on further investigation and their findings a review of HRAC group 15 (K3) might be required.

Bibliography

(1) Dücker R., Parcharidou E., and Beffa R. (2020). Flufenacet activity is affected by GST inhibitors in blackgrass (Alopecurus myosuroides) populations with reduced flufenacet sensitivity and higher expression levels of GSTS. Weed Science, 68 (5). 451-459.
(2) Dücker R. at al. (2019). Enhanced metabolism causes reduced Flufenacet sensitivity in black-grass (Alopecurus myosuroides Huds) field populations. Pest Manag Sci, 75. 2996-3004.
(3) Dücker R. at al. (2019). Glutathione transferase plays a major role in flufenacet resistance of ryegrass (Lolium spp.) field populations. Pest Manag Sci, 75. 3084-3092.
(4) Trentkamp S., Martin W, and Tietjen K. (2004). Specific and differential inhibition of very long chain fatty acid elongases from Arabidopsis thaliana by different herbicides. Proceedings of the National Academy of Sciences, USA 101. 11903- 11908.

What happens in countries currently using letter codes?

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- We should not expect to immediately replace the current classification codes with the new system.
- Countries currently using letters may require a long transition period for education and communication before a change to numbers could be implemented
- HRAC is committed to help facilitate the transition by supporting local education and policy needs.
- In the meantime, HRAC will continue to support the legacy letter-based code.

How it will be communicated

HERBICIDE RESISTANCE ACTION COMMITTEE

- Letters/brochures/PowerPoint presentation/Infographics to stakeholders including herbicide manufactures, regional/country HRACs, University researchers/Academia, regional and country weed science societies, regulatory officials, advisors, applicators, farmers and farmer associations – it is the responsibility of the regional/country HRAC to translate communications from English

- Letters to editors of key selected journals publishing herbicide/weed science content

- Encourage companies to print and distribute multiple copies of the new mode of action poster

- All of us have an interest in seeing this communicated broadly and adopted universally – we all have an important role to play

Global HRAC (Herbicide Resistance Action Committee) developed a Fact Sheet about the 2020 review of the Herbicide MoA classification.

HERBICIDE RESISTANCE ACTION COMMITTEE

To support the widespread adoption of responsible resistance management practices, CropLife International members have voluntarily made a commitment to include Mode of Action icons and groups on all crop protection product labels by 2023. In the meantime, Global HRAC updated the Herbicide MoA classification. It was necessary to capture new active ingredients and ensure the classification system reflects the current state of knowledge. In addition, to ensure global consensus between HRACs (Global and regional), CropLife (International and Australia) and some Weed Societies (such as WSSA), the classification was harmonized globally, and a transition was made from alphabetical to numerical codes which are more globally relevant and sustainable.

Countries currently using the legacy codes will require a transition period including education and communication before a change to numerical codes can be implemented. During this period, Global HRAC will continue to support legacy alphabetic codes and aims to fully implement the numerical code by the end of 2023.

Visit the Global HRAC website and download the FactSheet
https://hracglobal.com/tools/2020-review-of-the-herbicide-moa-classification

Fact Sheet
Download File (0.21MB)

Fact Sheet in powerpoint version

HERBICIDE RESISTANCE ACTION COMMITTEE

Important Changes To Herbicide Mode Of Action Labeling

Fact Sheet

HERBICIDE RESISTANCE ACTION COMMITTEE

1 Why was the Herbicide mode of action classification changed?

The previous revision of the **Herbicide Resistance Action Committee** (HRAC) mode of action (MoA) classification was performed in 2010. This update was necessary to capture new active ingredients, ensure the MoA classification system reflects the current state of knowledge and creates a harmonized system more globally relevant.

2 What was changed?

Transition from alphabetical to numerical mode of action codes

Mode of Action Example:

Inhibition of ALS

B → 2

Legacy HRAC Code → New HRAC Code

New MoA Label Icon

For guidance on how to label mixtures or any other questions, visit **hracglobal.com**

Additional examples of common MoAs

Mode of Action	Legacy HRAC	New HRAC
Inhibition of ACCase	A	1
Auxin mimics	O	4
Inhibition of EPSP synthase	G	9
Inhibition of glutamine synthetase	H	10
Inhibition of PPO	E	14
Inhibition of VLCFAs	K3	15
Inhibition of HPPD	F2	27

Other important changes

- Addition of **5 new or reclassified MoAs**
- Rationalization of **chemical family names**
- Addition of **15 new active ingredients**

3 Who proposed the changes?

HRAC appointed a Working Group of herbicide technical experts from CropLife International member companies to prepare the update. Additionally, input was incorporated from regional HRAC organizations, CropLife Australia, as well as weed science societies such as the WSSA to ensure global consensus going forward.

