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Qualifications for Exemption in § 340.1(b) – A case study: the Confirmed CR 20-358-01cr

- Camelina is an oil crop in the family Brassicaceae, an allohexaploid that contains three sub-genomes, AABBCC (three copies, or homeologs, of each gene).
- The targeted gene (CBI) for altered seed oil profile was edited for only one of the three homeologous genes. The exemption is pursuant to § 340.1(b)(1) - a single genetic modification leading to deletion of any size.
- Null segregants were obtained through conventional breeding procedures to remove the genetic sequences that allow CRISPR/Cas9 editing to take place such that only the genome edits remain.
- If the developer wanted to make the same corresponding changes to all the subgenomes, such lines would not qualify for exemption in § 340.1(b)(1) and the developer can request additional exemption through submitting proposal (§ 340.1(b)(4)) or go through the Regulatory Status Review (**RSR**) process.

Would a multiplex genome edited camelina qualify for a confirmation request (CR)?

- Multiplex genome-edited camelina null segregant lines developed by CRISPR/Cas technology that had been determined not to require regulation under the legacy regulations through the “Am I Regulated” process (20-010-01_air)
- Only a single modification in plants is qualified for exemption from the revised regulations. Therefore, while the above multiplex genome edited lines are exempted through the AIR process, new plants with such multiplex genome-edited modifications would not qualify for CR. But developers can request for an additional exemption through § 340.1(b)(4) or go through the **RSR** process.

Exemptions in § 340.1(c): Previously Reviewed Plants

Plants modified to contain a plant-trait-MOA combination that is the same as one that was previously evaluated and determined by APHIS not to be regulated are also exempt from the regulations.

Previous evaluations may have occurred under the:

- Petition process (under the legacy regulations); or
- RSR process (under the revised regulations)



Qualifications for Exemption in § 340.1(c) – A case study: comparison between two maize lines

Characteristics	HCEM485 (petition extension 09-063-01p under the legacy regulations).	GA21 (petition 97-099-01p under the legacy regulations)	
Plant Species	<i>Zea Mays</i>	<i>Zea Mays</i>	Same
Traits	Herbicide resistance (to glyphosate)	Herbicide resistance (to glyphosate)	Same
Gene construct	a) Promoter: 5' region of the maize EPSPS-encoding gene.	a) Promoter: 5' region of the rice actin 1 gene.	Different
	b) Gene: double mutated EPSPS-encoding gene	b) Gene: double mutated EPSPS-encoding gene	Same
	c) Terminator: 3' nontranslated region of the maize EPSPS-encoding gene.	c) Terminator: 3' nontranslated region of the <i>Agrobacterium</i> nopaline synthase gene (<i>nos</i>).	Different
Mechanisms of Action	An insensitive form of EPSPS (5-enolpyruvylshikimate-3-phosphate synthase) with a decreased binding affinity for glyphosate herbicides.	An insensitive form of EPSPS (5-enolpyruvylshikimate-3-phosphate synthase) with a decreased binding affinity for glyphosate herbicides.	Same

HCEM485 were submitted today for CR, it would qualify for § 340.1(c) exemption based on the same P-T-MOA shown in GA21.

Qualifications for Exemption in § 340.1(c) – Same MOA

- Will different promoters always result in the same MOAs?
 - E.g., constitutive vs. temporal and spatial expressions; expression levels
- Will the expression of different genes lead to different MOAs?
 - E.g., corn *epsps* gene vs. *Agrobacterium* cp4 *epsps* gene; *bar* gene vs. *pat* gene

Qualifications for Exemption in § 340.1(c) – Same Plant Species

- In a petition extension request, antecedent can be a different crop (species), e.g., if APHIS had never reviewed a glyphosate-resistant (EPSPS) soybean but had reviewed a glufosinate-resistant soybean and a glyphosate-resistant (EPSPS) corn, both glufosinate-resistant soybean and glyphosate-resistant corn can be used as antecedents.
- For exemption § 340.1(c) the Plant-Trait-Mechanism of action (MOA) must be the same as those of modified plants for which APHIS has conducted an RSR and found not to be subject to the regulations under 7 CFR part 340.
- The 'Plant' in P-T-MOA refers to the same plant species in combination with trait and MOA.

RSR vs Petition

- Data package
- Petition: A set of data requirement from developers is mandated in the legacy regulations to conduct Plant Pest Risk Assessment (PPRA) regardless of whether the plant could possibly pose a plant pest risk.
- RSR: Minimal or no data requirement from developers to conduct PPRA.

RSR vs Petition - Data and Information Requirements for RSR

- The RSR process differs from the petition process in that APHIS is requesting much less information from developers for the initial review.
- Based on the risk assessments in accordance with the petition process over 30 years, APHIS has discovered that the introduced trait of the modified organism and MOA provide the most reliable indicator of the organism's potential for plant pest risk.
- In many cases, APHIS will be able to evaluate the plant pest risks associated with a modified organism without field-test data.
- APHIS will seek additional information, potentially including data from controlled field experiments, in cases where APHIS identifies a plausible pathway to increased plant pest risk.

RSR vs Petition - Data and Information Requirements for RSR

- Information required for RSR submission is described in § 340.4(a)(4).
 - (i) A description of the comparator plant(s), to include genus, species, and any relevant subspecies information;
 - (ii) The genotype of the modified plant, including a detailed description of the differences in genotype between the modified and unmodified plant; and
 - (iii) A detailed description of the new trait(s) of the modified plant.

- APHIS will be publishing additional guidance soon.

Exemptions and RSR

- 7 CFR340.1(b)(1-3) exemptions are based on what could be achieved through conventional breeding and not based on plant pest risk assessments.
- 7 CFR 340.1(c) exemption is based on P-T-MOAs that were determined to be not regulated pursuant to either the legacy petition process or the new RSR process.
- RSR: RSR is not about a modified plant that could otherwise be achieved through conventional plant breeding, but rather for identifying and evaluating plausible pathways to plant pest risk in modified plants that are not eligible for exemption.



Thank you

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