The Content of the Glyphosate AIR5 Renewal Dossier

A presentation by the Glyphosate Renewal Group (GRG)

June/July 2021

Glyphosate Renewal Group

Agenda

1) Introduction to glyphosate
2) Glyphosate Renewal Group (GRG) and transparency initiative
3) Regulatory process and characteristics of this unique dossier
4) Representative uses in the renewal dossier
5) Environmental Monitoring Data & Water Treatment
6) Biodiversity & Conservation Agriculture
7) Toxicology
8) Public literature
9) Societal and agronomic impact of losing glyphosate

Introduction to glyphosate

Glyphosate Renewal Group

Weed control is critical for sustainable agriculture

Glyphosate Renewal Group

Glyphosate in brief

WHY

WHAT

GLYPHOSATE BASED FORMULATED PRODUCTS

HOW

Glyphosate is an essential component of the available toolbox to control weeds

WHY

Weeds are the biggest factor affecting the growing of crops.

Farmers need multiple tools to control them.

WHAT

A very effective non-selective herbicide.

One of the world's most important tools for managing problematic weeds.

HOW

Sprayed directly on weeds & grasses.

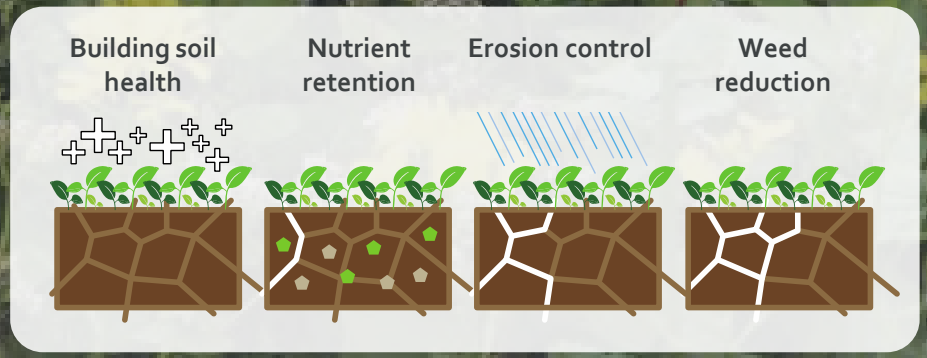
Taken up by green leaves, allowing targeted application.

Glyphosate Renewal Group

Why Glyphosate?

Glyphosate supports farmers in providing food to meet the needs of a growing population worldwide

Growing crops › Making farming more sustainable › Value beyond the farm



SAFE & EFFICIENT

A **safe and efficient** component of Integrated Weed Management. Helps farmers secure best harvests from available agricultural fields.

COVER CROPS / NO-TILL

Enables greater **biodiversity.** Helps create wildlife habitats.

Preserves **soil health,** reduces fuel inputs and thereby greenhouse gas emissions.

SAFETY OF INFRASTRUCTURE

Key to ensuring the safety of infrastructure, like railways, and controlling invasive weeds in natural areas.

GRG and our transparency initiative

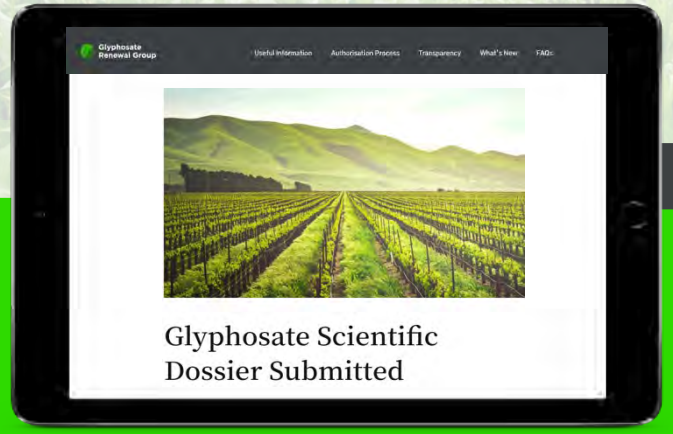
Glyphosate Renewal Group

Glyphosate Renewal Group (GRG)

The Glyphosate Renewal Group (GRG) is a collection of companies seeking the renewal of the EU authorisation of the active substance glyphosate in 2022.

The Group's member companies joined their resources to prepare a single dossier, published in 2020, with scientific studies and information on the safety of glyphosate.

www.glyphosate.eu/transparency/scientific-dossier/



Current members of the GRG

AFRASA · Barclay CROP PROTECTION · BAYER · Ciech Sarzyna · SINON · Nufarm · Albaugh Your Alternative℠ · syngenta Crop Protection

JUNE 2020

This dossier is submitted to the evaluating Member States as part of the EU regulatory procedure to continue the authorization of glyphosate and glyphosate-containing products on the EU market.

Glyphosate Renewal Group

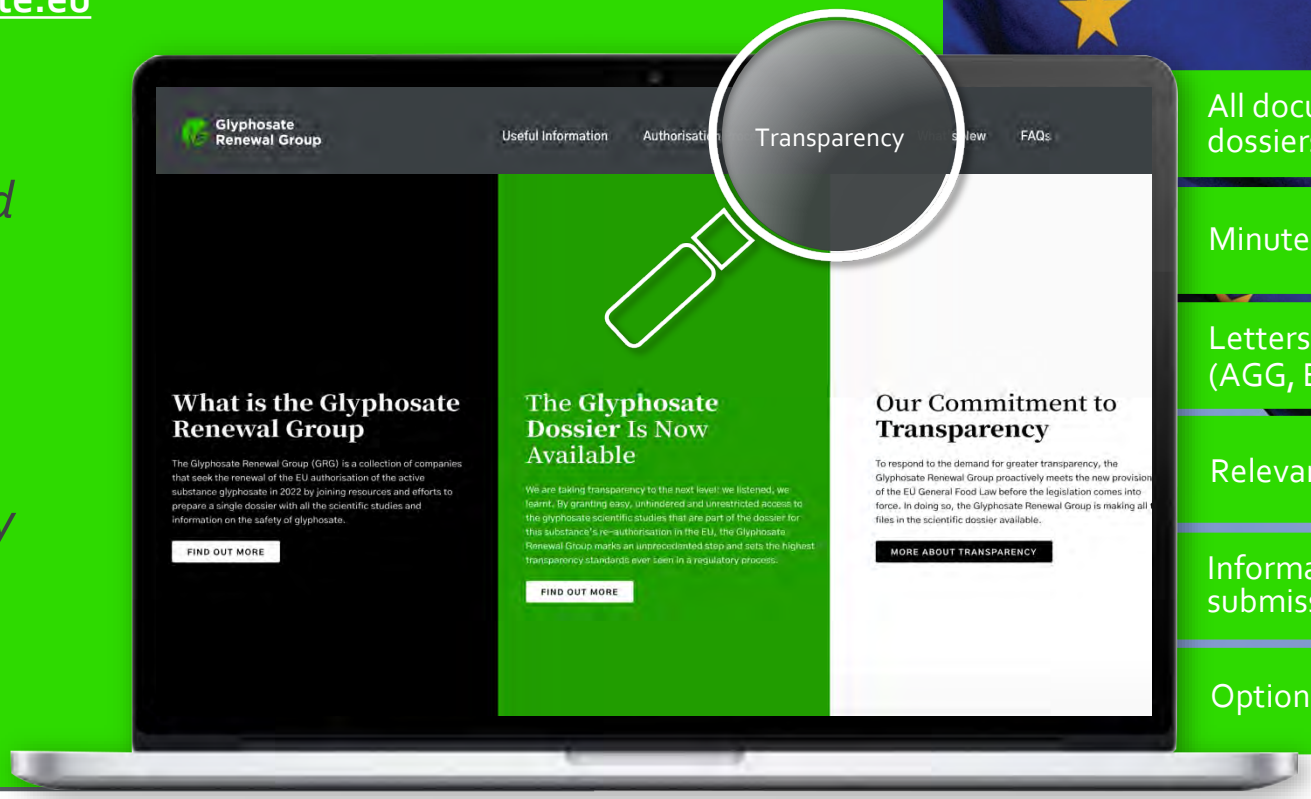
Look for yourself: the 2020 dossier

GRG committed to unprecedented transparency

For 1st time, anyone can access scientific data and beyond on…

www.glyphosate.eu

This increased transparency and dialogue help foster public trust in our regulatory system



- All documents and **study reports** in submitted dossiers (except personal and confidential data)
- Minutes / presentations of discussions with **AGG**
- Letters **exchanged with authorities** (AGG, EFSA, DG SANTE)
- Relevant public **scientific literature** in dossier
- Information for last **(2012)** and current **(2020)** submissions
- Option to **submit comments and questions**

Glyphosate Renewal Group

ECHA: European Chemicals Agency. AGG: Assessment Group on Glyphosate. DG SANTE: Commission department responsible for EU policy on food safety and health.

GRG recognised as another trusted source
Visit the GRG website here

DG SANTE
Glyphosate | Food Safety (europa.eu)

AGG
Assessment Group | Food Safety (europa.eu)

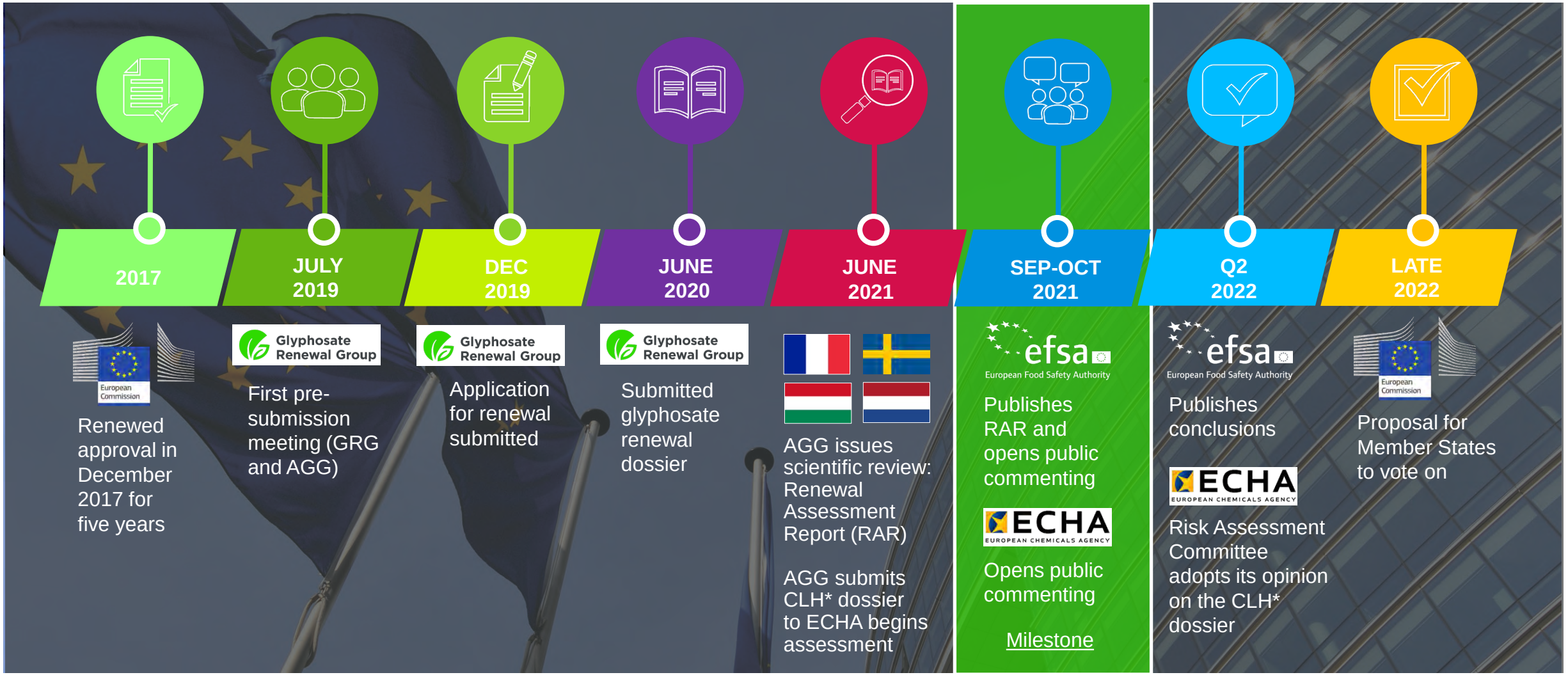
EFSA
Scientific topic: Glyphosate | European Food Safety Authority (europa.eu)

