Opportunities for streamlining the risk assessment of GM stacked events obtained by conventional crossing

CropLife EUROPE

19/03/2025

Outline

1. Rationale
2. GM stacked events obtained by conventional crossing
3. Information required for GM single event vs. stacked events applications
4. Risk assessment for GM stacked events obtained by conventional crossing
5. Proposal for a streamlined risk assessment of GM stacked events
6. Conclusion

Rationale

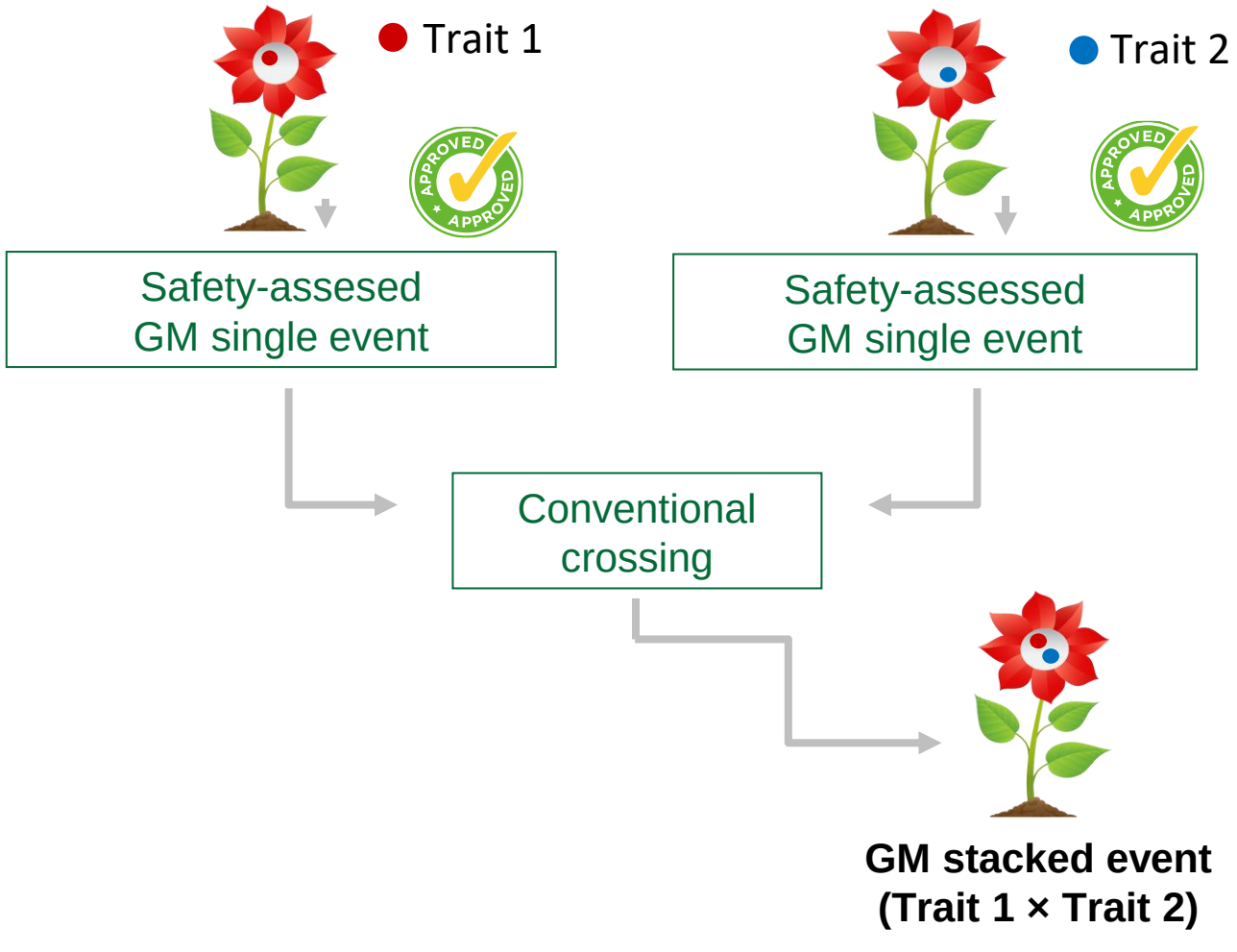
- New EU Commission pursuing **regulatory simplification** and **better implementation** as critical to support **competitiveness**.
- "Meaningful simplification" needed to ensure **agrifood sector remains competitive** and **resilient** (Vision for Ag and Food)