CropLife

4 Why change from letters to numbers?

HRAC believes that a numerical code system is more globally relevant and sustainable compared to an alphabetic code based on English/Latin letters. Another concern about the English alphabet is that there are only 26 letters. Today there are 26 recognized MoAs.

Over the next 10 years we anticipate up to 4 new modes of action to be commercialized, which will exceed the 26-letter maximum.

26 LETTERS IN THE ENGLISH **ALPHABET**

MODES OF **ACTION** RECOGNIZED **26**

4 NEW MODES of ACTION **EXPECTED** OVER THE NEXT **TEN YEARS**

Moving to numbers means there will be a common code shared globally.

5 When will the changes take place?

Countries currently using the legacy system will require a long transition period including education and communication before a change to numbers can be implemented. During this period, HRAC will continue to support legacy alphabetic codes. We hope to fully implement the numerical code by the end of 2023.

2023

Questions?

For more information about the Herbicide mode of action changes, visit the HRAC website

hracglobal.com

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Inhibition of HPPD	F2	**27**

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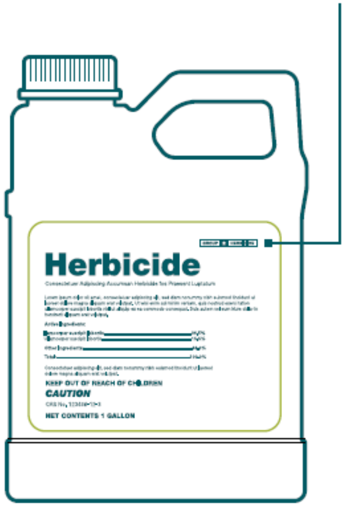
New MoA Label Icon

GROUP 2 HERBICIDE

GROUP 2(B)* HERBICIDE



*Some may choose to include both legacy and new codes.

For guidance on how to label mixtures or any other questions, visit **hracglobal.com**

HERBICIDE RESISTANCE ACTION COMMITTEE

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CropLife INTERNATIONAL

HERBICIDE RESISTANCE ACTION COMMITTEE

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HERBICIDE RESISTANCE ACTION COMMITTEE

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Questions?

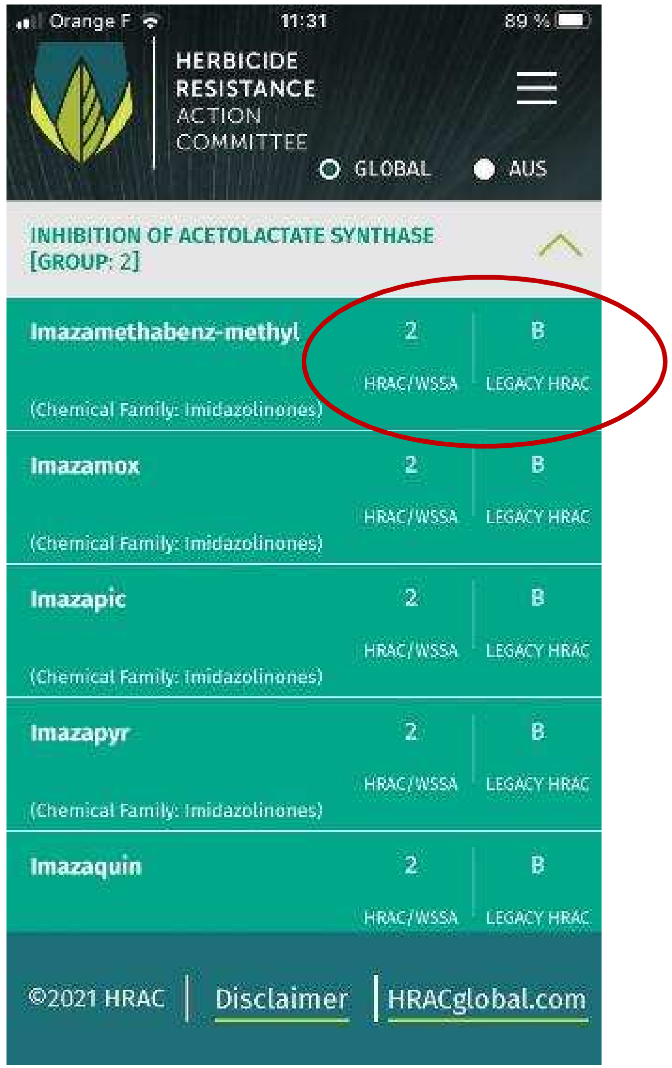
For more information about the Herbicide mode of action changes, visit the HRAC website