ECHA
Glyphosate - ECHA (europa.eu)

Regulatory process and characteristics of this unique dossier

Glyphosate Renewal Group

The regulatory process for this dossier: a summary



* Harmonised Classification and Labelling

The most extensive and comprehensive dossier ever

Containing 2-4 times more information than a typical renewal dossier

Scientific studies

~1,500

Public literature review

>12,000

New data requirements

~100 *new studies in total*

180,000

Overall pages

>150

Individuals involved

23

Representative uses to cover agriculture and non-agriculture uses

4

Evaluating Member States

Further items addressed 2020

The new dossier provides content that goes far beyond what is required

- Comprehensive water & environmental **monitoring report** across EU Member States
- Evaluation & mitigation measure proposals to preserve **biodiversity**
- Benefits of glyphosate for **conservation agriculture** & **integrated weed management**
- **Societal & agronomic benefits** of glyphosate

*Look for yourself on **www.glyphosate.eu***

AGG's Procedure and Outcome of dRAR Overview Document

- On 15 June 2021, the AGG dispatched the dRAR / CLH dossier to EFSA / ECHA
- AGG made an overview document about procedure & outcome available on their website
- **Overall conclusion of the assessment by AGG:**
- Based on the current assessment, AGG considers that **glyphosate does meet the approval criteria** set in Reg. (EC) No 1107/2009
- AGG considers that **authorisation in at least one Member State is expected to be possible** for at least one plant protection product containing the active substance for at least one representative use

AGG's Procedure and Outcome of dRAR Overview Document

Main findings

- **Human Health:**
  - **No new classification proposed,** existing one proposed to maintain ("*causes serious eye damage*")
  - AGG concludes that **glyphosate meets the approval criteria for human health** as laid down in Reg. (EC) No 1107/2009 and its amendments
- **Consumer safety:**
  - an application to set an **MRL in honey** is included
  - **No chronic or acute consumer risk is expected** from treatment of crops with glyphosate according to the representative uses for the current renewal process

AGG's Procedure and Outcome of dRAR Overview Document

- **Endocrine disruption:**
  - AGG proposes that **ED criteria are not met,** as laid down in Reg. (EC) No 1107/2009 as amended by Reg. (EU) No 2018/605
- **Fate and behaviour in the environment:**
  - The results from **public monitoring programs** were also taken into account
- **Ecotoxicology:**
  - Based on available ecotoxicological information for glyphosate the current classification "*Toxic to aquatic life with long lasting effects*" should be retained
  - GRG addressed **impact of use of glyphosate on biodiversity via indirect effects and trophic interaction,** taking into account the methodology of definition of Specific Protection Goals
  - AGG proposes that impacts on biodiversity are further considered during peer review process, and if relevant, by risk managers. When plant protection products are assessed by **national competent authorities, specific mitigating measures can be laid down to mitigate the effect of glyphosate on biodiversity**.

Representative uses in the renewal dossier

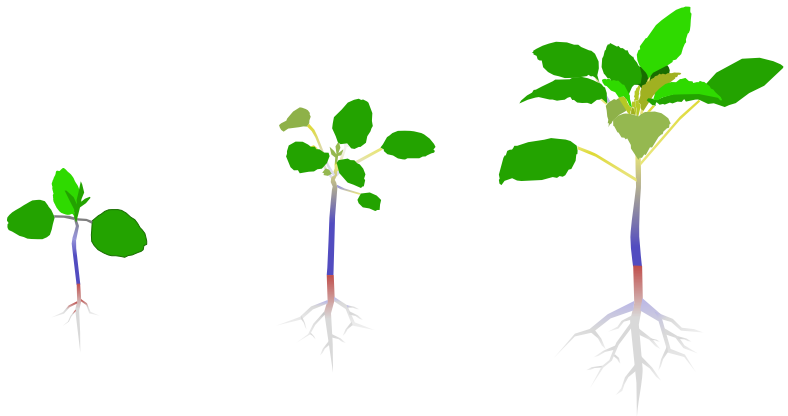
Glyphosate Renewal Group

Flexible application during the crop cycle

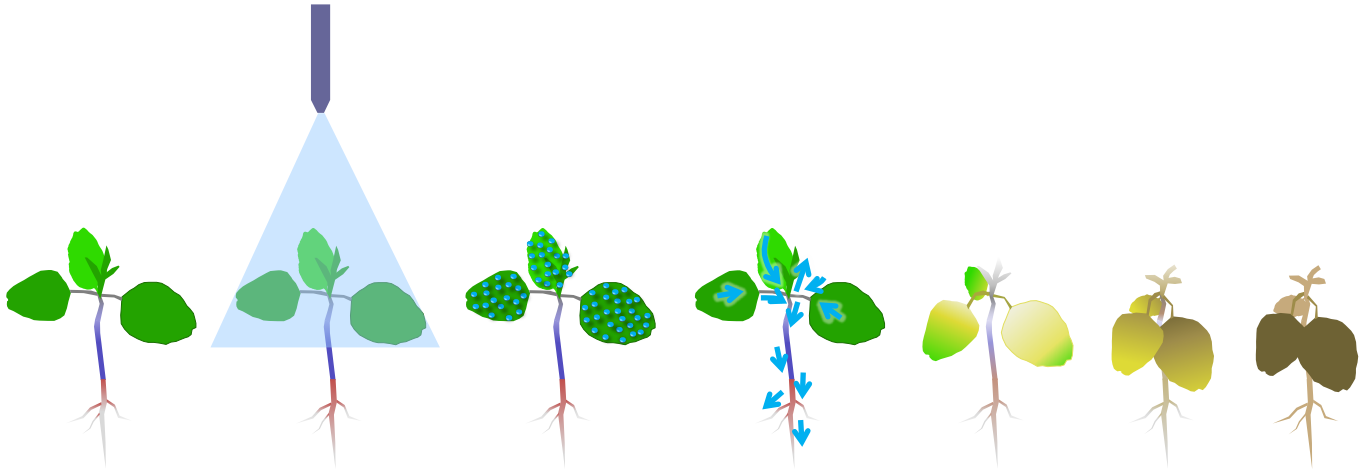
Farmers need a varied toolbox of products and practices to keep weeds off balance. Glyphosate is a key part of such Integrated Weed Management (IWM).

Weeds after glyphosate treatment

UNTREATED



TREATED



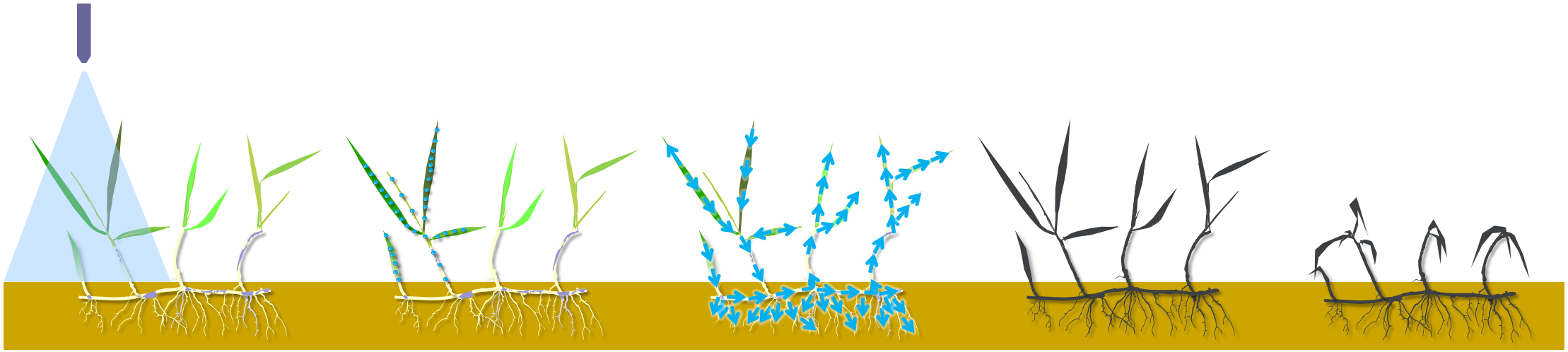
Herbicides containing glyphosate are applied at various stages of the cropping cycle to manage dominant weeds in a wide range of arable crops.

Glyphosate is absorbed through plant leaves and carried by the sap stream into the plant roots, where it stops a specific enzyme pathway (the shikimic acid pathway), preventing weeds from absorbing nutrients from the soil.

Flexible application during the crop cycle

Farmers need a varied toolbox of products and practices to keep weeds off balance. Glyphosate is a key part of such Integrated Weed Management (IWM).

Rhizomatous weeds after glyphosate treatment



23 representative uses in renewal dossier

1/2

Scenario	Situation	Kg ai/ha	Applic.	Max/year
1. Before new Row Crop Pre Sowing, Pre Planting (Root & tuber vegetables, Bulb vegetables, Fruiting vegetables, Brassica, Leafy vegetables, Stem vegetables, Sugar beet)	All weeds >BBCH13 All weeds BBCH13-21 Annuals	1.44 1.08 0.72	1X 1X 1X	1.44 1.08 0.72
2. Stubbles Post Harvest, Pre Planting (Root & tuber vegetables, Bulb vegetables, Fruiting vegetables, Brassica, Leafy vegetables, Stem vegetables, Sugar beet)	All weeds All weeds Annuals	1.08-1.44 0.72-1.08 0.72	1-2X 1-3X 1-3X	2.16 2.16 2.16
3. Cereal volunteers (Root & tuber vegetables, Bulb vegetables, Fruiting vegetables, Brassica, Leafy vegetables, Stem vegetables, Sugar beet)	Cereal volunteers	0.54 0.54	1X 1X/3 years	0.54 0.54/3 years
4. Orchards Post Emergence (stone and pome fruits, kiwi, tree nuts, banana, table olives)	Band or Spot trt (=max 50%)	1.08-1.44 0.72-1.08 0.72	1-2X 1-3X 1-3X	2.88 2.88 2.16
5. Vines Post Emergence (table and wine grape, leaves not intended for human consumption)	Band or Spot trt (=max 50%)	1.08-1.44 0.72-1.08 0.72	1-2X 1-3X 1-3X	2.88 2.88 2.16

23 representative uses in renewal dossier

Scenario	Situation	Kg ai/ha	Applic.	Max/year
6. Vegetables Post Emergence (Root and tuber vegetables, Bulb vegetables, Fruiting vegetables, Legume vegetables, Leafy vegetables)	Inter-row (=max 50%)	1.08 0.72	1X 1X	1.08 0.72
7. Railroad tracks	Non-ag	1.8 1.8	2X 1X	3.6 1.8
8. Invasive Giant hogweed	Spot trt	1.8	1X	1.8
9. Invasive Japanese knotweed	Spot trt	1.8	1X	1.8
10. Couch grass (Root & tuber vegetables, Bulb vegetables, Fruiting vegetables, Brassica, Leafy vegetables, Stem vegetables, Sugar beet)	Couch grass Spot trt (=max 20%)	1.08 0.72 0.72	1X 1X 1X/3 years	1.08 0.72 0.72/3 years