- **Improving regulatory efficiency incl. streamlining processes** is an objective of EFSA's 2021-2027 Strategy
- EFSA is exploring "*opportunities to* **improve speed and save efforts by reducing re-work and streamlining processes**" as a focus of 2025 work (EFSA Programming document 2024-2026)
- Ongoing EFSA discussions on the risk assessment of GM stacked events [GMO Panel Plenary meeting; CompERA/Food & Feed safety/Molecular Characterization working groups]

- A CropLife Europe member submitted a streamlined data package for a GM stacked events application

Opportunity to streamline risk assessment for GM stacked events obtained by conventional crossing, fostering innovation while maintaining safety

Conventional crossing to obtain GM stacked events is the same process as for conventional varieties



Previously risk-assessed events :
As safe as conventional counterpart

Conventional crossing :
Safe process

No scientific basis for harm:
leveraging safety of single events & of conventional crossing

Information required for GM SINGLE transformation events

Molecular characterization

- **Information relating to the genetic modification**
  - Methods of genetic modification
  - Nature and source of vector
  - T-DNA
    - Source of donor nucleic acid(s)
    - Size and intended function
    - Complete sequence
    - History of safe use
    - Bioinformatics (toxin/allergens)
- **Information relating to the GM plant**
  - Description of the trait(s), MOA
  - Inserted sequence(s)
    - Size and copy number,
    - Insert organization,
    - Junction and insertion site analysis,
    - Complete sequence of insert and flanking regions
    - Bioinformatics (gene disruption)
    - Other new ORFs – bioinformatics
  - Expression of the insert(s)
  - Genetic and phenotypic stability
    - Phenotypic stability
    - Inheritance patterns
  - Horizontal gene transfer
- **Additional information relating to the GM plant required for environmental safety aspects**

Comparative analysis

- Field trials: 8 sites x 4 reps
- Conventional counterpart and additional comparators
- Composition
- Endogenous allergens (if applicable)
- Agronomic and phenotypic characteristics
- Effects of processing

Toxicology

- **Testing of NEPs**
  - Molecular and biochemical characterization of NEPs
  - Bioinformatics (toxins, anti-nutrients)
  - Influence of temperature and pH
  - Digestibility
  - Repeated-dose 28-d toxicity
- **Testing of new constituents other than proteins**
- **Information on altered levels of FF constituents**
- **Testing of whole GM food or feed**
  - 90-d feeding study

Allergenicity

- **Assessment of allergenicity of the NEPs**
  - Bioinformatics (allergens, celiac)
  - Serum screening (if applicable)
  - Pepsin resistance and *in vitro* digestibility tests
- **Assessment of allergenicity of the whole genetically modified plant**
- **Adjuvanticity**

Nutritional assessment

- Nutritional assessment (as applicable)
- Broiler study (if applicable)

Exposure assessment

- Human anticipated intake
- Animals anticipated intake

Risk characterization

Environmental risk assessment

- Weight of evidence approach

Additional information

- Literature searches
- List of unpublished studies

Other information

- Method of Detection
- Sequencing information
- Post market monitoring (if applicable)
- Post market environmental monitoring plan

After approval

- Literature searching
- Trade data

- Crop biology

Information required for GM STACKED events obtained by conventional crossing

Molecular characterization

- **Information relating to the genetic modification**
  - ~~Methods of genetic modification~~
  - ~~Nature and source of vector~~
  - T-DNA
    - ~~Source of donor nucleic acid(s)~~
    - ~~Size and intended function~~
    - ~~Complete sequence~~
    - ~~History of safe use~~
    - Bioinformatics (toxin/allergens)
- **Information relating to the GM plant**
  - ~~Description of the trait(s), MOA~~
  - Inserted sequence(s)
    - ~~Size and copy number,~~
    - ~~Insert organization,~~
    - ~~Junction and insertion site analysis,~~
    - Complete sequence of insert and flanking regions*
    - Bioinformatics (gene disruption)
    - Other new ORFs – bioinformatics
    - **Potential interaction (between unintended modifications)**
  - Expression of the insert(s)
    - **Potential interaction (between events)**
  - Genetic and phenotypic stability
    - ~~Phenotypic stability~~
    - ~~Inheritance patterns~~
    - **Re-sequencing***
  - Horizontal gene transfer
- **Additional information relating to the GM plant required for environmental safety aspects**