→ **hracglobal.com**

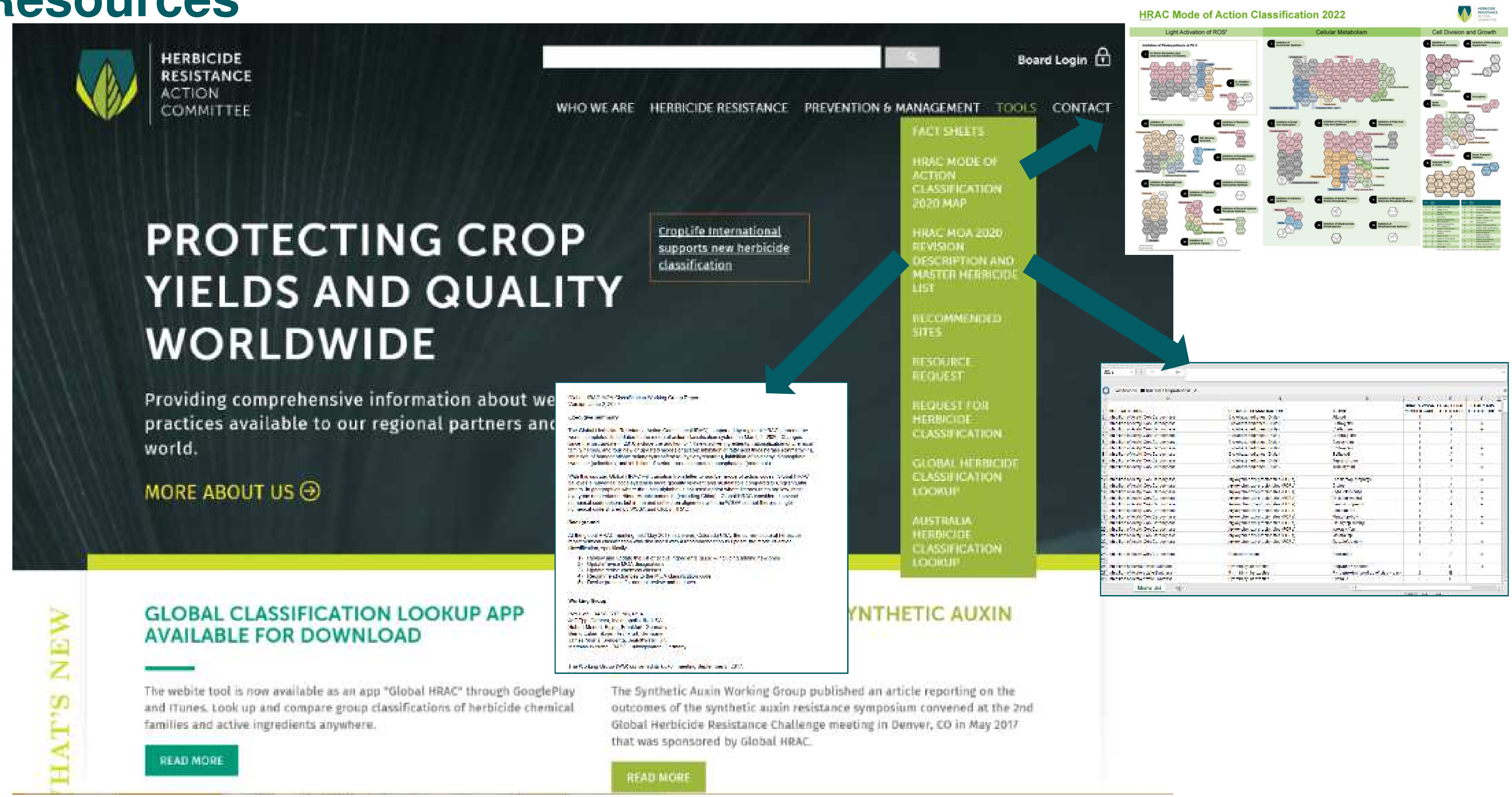
Global HRAC App

- Please download it and advertise for our App within your organisations !
- It has been updated with the new classification system

- Use App as communication tool.