Glyphosate is a "once in a century herbicide"

Used in hundreds of crops and providing economic benefits outside of agriculture

Pre-planting

Railways

Post-harvest

Orchards

Vines

Groundcovers in permanent crops

Glyphosate Renewal Group

Environmental Monitoring Data & Water Treatment

Environmental monitoring across EU Member States

The GRG initiated a collection & assessment of public monitoring data for water (groundwater, surface water, drinking water), soil, sediment and air

The GRG sponsored 2 new applicant studies designed to be a comprehensive overview at EU level, covering various spatial extents & temporal scales

Safe use demonstrated in the environment in Europe following use of Glyphosate products according to the label;
No risk posed to ecosystems or to human health via drinking water;
Where local issues are detected: targeted elucidation & stewardship measures

Public monitoring data demonstrate compliance with the regulatory framework (Regulation 1107/2009/EC, Water Framework Directive, Groundwater Directive, Priority Substances Directive, Drinking Water Directive)

There is no risk posed to human health via drinking water

Glyphosate Renewal Group

Environmental monitoring – Results

- *Rates of compliance* with key RACs and thresholds for both GLY and AMPA are high
- Exploration of exceedances: mostly sporadic and non-systematic both spatially and temporally, likely false positives
- For GW <0.1% of exceedances are consecutive

Compartment	Dataset Size	GLY		AMPA	
		RAC[1] (µg/L)	Compliance (%)	RAC[1]/ Threshold (µg/L)	Compliance (%)
Soil	Small	94.6 mg/kg	100	26.4 mg/kg	100
Groundwater	Very Large	0.1	99.38	10.0[2]	99.998
Surface Water	Very Large	400	99.994	1200	99.999
Transitional Water	Very Small	400	100	1200	100
Drinking Water	Large/Very Large	0.1	99.84	0.1[3] 10.0[2]	99.78 100
Sediment	Small/Medium	NA	-	NA	-
Air	Very Small	NA	-	NA	-

NA - Not applicable
[1] - Regulatory acceptable concentration
[2] - RAC for non-relevant metabolite
[3] - Threshold value chosen to allow statistical comparisons only

Glyphosate Renewal Group

Biodiversity & conservation agriculture

Evaluation and mitigation measure proposals to preserve biodiversity

The GRG has proposed specific avenues to increase the contribution of glyphosate to biodiversity in Europe, including:

The GRG has proposed significant use rate reductions in Europe…

up to 50%

- Use and adherence of glyphosate-based products as part of Integrated Weed Management (IWM) programs
- A commitment to improving the use of glyphosate by including clear language and instructions on product labels consistently across Member States.
- Proposal to connect a specific biodiversity condition to the use of glyphosate-based products

The Last Annex I Renewal December 2017

L 333/10 EN Official Journal of the European Union 15.12.2017

COMMISSION IMPLEMENTING REGULATION (EU) 2017/2324

of 12 December 2017

renewing the approval of the active substance glyphosate in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011

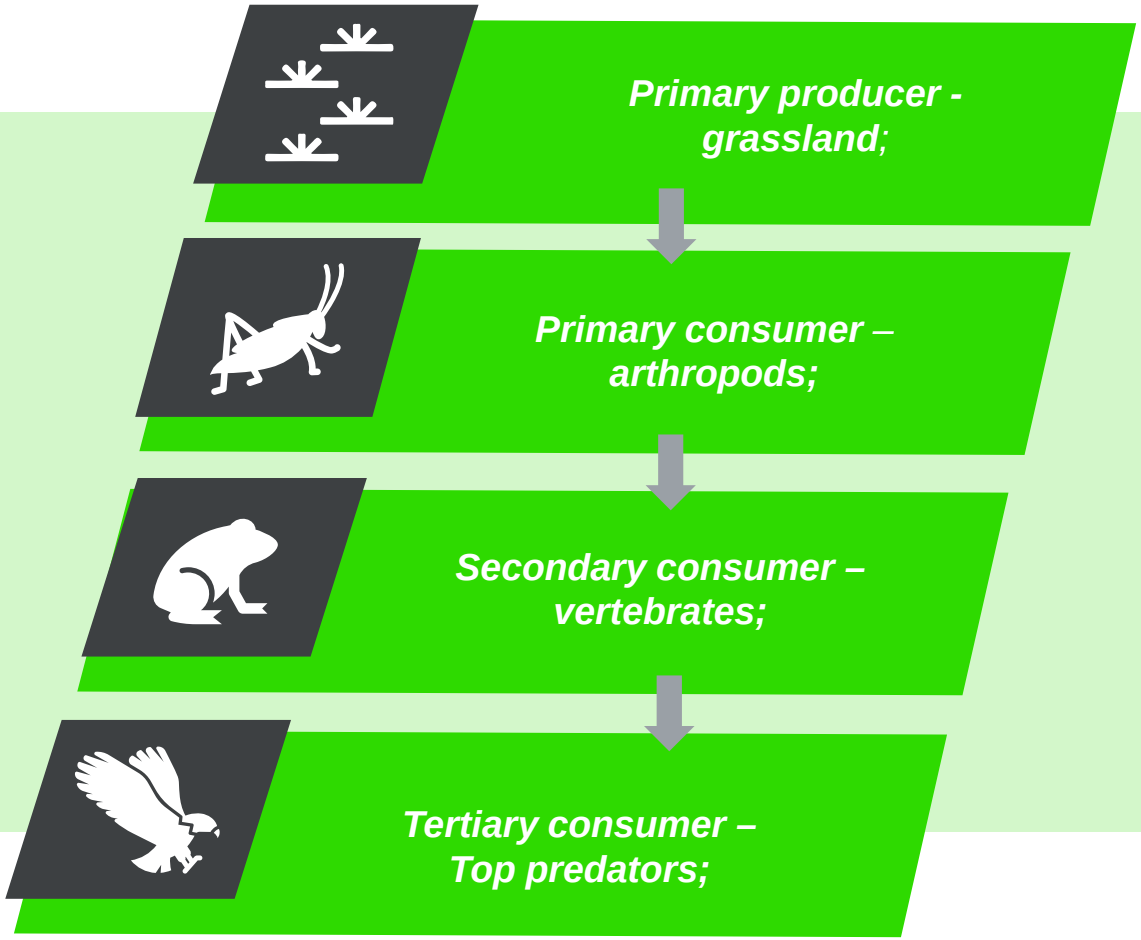
Member States shall pay particular attention to:

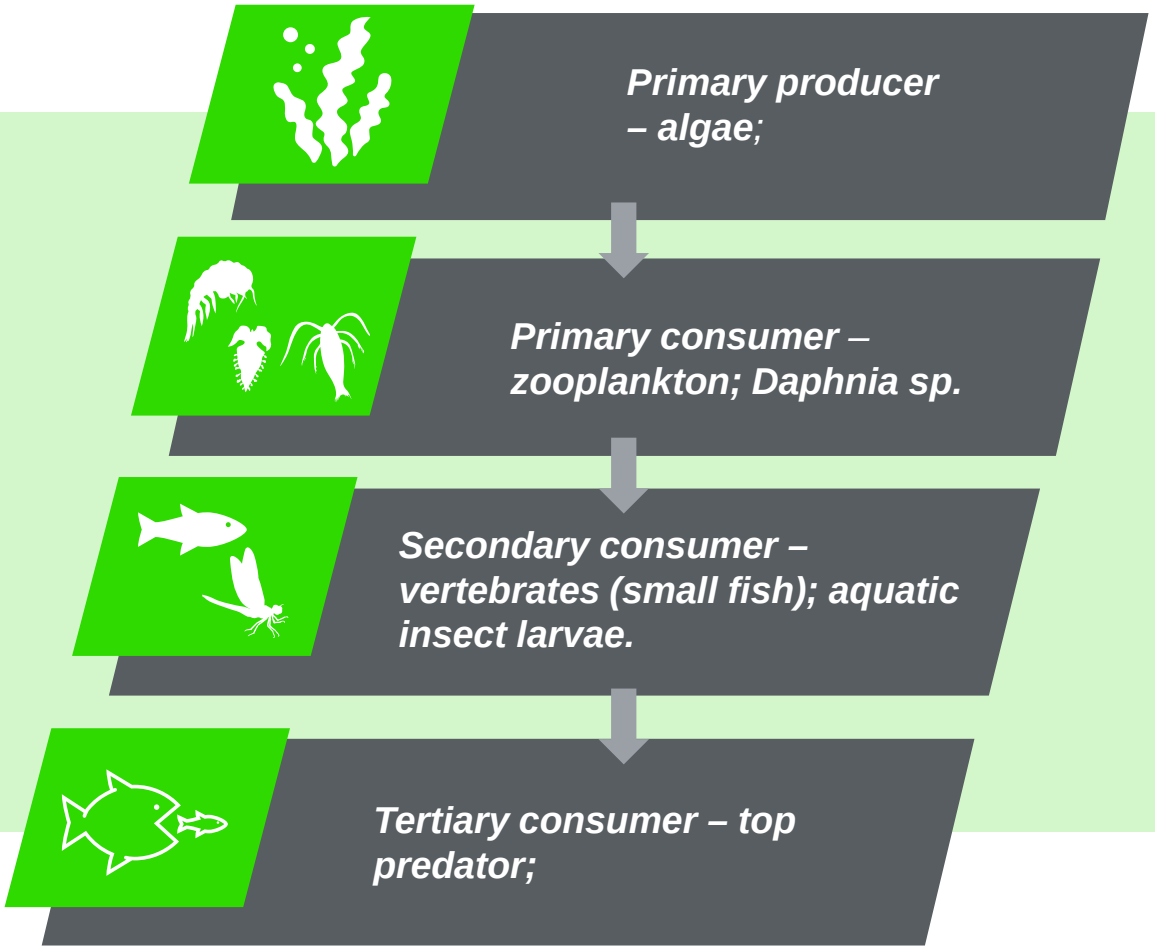
- the risk to terrestrial vertebrates and non-target terrestrial plants

- the risk to diversity and abundance of non-target terrestrial arthropods and vertebrates via trophic interactions

- the potential for impacts through trophic interaction along the food chain

Trophic Interactions within Food Chains





Direct effects leads to indirect effects on food chain;
- Impact on arthropods may impact toad and raptor populations.
- Impact on Daphnia sp. may impact fish populations.

Glyphosate biodiversity assessment

Key considerations

- Proposed use patterns - reductions (up to 50%) in rates relative to the last renewal (2017)
- Acceptable direct effects risk assessment for birds, aq. organisms, non -target arthropods, bees, soil organisms and non -target terrestrial plants (with mitigation measures)
- Glyphosate: Rarely measured in environment at levels of regulatory concern
  - 99.99% of the glyphosate surface water monitoring detects < Regulatory Acceptable Concentration (RAC) (Hughes, 2020)
  - Soil levels below < RAC
  - Glyphosate detected at a low frequency and very low levels in honey
- Challenges ;
  - Small mammal chronic risk assessment – refinement needed (residues on food items)
  - Indirect effects assessment
    - In-field weed control → bird indirect effects through trophic interactions - habitat loss; bird & mammal dietary items (arthropods / herbs), cover for ground nesting birds)

Biodiversity: General Protection Goal in Regulation (EC) No 1107/2009

- **Biodiversity** mentioned twice in Regulation (EC) No 1107/2009;
  - Regulation (EC) No. 1107/2009 Article 4 (3e): "*impacts on biodiversity and the ecosystem must be avoided*"
  - **Defined**: 'Variability among organisms and ecological complexes of which they are part..'