Comparative analysis

- Field trials: 8 sites x 4 reps*
- Conventional counterpart and additional comparators*
- Composition*
- Endogenous allergens (if applicable)*
- Agronomic and phenotypic characteristics*
- Effects of processing
- **Potential interaction (between events)**

Toxicology

- **Testing of NEPs**
  - ~~Molecular and biochemical characterization of NEPs~~
  - Bioinformatics (toxins, anti-nutrients)
  - ~~Influence of temperature and pH~~
  - ~~Digestibility~~
  - ~~Repeated-dose 28-d toxicity~~
- **Testing of new constituents other than proteins**
- **Information on altered levels of FF constituents**
- ~~Testing of whole GM food or feed~~
  - ~~90-d feeding study~~
- **Potential adverse effect due to stacking**

Allergenicity

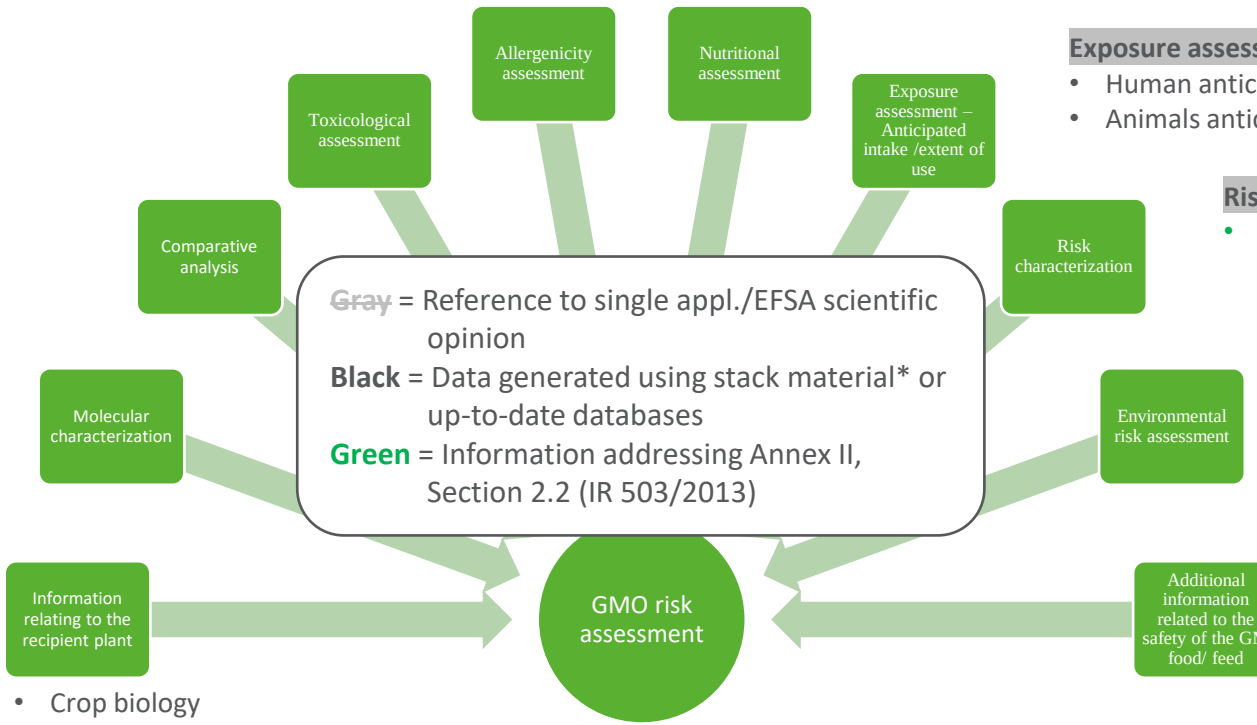
- **Assessment of allergenicity of the NEPs**
  - Bioinformatics (allergens, celiac)
  - ~~Serum screening (if applicable)~~
  - ~~Pepsin resistance and *in vitro* digestibility tests~~
  - **Potential for increased allergenicity (between NEPs)**
- **Assessment of allergenicity of the whole genetically modified plant**
- **Adjuvanticity**