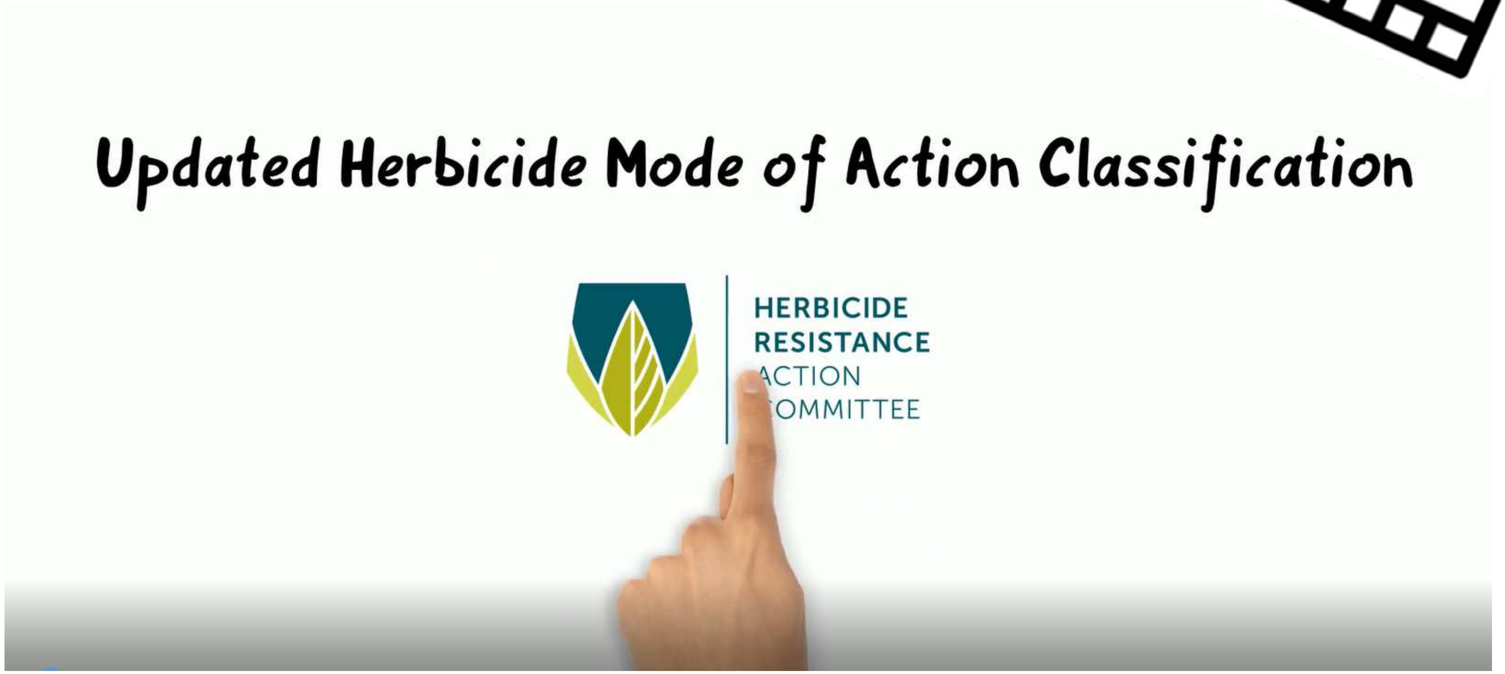


Resources

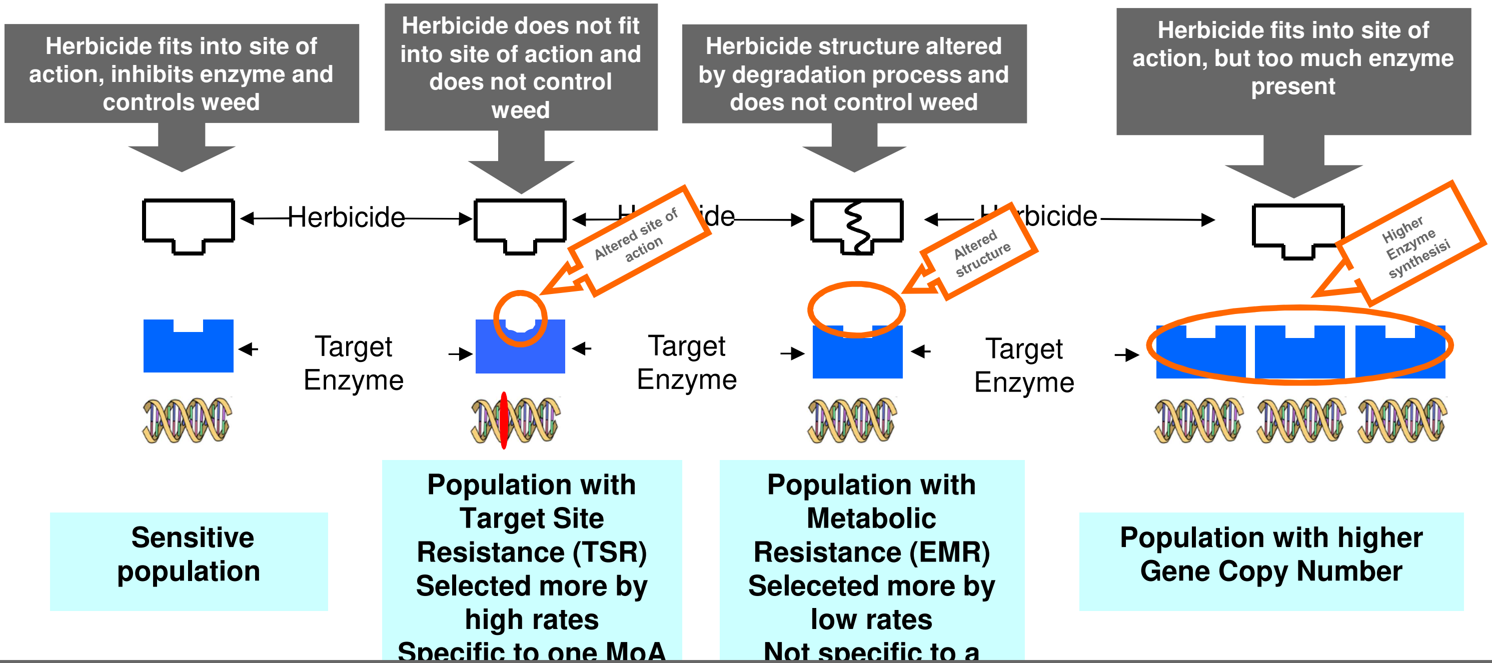

HERBICIDE RESISTANCE ACTION COMMITTEE
Board Login
WHO WE ARE
HERBICIDE RESISTANCE
PREVENTION & MANAGEMENT
TOOLS
CONTACT
FACT SHEETS
HRAC MODE OF ACTION CLASSIFICATION 2020 MAP
HRAC MOA 2020 REVISION DESCRIPTION AND MASTER HERBICIDE LIST
RECOMMENDED SITES
RESOURCE REQUEST
REQUEST FOR HERBICIDE CLASSIFICATION
GLOBAL HERBICIDE CLASSIFICATION LOOKUP
AUSTRALIA HERBICIDE CLASSIFICATION LOOKUP
PROTECTING CROP YIELDS AND QUALITY WORLDWIDE
CropLife International supports new herbicide classification
Providing comprehensive information about we
practices available to our regional partners and
world.
MORE ABOUT US
WHAT'S NEW
GLOBAL CLASSIFICATION LOOKUP APP AVAILABLE FOR DOWNLOAD
The webite tool is now available as an app "Global HRAC" through GooglePlay and iTunes. Look up and compare group classifications of herbicide chemical families and active ingredients anywhere.
READ MORE
YNTHETIC AUXIN
The Synthetic Auxin Working Group published an article reporting on the outcomes of the synthetic auxin resistance symposium convened at the 2nd Global Herbicide Resistance Challenge meeting in Denver, CO in May 2017 that was sponsored by Global HRAC.
READ MORE
HRAC Mode of Action Classification 2022
Light Activation of ROS
Cellular Metabolism
Cell Division and Growth

Coming soon: 3’ video

https://hracglobal.com/files/simpleshow_CropLife_Mode_of_Action_Alteration_220224.mp4



Mechanisms Involved in Herbicide Resistance



Other mechanisms such as uptake, translocation, sequestration are even more difficult to study. Case by case approach.

Different mechanisms imply to develop several diagnostic tests to characterize herbicide resistance. One plant can show several herbicide resistance mechanisms