However - No specific and comprehensive guidance for biodiversity assessment

Problem - Current EU level RA guidance does not provide methods to assess **indirect effects** across all taxa groups.

Complexity / multiple elements influence biodiversity at landscape level

- Minimizing impact of **indirect effects** to birds through trophic interactions should be considered as a **risk management issue at MS level** to address specific species concerns

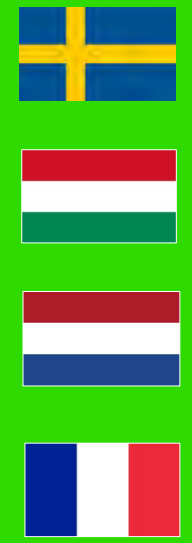
Pre-submission meeting feedback from AGG

- The AGG indicated that the biodiversity assessment should provide;

A comprehensive evaluation of glyphosate and Its' impact on biodiversity

- proposal(s) for compensatory / mitigation measures that protect biodiversity

- Assessment should consider:
  - Existing non-target organism risk assessments & guidance
  - **In-field and off-field** habitats
  - **Relevant peer-reviewed literature**
  - **Monitoring data** considered within the context of the biodiversity assessment
  - **Environmental mixtures -** glyphosate monitoring data / product data
  - **Ecosystems Services Approach -** recommended by EFSA to inform development of Specific Protection Goals (EFSA, 2016)



Specific Protection Goals

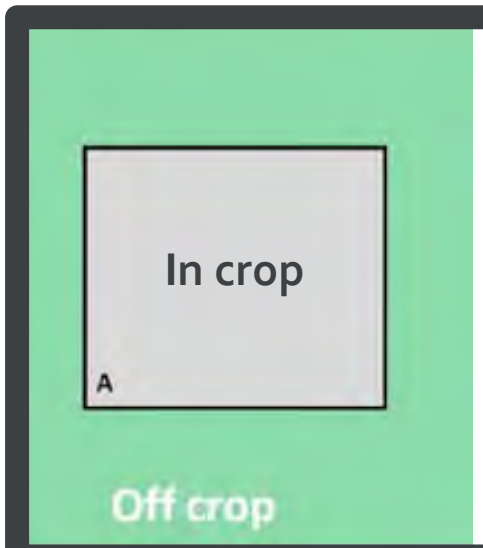
Protection goals

Problem formulation

Risk assessment

Risk management

- Ecological assessment requires **Specific Protection Goals (SPGs)** specifying
  - what to protect, where to protect,
  - level of protection,
  - over what time period (EFSA, 2010)



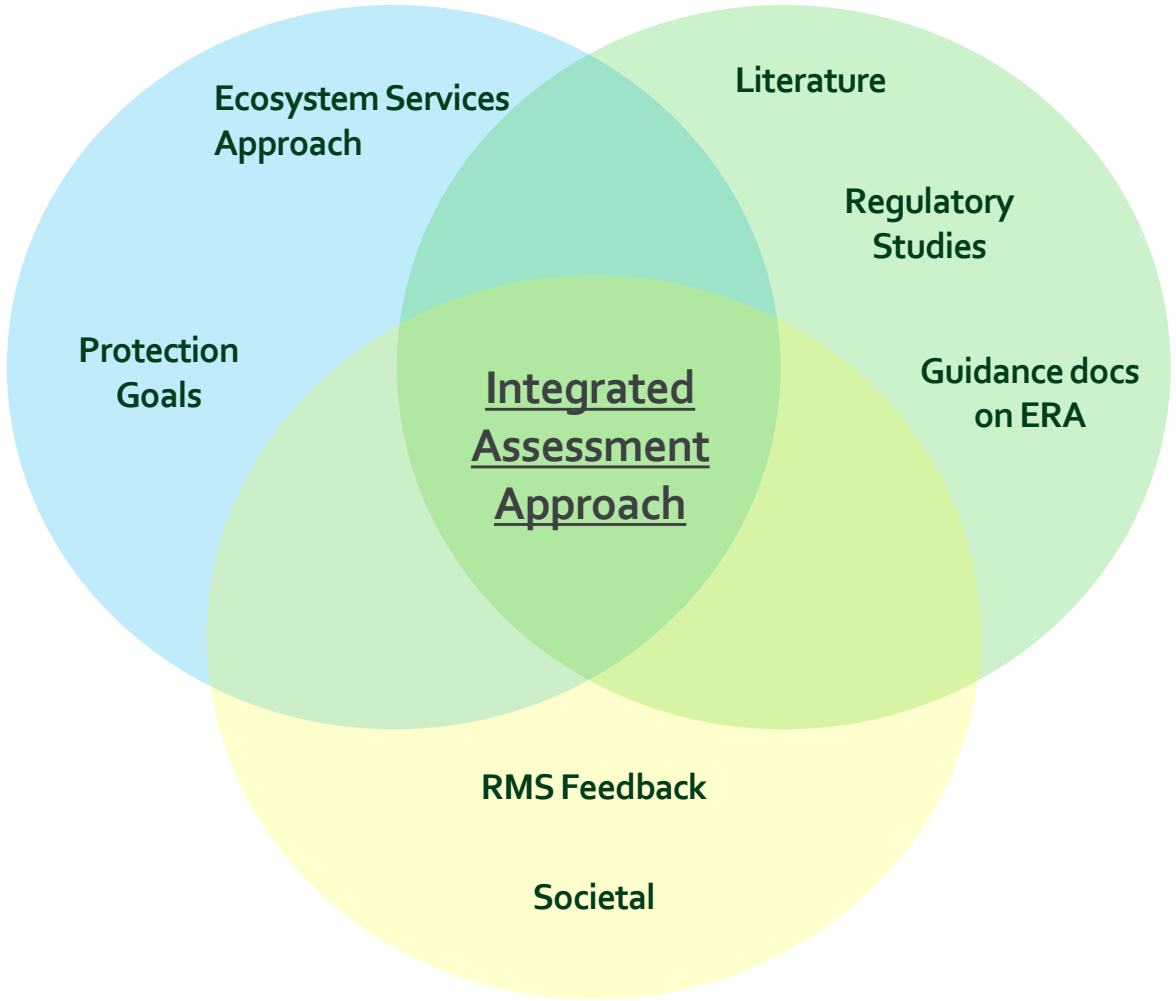
- For some taxa there are justifiably different protection goals for **in-crop** and **off-crop** (e.g. trade-off)

Glyphosate Biodiversity Assessment → our Approach

Setting precedence for risk assessment and impact mitigation on biodiversity

Step 1 NEW	Step 2	Step 3	Step 4 NEW
Define • **Specific Protection Goals - *SPGs** - each ecotoxicological taxa group area (EFSA 2016)	**Consider** • **Relevant studies &** • **Public literature** - that address **direct** & **indirect effects**	**Evaluate** • **Have SPGs been met ?** - includes use of **standard mitigation measures**	**Propose** • **Are non-standard mitigation options required ?** - are these protective of **indirect effects; risk Manager decision driven by local MS need**

Considerations Taken for the Biodiversity Assessment



- **For each taxonomic group, presents;**
  - Specific Protection Goals (SPGs)
  - Assessment Endpoints
  - Measurement Endpoints / study types
  - Provides **rationale why SPGs are protective of biodiversity** or
  - Informs **mitigations / risk management options (Step 4 if necessary)**

The relationship between protection goals, assessment endpoints and measurement endpoints. Example: bees oral & contact exposure

Specific Protection Goals	Assessment Endpoints	Measurement Endpoints	Tiered Study Types
No significant effect on colony survival and development and hive products **Pollination services**	Population size and stability	Adult survival and larval emergence	Adult honeybee acute contact & oral (LC_{50}) Adult Bumble bee acute (LC_{50}) Adult solitary bee acute (LC_{50}) Adult chronic (NOAEC) Larval emergence (NOAEC) Brood study (NOAEC)
Bee biodiversity	Species richness (functional composition) and abundance	Adult survival and larval emergence	Adult honeybee acute contact & oral (LC_{50}) Adult Bumble bee acute (LC_{50}) Adult solitary bee acute (LC_{50}) Adult chronic (NOAEC) Larval emergence (NOAEC) Brood study (NOAEC)

Glyphosate Biodiversity Assessment → Conclusions

- **Low likelihood of indirect effects to biodiversity**
  for aquatic, soil (microbes & macro-organisms, worms, soil mites) and bee areas
- **Cannot exclude indirect effects** from **in-crop weed control** on arthropods & birds

⇒**Requirement of additional mitigation measures to be decided by MS risk managers**
based on local conditions

⇒**Options for additional mitigation measures proposed** (based on MAgPIE recommendations (2017))

- **Non-spray in-crop area** in part of field
- **Multi-functional field margins** (with e.g. biodiversity enhancing seed mixtures)
- **Land sparing**: Compensation areas as biodiversity refuge

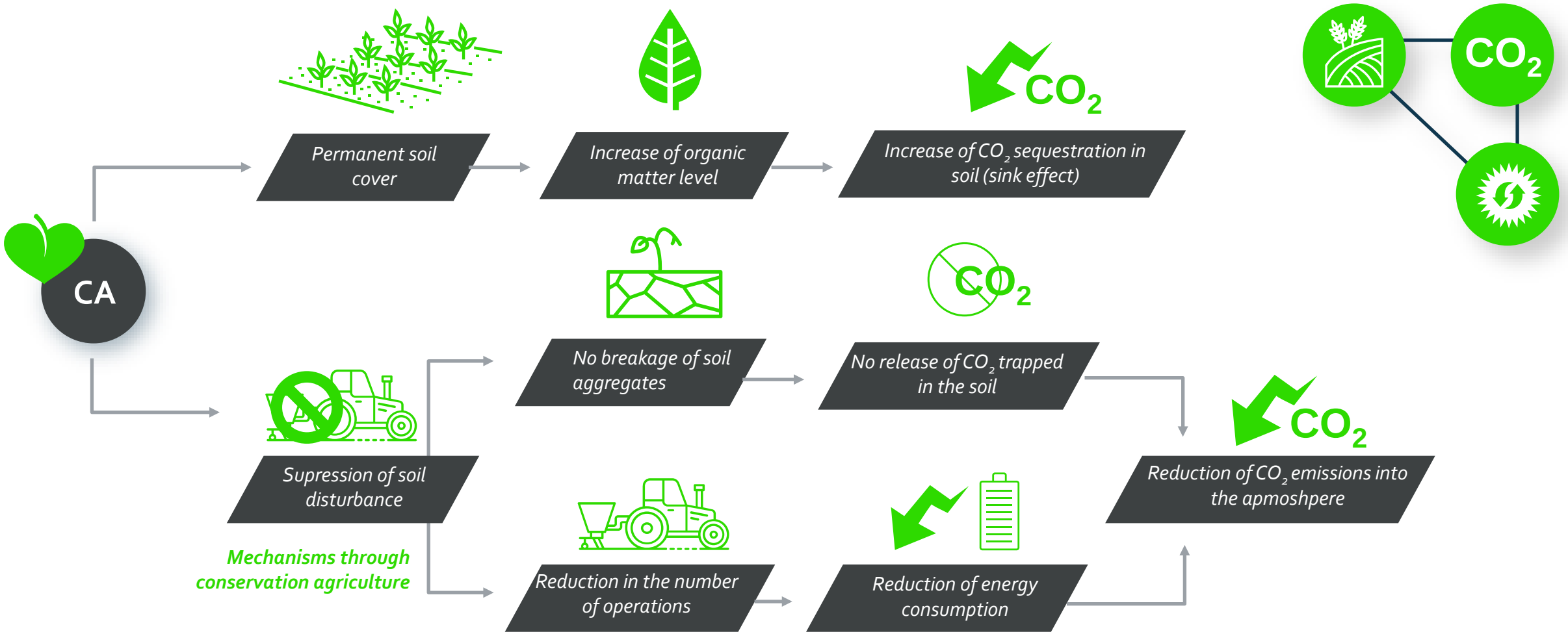
Benefits of glyphosate for conservation agriculture and integrated weed management (IWM)

Glyphosate-based products are an essential tool in IWM, due to its high efficacy and unique mode of action, and the fact that it is translocated throughout the plant, including down to roots, rhizomes and tubers below ground.