Nutritional assessment

- Nutritional assessment (as applicable)
- ~~Broiler study (if applicable)~~
- **Potential changes in nutritional value due to stacking**

Exposure assessment

- Human anticipated intake
- Animals anticipated intake



- Crop biology

Risk characterization

- **Additional risk arising from stacking**

Environmental risk assessment

- Weight of evidence approach

Additional information

- Literature searches
- List of unpublished studies

Other information

- Method of Detection
- Sequencing information
- Post market monitoring (if applicable)
- Post market environmental monitoring plan

After approval

- Literature searching
- Trade data

Risk assessment of GM stacked events obtained by conventional crossing

Implementing Regulation (EU) No 503/2013
Annex II, Section 2.2

Risk assessment (RA) of genetically modified food and feed containing stacked transformation events

=

RA of each single transformation event or, in accordance with Article 3(6) of this Regulation, to refer to **already submitted application(s)**

+

Assessment of the following aspects:

a) stability of the transformation events;

b) expression of the transformation events;

c) potential synergistic or antagonistic effects resulting from the combination of the transformation events

⇨

- No potential interactions identified

  => no additional RA

- Potential interactions identified

  => additional RA in accordance with Regulation

Proposal for a streamlined risk assessment of GM stacked events

IR (EU) No 503/2013 Annex II, Section 2.2 data requirements	RA of each single transformation event or, in accordance with Article 3(6) of this Regulation, to refer to already submitted application(s)	Stability of the transformation events	Expression of the transformation events	Potential synergistic or antagonistic effects resulting from the combination of the transformation events
Problem Formulation	Are individual GM single events deemed as safe as their conventional counterparts?	Are there molecular changes in the GM stacked events that alter the stability of the events?	Are there changes in the expression levels of the NEPs that alters the levels of exposure to the NEPs?	Are there likely interactions that can alter the risk assessment (*e.g.* hazard or exposure) compared to the single events?

Data package	• Reference to single appl./EFSA scientific opinion
	• Reg. (EC) No 1829/2003 Art. 9(3) and 21(3) oblige the authorisation holder to inform without delay to the Commission any new scientific or technical information that might influence the evaluation of the safety in use of GM food and feed
		• Confirm that inherited inserts are identical to those of each respective parental single event
		• Confirm the conventional crossing has not altered the inherited inserts at molecular level
			• Confirm the expression levels of the NEPs are similar in the stack and the singles
			• Confirm the NEPs are expressed as intended when combined by conventional crossing
			  ○ If so, the exposure levels as provided for the singles apply to the stack.
			  ○ If not, conduct further analysis.
				If unlikely, provide scientific justification confirming absence of synergistic and antagonistic effects based on
				1) distinct mode of action;
				2) distinct biological function;
				3) lack of interactions between the NEPs in the stack that could lead to adverse effects (toxicity, allergenicity, and/or nutrition)
				If likely, conduct further analysis in accordance with the regulation

Conclusion

The new **Commission's initiative** and **EFSA's 2021-2027 Strategy** foresee **regulatory simplification** and **better implementation** which is vital for enhancing EU competitiveness and ensuring resilience of the EU agri-food system.

Current risk assessment practices for GM stacked events are disproportionate to the risk posed by conventional crossing.

Streamlining the risk assessment for GM stacked events obtained by conventional crossing is an opportunity to improve regulatory efficiency and promote innovation **without compromising safety**.

CLE advocates for a fit-for-purpose, **science-driven approach** to the risk assessment of GM stacked events obtained by conventional crossing in line with Section 2.2 of Annex II of Implementing Regulation (EU) No 503/2013. This can be implemented **without legislative changes**.

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FOR MORE INFORMATION

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