A diversified use of the toolbox of chemical and non-chemical measures supports effective weed resistance management and the reduction of the weed seed bank in soil.

The main alternative to a glyphosate-based weed control strategy would be increased use of cultivation (ploughing) which has been shown to have negative impacts on biodiversity, soil health and water quality.

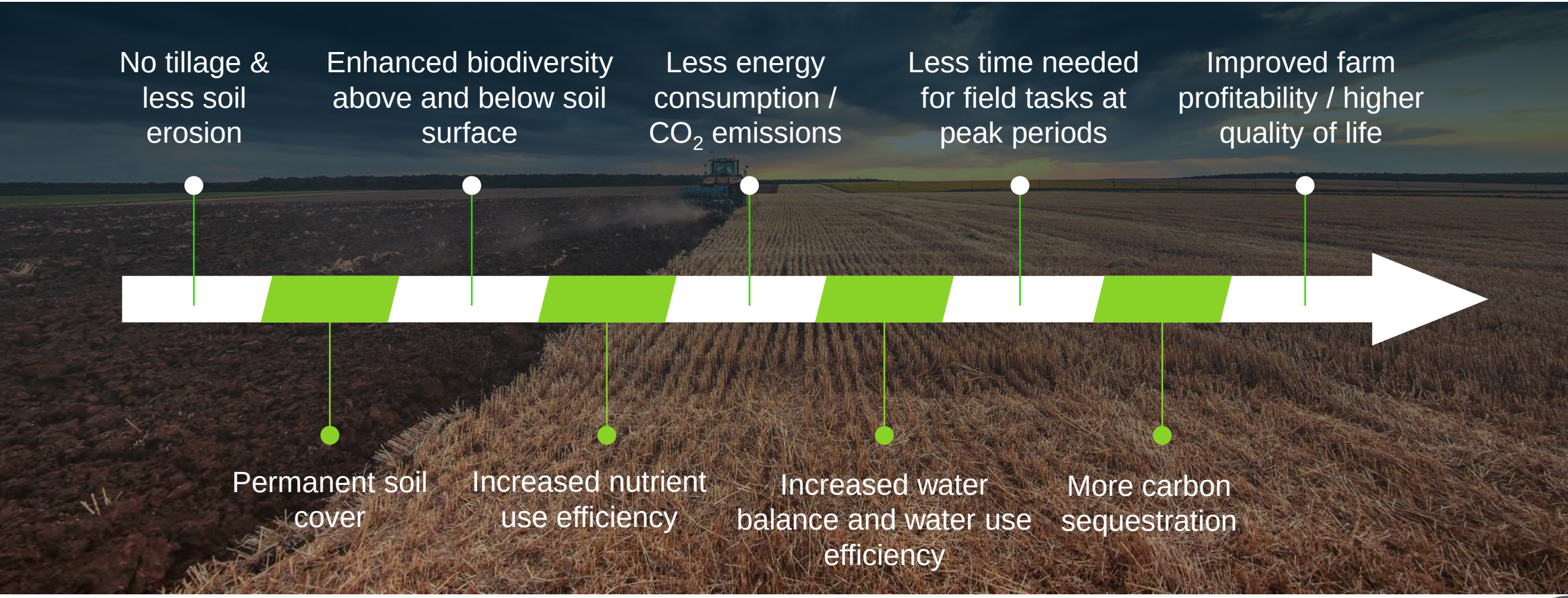
Climate change mitigation through Conservation Agriculture



González-Sánchez et al., 2017

Conservation Agriculture

One of the greatest benefits of Glyphosate: *the ability to foster healthier soils by reducing the need for tillage (plowing)*



Runoff and Erosion control

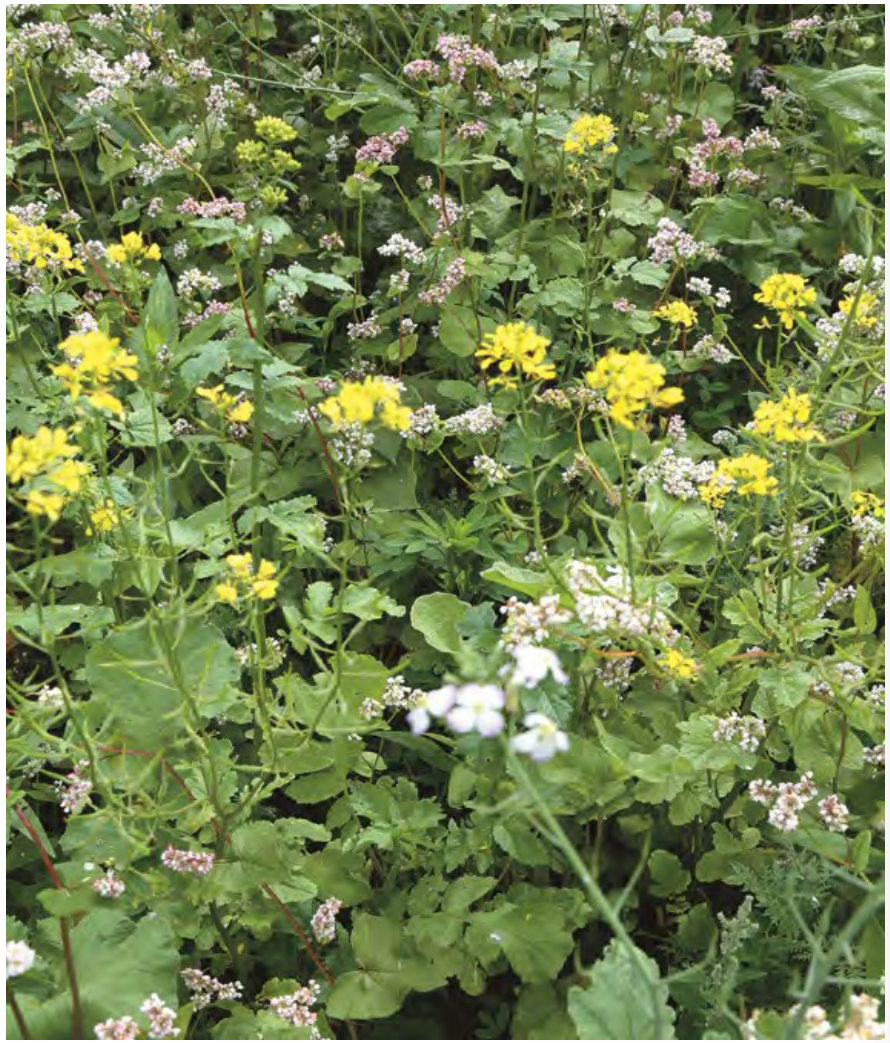
The same field, the same slope, the same crop!

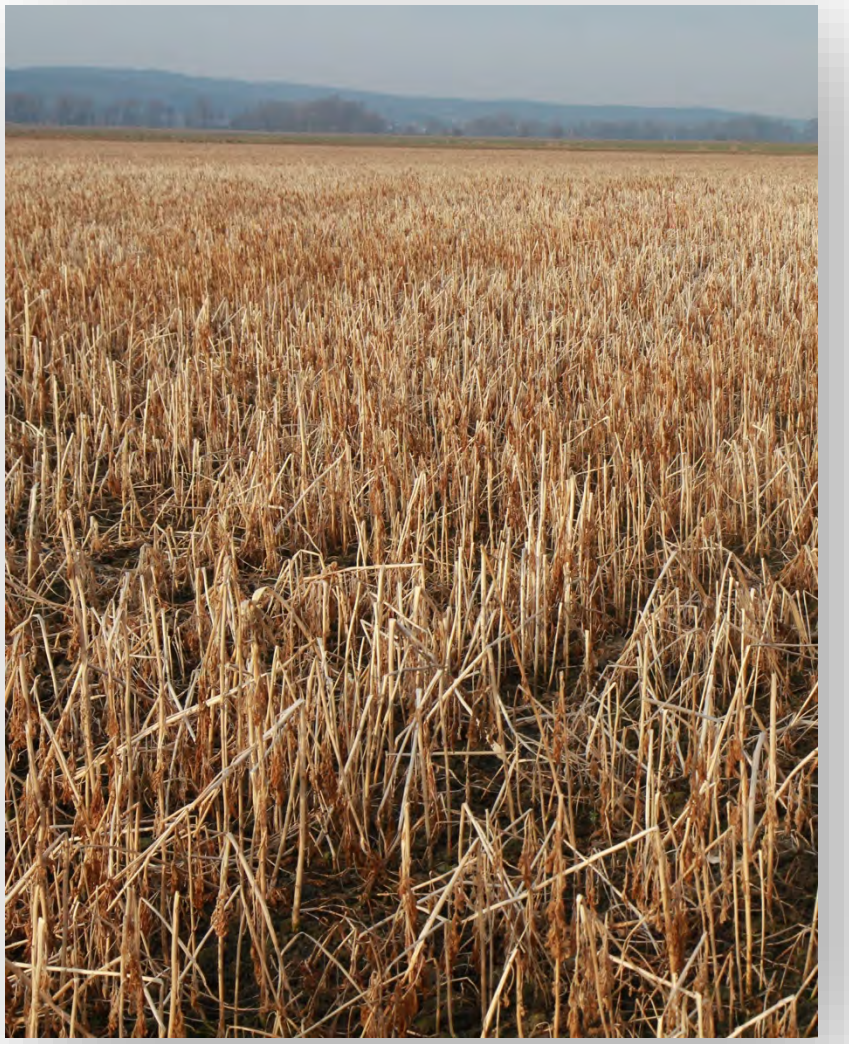
Conventional tillage

Conservation Agriculture

No-tillage + residues

Intermediate „Cover Crops“ to avoid Bare Soil





No-tillage in Spain

Benefits of Conservation Agriculture

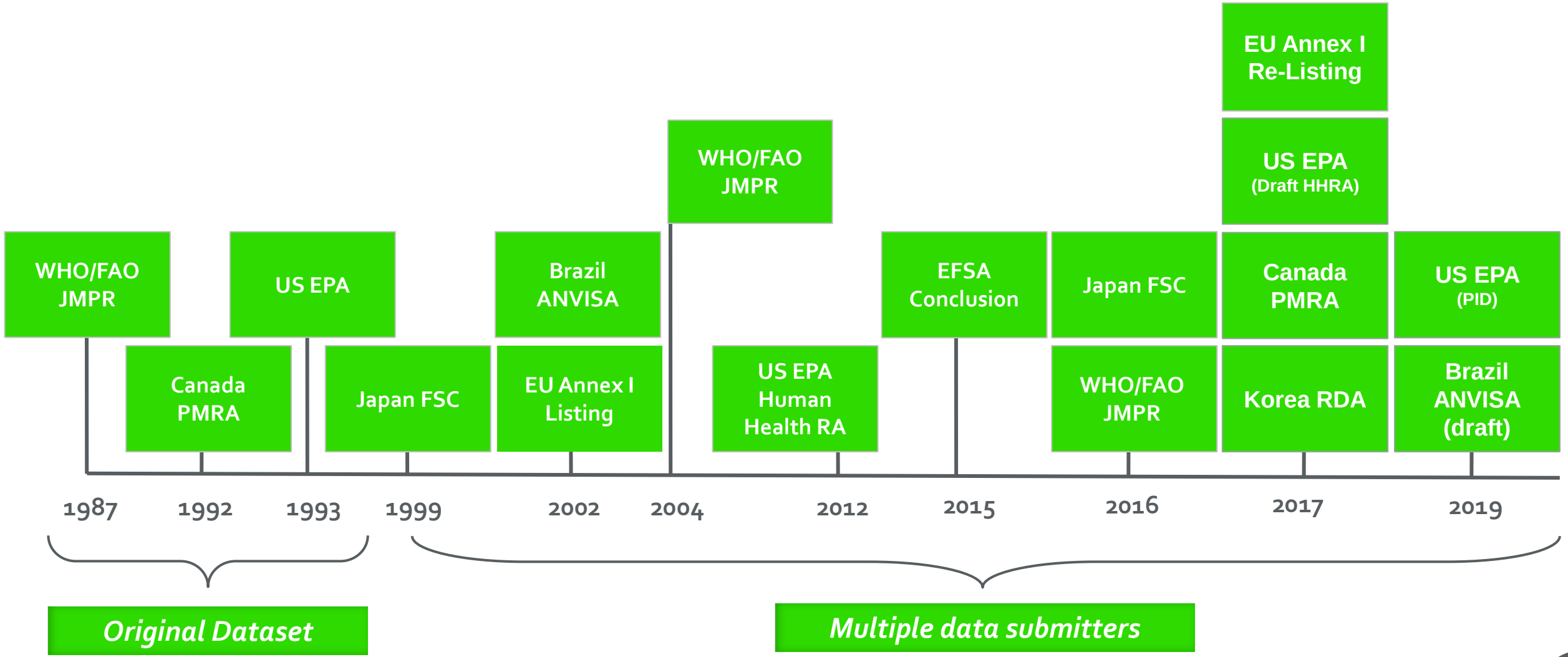
1. ***Carbon sequestration:*** *carbon is stored in soil instead of being released with tillage*
2. ***Protection of soil fertility:*** *the soil can retain higher water and moisture levels.*
3. ***Increased profitability***
4. ***Less time*** *needed for field tasks*
5. ***Improved*** *water balance and* ***increased*** *water use efficiency*
6. ***Increased soil carbon sink effect*** *(organic matter)*
7. ***Less CO_2 emissions / energy***
8. ***Biodiversity friendly***

Toxicology

Outline

- Previous evaluations
- Critical points under AIR
  - Genotoxicity /carcinogenicity
  - Reproductive
  - ED
  - Metabolites
  - Conclusion on safety profile & Challenges

Key Regulatory Reviews of Glyphosate



Glyphosate Renewal Group

Recent Regulator Conclusions

efsa
European Food Safety Authority
EFSA Journal 2015;13(11):4302

CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance glyphosate[1]

European Food Safety Authority (EFSA)[2]

European Food Safety Authority (EFSA), Parma, Italy

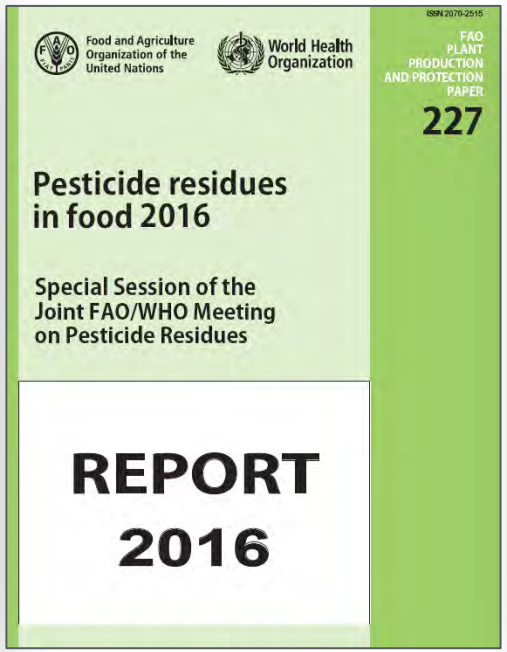
ABSTRACT

The conclusions of the European Food Safety Authority (EFSA), following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State Germany, for the pesticide active substance glyphosate are reported. The context of the peer review was that required by Commission Regulation (EU) No 1141/2010 as amended by Commission Implementing Regulation (EU) No 380/2013. The conclusions were reached on the basis of the evaluation of the representative uses of glyphosate as a herbicide on emerged annual, perennial and biennial weeds in all crops [crops including but not restricted to root and tuber vegetables, bulb vegetables, stem vegetables, field vegetables (fruiting vegetables, brassica vegetables, leaf vegetables and fresh herbs, legume vegetables), pulses, oil seeds, potatoes, cereals, and sugar- and fodder beet; orchard crops and vine, before planting fruit crops, ornamentals, trees, nursery plants etc.] and foliar spraying for desiccation in cereals and oilseeds (pre-harvest). The reliable endpoints, concluded as being appropriate for use in regulatory risk assessment and derived from the available studies and literature in the dossier peer reviewed, are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are identified. Following a second mandate from the European Commission to consider the findings from the International Agency for Research on Cancer (IARC) regarding the potential carcinogenicity of glyphosate or glyphosate-containing plant protection products in the on-going peer review of the active substance, EFSA concluded that glyphosate is unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification with regard to its carcinogenic potential according to Regulation (EC) No 1272/2008.

KEY WORDS

glyphosate, peer review, risk assessment, pesticide, herbicide

EFSA concluded that glyphosate is ***unlikely to pose a carcinogenic hazard to humans and the evidence does not support classification*** *with regard to its carcinogenic potential according to Regulation (EC) No 1272/2008.* ***EFSA – Approved October 2015***



Food and Agriculture Organization of the United Nations
World Health Organization

ISSN 2070-2515

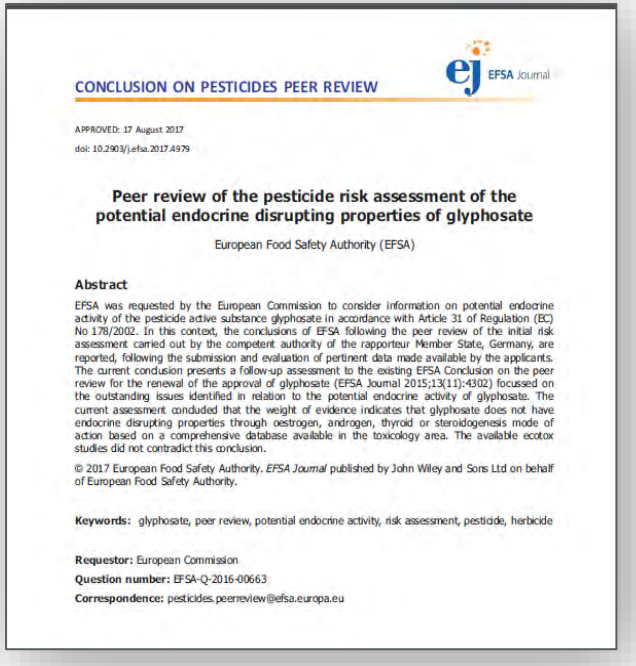
FAO PLANT PRODUCTION AND PROTECTION PAPER
227

Pesticide residues in food 2016

Special Session of the Joint FAO/WHO Meeting on Pesticide Residues

REPORT 2016

Glyphosate is unlikely to pose a carcinogenic risk to humans from exposure through the diet; glyphosate is unlikely to be genotoxic at anticipated dietary exposures
JMPR – June 2016



CONCLUSION ON PESTICIDES PEER REVIEW

ej EFSA Journal

APPROVED: 17 August 2017

doi: 10.2903/j.efsa.2017.4979

Peer review of the pesticide risk assessment of the potential endocrine disrupting properties of glyphosate

European Food Safety Authority (EFSA)

Abstract

EFSA was requested by the European Commission to consider information on potential endocrine activity of the pesticide active substance glyphosate in accordance with Article 31 of Regulation (EC) No 178/2002. In this context, the conclusions of EFSA following the peer review of the initial risk assessment carried out by the competent authority of the rapporteur Member State, Germany, are reported, following the submission and evaluation of pertinent data made available by the applicants. The current conclusion presents a follow-up assessment to the existing EFSA Conclusion on the peer review for the renewal of the approval of glyphosate (EFSA Journal 2015;13(11):4302) focussed on the outstanding issues identified in relation to the potential endocrine activity of glyphosate. The current assessment concluded that the weight of evidence indicates that glyphosate does not have endocrine disrupting properties through oestrogen, androgen, thyroid or steroidogenesis mode of action based on a comprehensive database available in the toxicology area. The available ecotox studies did not contradict this conclusion.

Keywords: glyphosate, peer review, potential endocrine activity, risk assessment, pesticide, herbicide

Requestor: European Commission
Question number: EFSA-Q-2016-00663
Correspondence: pesticides.peerreview@efsa.europa.eu

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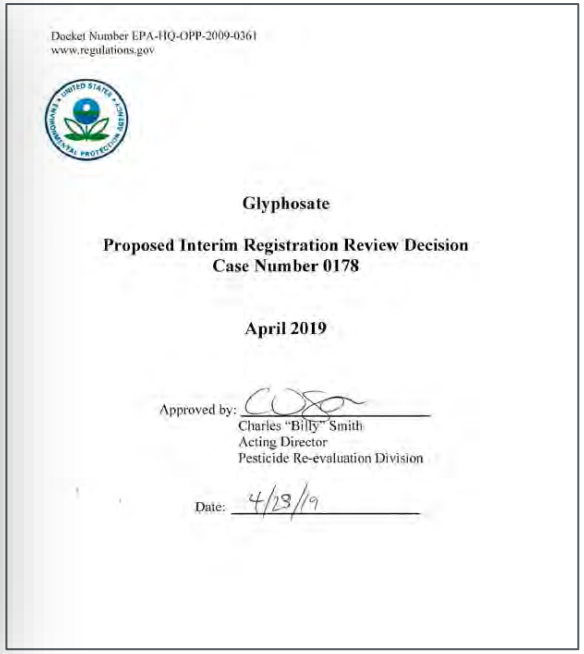
EFSA – Approved August 2017



Docket Number EPA-HQ-OPP-2009-0361
www.regulations.gov

Glyphosate

Proposed Interim Registration Review Decision Case Number 0178

April 2019

Approved by:
Charles "Billy" Smith
Acting Director
Pesticide Re-evaluation Division

Date: 4/23/19

The EPA conducted an independent evaluation of the carcinogenic potential of glyphosate and has determined that glyphosate is " not likely to be carcinogenic to humans."
EPA PID – April 2019

Outlined in the Renewal Assessment Report which supports the 2015 EFSA conclusions ***(BfR, 2015)***

- 2001 Monograph relied on several data sets from registrants rather than on one 'key study'
- A1R 2 even more toxicology data; packages from:
- **Monsanto**
- **Cheminova**
- **Syngenta**
- **Arysta**
- **Feinchemie (Adama)**
- **Nufarm**

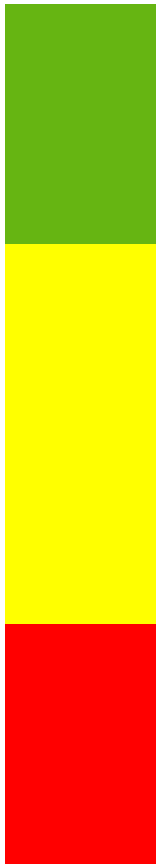
More than 900 scientific publications (published since 2000 until 2014) and other relevant information was considered.

All these publication were assessed for relevance, quality and reliability and were used for risk assessment only on condition that the respective criteria had been met

Safety Profile of Active Ingredient

Low Regulatory Risk based on EFSA 2015 conclusions

Endpoint	Regulatory Risk	Classification
Acute Toxicity		Irritating to eyes (a.i. only); **Cat. 1, R41; Classif. H318**
Developmental & Reproductive		Not a reproduction/developmental toxicant
Genotoxicity		Not genotoxic
Carcinogenicity		Not carcinogenic
Endocrine Disruption		Not an endocrine disruptor
Other		Not neurotoxic or immunotoxic



Low Risk

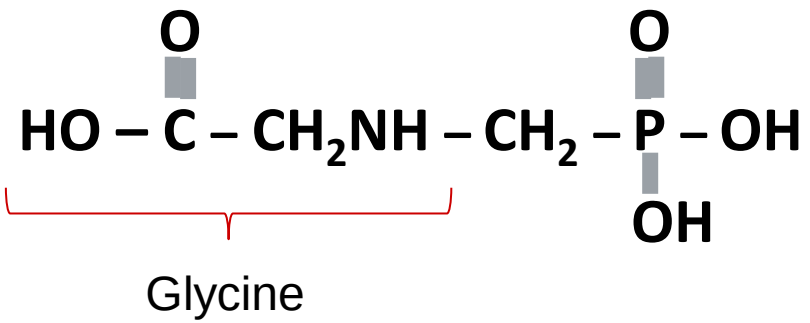
Medium; require refinements

High Risk

The Kinetics of Glyphosate are Well Documented

This pattern of toxicokinetics and metabolism is independent of sex, dose level, or repeated administration **(EU, 2015)**

- Glyphosate is rapidly absorbed from the gut (oral absorption ~20%; mostly excreted unchanged in feces)
- Systemic glyphosate rapidly excreted via urine (within 48 hours; $T_{1/2}$ = 6-12 hours)
- Essentially no metabolism of absorbed glyphosate
- Shows no potential for bioaccumulation
- Very low dermal absorption; multiple formulations tested (human *in vitro* < 1% absorption)



Glycine conjugation is one type of
- phase II metabolism

Glyphosate *in vivo* behaves as
- conjugated methyl phosphonate

Therefore no surprise
- **No metabolism**
- **Rapid urinary excretion**
- **Polar - no bioaccumulation potential**

Genotoxicity Studies

No evidence of a genotoxic potential in an adequate range of *in vitro* and *in vivo* studies **(BfR, 2015, RAR vol. 3)**

Study Type	Assays (# acceptable)	Results
in vitro	Ames (12; 4 supplementary) Mouse Lymphoma (2) HGPRT (1) Chromosomal Aberration (3; 1 supplementary) Unscheduled DNA synthesis (1) DNA Repair Test - Rec assay; (1 supplementary)	All Negative
in vivo	Micronucleus - MN (9) Chromosomal Aberration (2)	Negative 1 MN (F weak +ve @HDT, 5000 mg/kg)

2021 NEW STUDIES ACCORDING TO 2018 AND 2020 OECD TG:

in vitro HPRT and *in vitro* micronucleus assay in human lymphocytes both confirmed the lack of genotoxicity potential of glyphosate

Genotoxicity studies for glyphosate-based formulations (GBFs) and formulation components

GBFs do not cause point (gene) mutations and are devoid of a clastogenic potential *in vivo* **(BfR, 2015, RAR vol. 3)**

Test Substance	Assays	Number of Studies	Results
Glyphosate Based Formulations	Ames	4	Negative
	Micronucleus (*in vivo*)	4	Negative
Surfactants	Ames	3	Negative
	Micronucleus (*in vitro*)	1	Negative
	Mam. cytogenetics	1	Negative

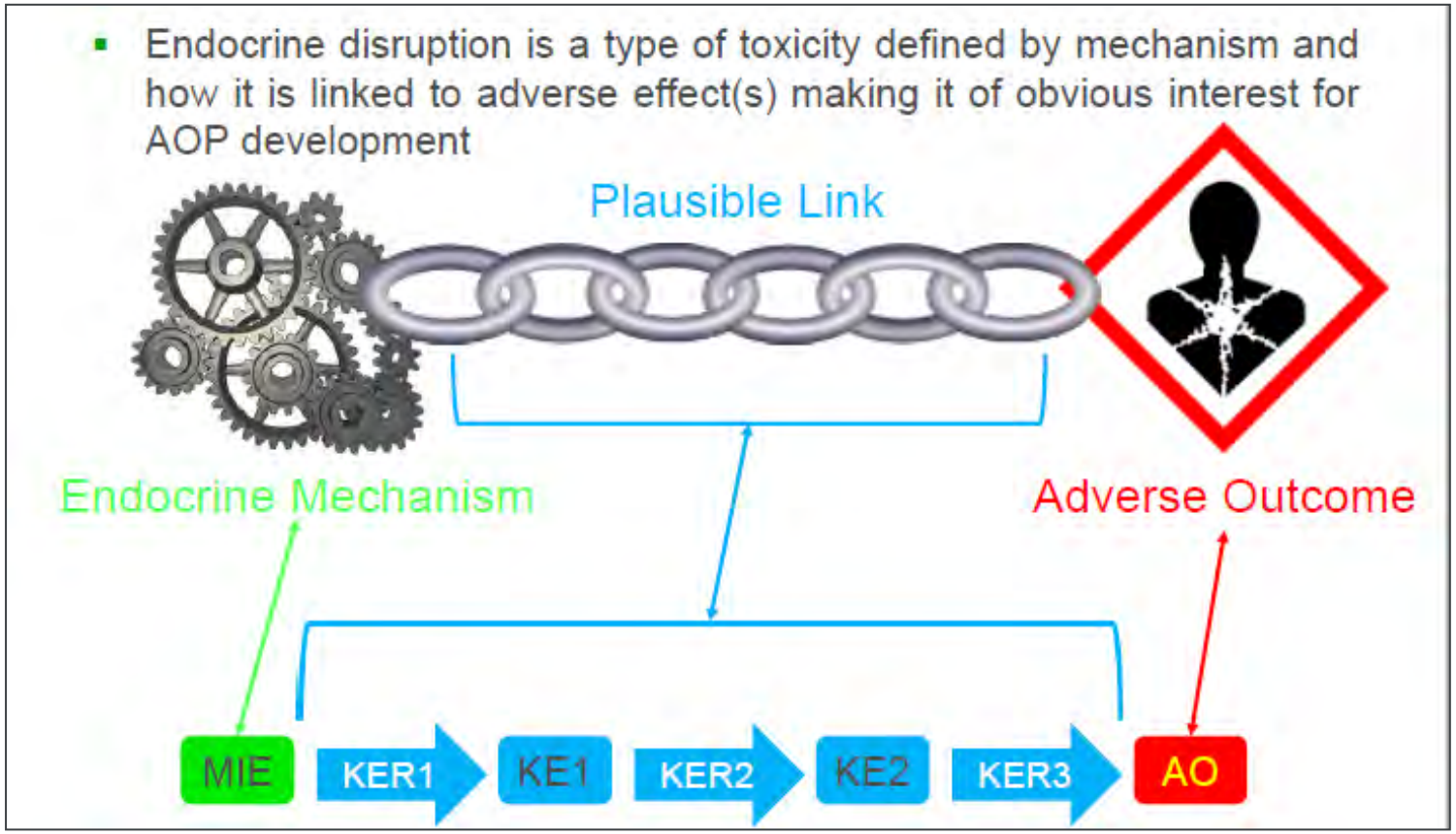
NOTE: Ongoing testing of formulations to support Art 43 submissions

Above studies were reviewed in AIR 2

ECHA/EFSA Guidance for the identification of endocrine disruptors

ED identification criteria

[…] *an active substance shall be considered as having endocrine disrupting properties that may cause adverse effects on (non)-target organisms if it is a substance that (1) shows an adverse effect in (non)-target organisms, (2) has an endocrine mode of action (MoA), and (3) the adverse effect is a consequence of the endocrine MoA*.



*EDSP Screening Showed **No Interaction** with the Endocrine System (NI = No Interaction)*

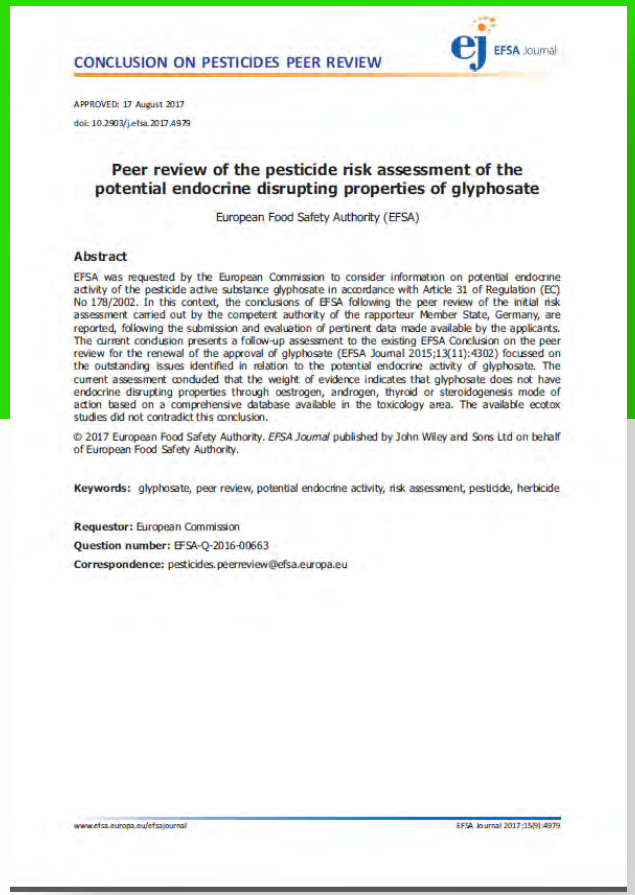
Screening Assays *	Modes of Action							
	Receptor Binding				Steroidogenesis		HPG Axis	HPT Axis
	E	Anti-E	A	Anti-A	E	A		
In vitro								
ER Binding	NI	NI						
ERα Transcriptional Activation	NI							
AR Binding			NI	NI				
Steroidogenesis					NI	NI		
Aromatase					NI			
In vivo								
Uterotrophic rat	NI							
Hershberger rat			NI	NI		NI		
Pubertal Male rat			NI	NI		NI	NI	NI
Pubertal Female rat	NI	NI			NI		NI	NI
Amphibian Metamorphosis								NI
Fish Short-term Reproduction	NI	NI	NI	NI	NI	NI	NI	

* Blank cells represent modalities that were not tested by a given screening assay

Endocrine Disruption – preparation of Appendix E (Lines of evidence) and Appendix I (ED Assessment) No new information since 2017 EFSA ED conclusion

OECD Conceptual Framework			
Level 1	Existing data and new-nontesting information		
Level 2	In vitro assays on selected endocrine mechanisms	5 EDSP assays	Estrogen Receptor(ER) Binding assay ERα Transcriptional Activation assay Androgen Receptor (AR) binding assay Steroidogenesis Aromatase Inhibition assay
Level 3	In vivo assays on selected endocrine mechanisms	4 EDSP assays	Hershberger assay Uterotropic assay Fish short-term reproduction Amphibian metamorphosis
Level 4	In vivo assays on adverse selected endocrine mechanisms	2 EDSP	Pubertal developmental and Thyroid function in male and female rats
		In vivo toxicity studies	70 studies with rats, mice, dogs and rabbits
Level 5	In vivo assay covering life cycle changes		6 Two-generational reproductive toxicity Fish full life-cycle study Avian reproduction study

Endocrine Disruption Conclusion



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Keywords: glyphosate, peer review, potential endocrine activity, risk assessment, pesticide, herbicide

Requestor: European Commission

Question number: EFSA-Q-2016-00663

Correspondence: pesticides.peerreview@efsa.europa.eu

The weight of evidence indicates that ***glyphosate is not an ED.***
EFSA – September 2017

Submission followed EFSA guidance on endocrine disruption assessment in Appendix E and Appendix I.

Aminomethylphosphonic Acid (AMPA) – plant & soil metabolite

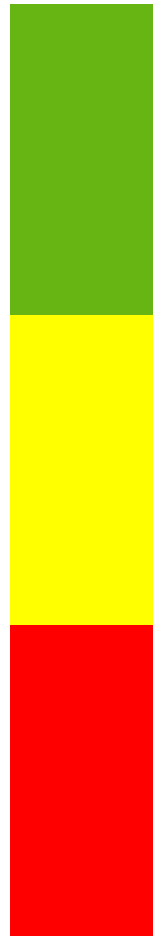
AMPA has a similar toxicological profile to glyphosate (EU, 2015)

- **Environmental metabolite and degradate of glyphosate**
- **A number of toxicological studies are available on the metabolite AMPA**
- **Overall it was concluded that AMPA presents a similar toxicological profile to glyphosate and the reference values of the latter apply to its metabolite AMPA.**

Safety Profile of Active Ingredient

Low Regulatory Risk based on current toxicological information although a lot of **challenges**

Endpoint	Regulatory Risk	Classification
Acute Toxicity		Irritating to eyes (a.i. only); **Cat. 1, R41; Classif. H318**
Developmental & Reproductive		**Not** a reproduction/developmental toxicant
Genotoxicity		**Not** genotoxic
Carcinogenicity		**Not** carcinogenic
Endocrine Disruption		**Not** an endocrine disruptor
Other		**Not** neurotoxic or immunotoxic



Low Risk

Medium; require refinements

High Risk

Public Literature

Glyphosate Renewal Group

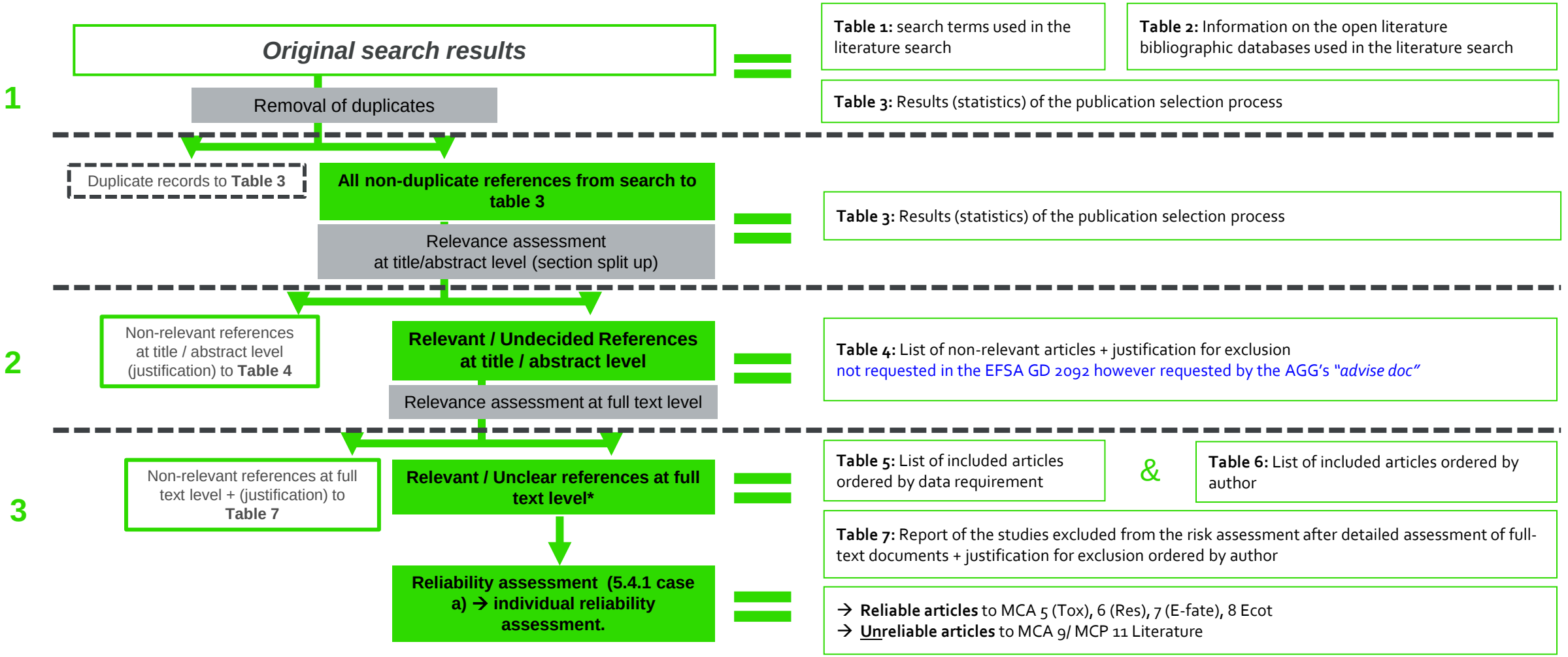
Databases used

Item	Databases information
Databases	CAB Abstracts, MEDLINE, Science Citation Index, BioMedSearch.com, Europe PubMed Central, NAL Catalog Agricola, PubMed, Toxicology Data Network, CAB Direct, SciFinder, Scopus, BIOSIS, FSTA, SciSearch.
Additional data sources not suggested by EFSA but covered by search	PQSCITECH, ESBIOBASE, TOXCENTER, HCAPLUS.

Publication period: January 2010 – June 2020

The Process - Workflow

References: EFSA GD 2092/2011 and Advice document AGG_Oct 2019



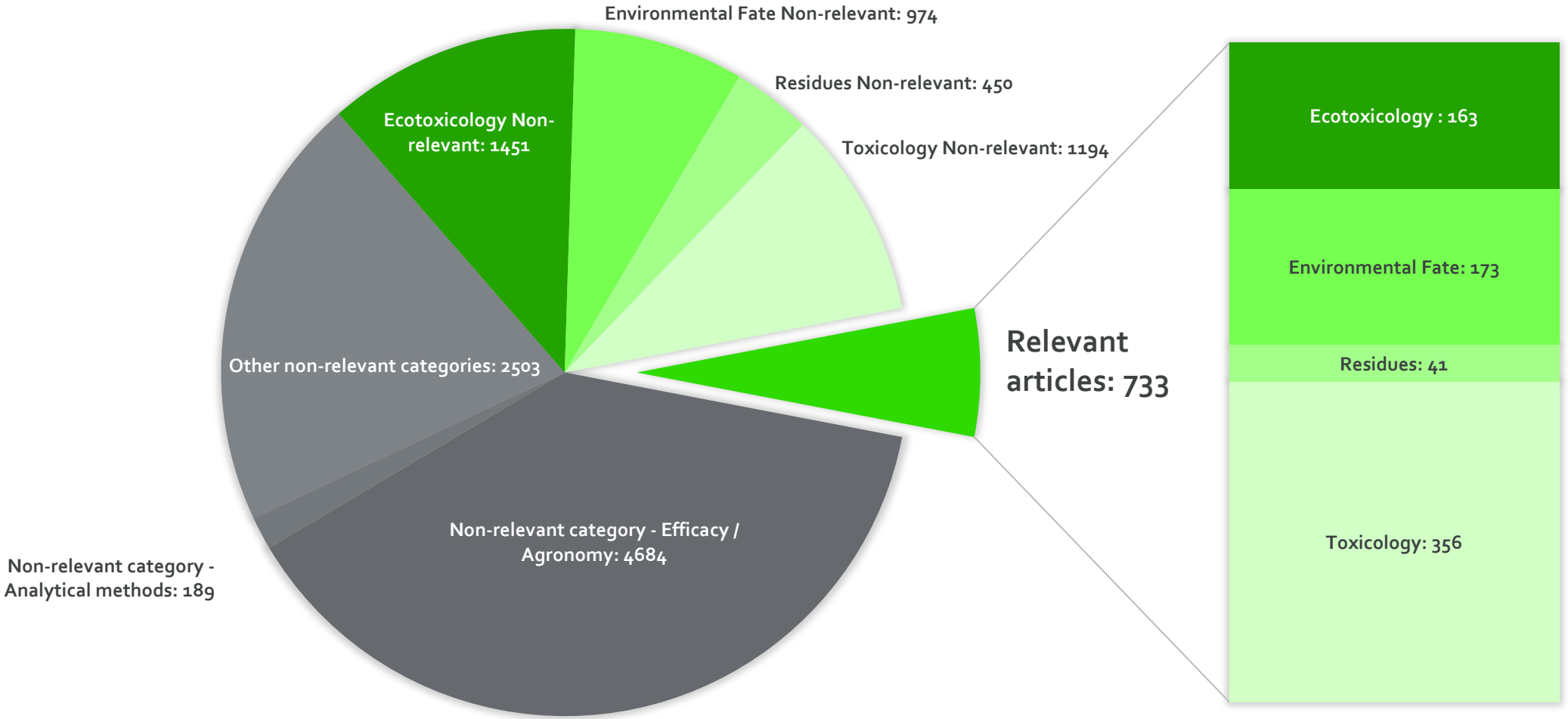
Glyphosate Renewal Group

*All articles evaluated in full text to be submitted in the electronic dossier in Caddy XML (as PDF files) not requested in the EFSA GD 2092 however requested by the AGG's "advise doc"

AIR5 Glyphosate literature search and evaluation

Publication period: January 2010 – end June 2020

Total number of articles:12178



Societal and agronomic impact of losing glyphosate

Potential impact of ban of Glyphosate on European farming

In the absence of glyphosate**, many existing production systems, **practices and rotations would become unviable.

***Reduction in production will have implications for EU's self-sufficiency in basic food commodities** such as cereals and potatoes, and negatively impact exports.*

*Yield reductions of **8-18% in wheat**, **8-19% in barley** and 1-3% in grape vines (table and wine growing grapes); A decline in production of wheat by up to 24 Mt, **potatoes by 10.4 Mt**, and grape **vines by 4.7 Mt .***

***Production losses are expected to cost the EU wheat sector up to €10.5 billion**, the potato sector just under €2 billion and the grape vine sector up to €4.2 billion.*

Source: Stewart Redqueen (2017); ANSES (2020); Garcia-Perez, Illman & Wynn (2020)

Safety of public transport infrastructure: Railway use

70%

Precision application technology is being introduced across Europe which can lead to use **reduction rates of up to 70%,** reducing the exposure of non-target plants and organisms

3

The Herbicide Resistance Action Committee (HRAC) recommends at least three modes of action for every weed – no new mode of action has been discovered in the last 30 years

Inability to use glyphosate on the European rail network would lead to increased reliance on selective herbicides with narrower spectrums of activities, and vulnerability to invasive species such as Milkweed, which is a threat to human and animal life

Glyphosate-based products are the products of choice for all **European railway companies** to keep tracks free from weeds

Summary

Key benefits of glyphosate for sustainable agriculture