

Risk Assessment Review Table

Tracking No: 2021-253-IAR-005-CMR

Title: Review of Risk Assessment on an Application from Institute for Agricultural Research (IAR), Zaria for Release into the Environment of Maize (*Zea mays* L.) Genetically Modified for Drought Tolerance and Insect Resistance – Stacked Events MON-89034 and MON-87460-4 (hereafter referred to as Maize with Events MON87460 x MON89034) in Nigeria

S/No	Concern	Potential hazard	Likelihood	Consequence	Acceptable risk?	Management
Environmental Risk Assessment						
1.	Potential for gene flow from TELA maize stacked events MON87460 x MON89034 to wild relatives whose hybrid offspring may become more weedy or more invasive	Increased fitness of wild relatives, thus causing increased competitive advantage leading to the development of super weeds (disruption of agricultural system)	<p>Highly unlikely due to the reasons below:</p> <p>There are no wild relatives of maize in Nigeria. All teosintes and subspecies of wild relatives occur only in Mexico and Guatemala (Sánchez-González and Ruiz-Corral, 1997).</p> <p>Although maize often appears as a volunteer plant in a subsequent rotation, it has no inherent ability to persist or propagate and therefore, cannot survive as a weed.</p> <p>According to the OECD consensus document on the Biology of <i>Zea mays</i> subsp. <i>mays</i> (maize), (OECD, 2003), maize has lost its ability to survive in nature due to its long domestication process and needs human intervention to disseminate its seed.</p> <p>Furthermore, maize is unable to reproduce sustainably outside of domestic cultivation, and maize plants are not invasive in nature.</p>	Minor Potential for the evolution of aggressive weeds or the extinction of rare species. (Ellstrand <i>et al.</i> , 1999).	Acceptable, because the risk is negligible	None
2.	Potential for gene flow from TELA maize stacked events MON87460 x MON89034 to conventional maize	Undesired genes in conventional maize genomes	<p>Likely</p> <p>Available information on the reproduction characteristics of maize shows that maize is a cross-pollinated species, with pollen produced in large quantities. A normal-sized hybrid tassel can</p>	Minor Although this is not a safety issue, the occurrence of	Acceptable, because the risk is Low .	Propose coexistence measures to be implemented (socio

			<p>produce up to 25 million pollen grains (Kiesselbach, 1999).</p> <p>Pollen dispersal in maize does not exceed 200m under normal environmental conditions. Infact, 90% of dispersed pollen falls within the first 10m.</p> <p>On average, maize pollen loses 100% viability after 2 to 3 hours of atmospheric exposure (Luna <i>et al.</i>, 2001; Aylor, 2003). Therefore, pollen flow can be effectively minimized through physical or temporal isolation measures.</p> <p>Expression of the introduced <i>Cry1A.105</i>, <i>Cry 2Ab2</i>, <i>NPTII</i> and <i>CspB</i> genes will not alter the nature of maize pollen nor the frequency or efficiency of horizontal gene transfer (HGT).</p> <p>TELA maize stacked event has no increased weediness potential compared to currently commercialized varieties</p>	this scenario has the capacity of disrupting trade		economic issues) to manage this concern.
3.	Potential for gene flow of <i>nptII</i> to bacteria, humans and animals	Antibiotic resistance	<p>Unlikely</p> <p>The <i>nptII</i> gene is ubiquitous in the environment and is naturally expressed by several soil bacteria. The NPTII gene from plant material can only be taken up by competent bacteria via natural transformation a process that occurs infrequently in many bacteria and in most environmental conditions, if the intact gene enters the bacteria, it will be rapidly degraded by restriction endonucleases in many bacterial cells. Gene transfer from plant to bacteria has only been demonstrated under laboratory conditions when regions of homology were already present in the recipient bacterium (Bennett <i>et al.</i>,2004; de Vries <i>et al.</i>,2001, Kay <i>et al.</i>,2002, and Tepfer <i>et al.</i>,2003)</p>	<p>Minor</p> <p>Increased antibiotic resistance to amino glycosides.</p>	Acceptable, because the risk is Low .	None

4.	Potential impact of the event MON87460 × MON89034 (TELA maize) stacked events on biodiversity	Unintended Adverse effects on biodiversity	<p>Highly Unlikely</p> <p>Experience with conventional domesticated maize shows that there is no potential for maize to be invasive in natural habitats or to persist in the agronomic environment without human intervention. Maize is a poor competitor, which outside of cultivation has no significant impact on biodiversity or the environment. Maize plants are non-invasive in natural habitats (Gould, 1968)</p> <p>Maize with events MON87460 and MON810 was not altered in its phenotypic, agronomic, reproductive, survival and dissemination characteristics when compared to conventional maize and, therefore, it is highly unlikely that maize with events MON87460 and MON810 will have effects on the biotic components and abiotic from the environment, compared to conventional maize.</p> <p>Thus, it is concluded that the probability of maize with events MON87460 and MON810 spreading into the environment by non-agricultural means and causing damage to ecosystem biodiversity is negligible, as maize is neither persistent nor invasive and these parameters are unchanged in maize with events MON87460 and MON810 compared to conventional maize.</p>	<p>Minor</p> <p>Loss of genetic diversity leading to extinction of species as well as imbalance of the ecosystem</p>	Acceptable, because the risk is low .	None
5.	Potential impact of the event and its gene products on non-target organisms	Unintended Adverse effects on non-target organisms	<p>Highly unlikely because:</p> <p>The release of the event will not result in altered impacts on non-target organisms, including humans.</p> <p>The event does not pose an increased risk to interacting non-target organisms. In the various field trials conducted with genetically modified maize, no adverse effects or agronomic differences were reported, except for intentionally introduced traits.</p> <p>There is available information based on findings from several studies on the environmental safety of <i>Cry1Ab</i>, <i>Cry2Ab2</i> and <i>Cry1A</i>, <i>CspB</i> and <i>NPTII</i> to non-target</p>	<p>Marginal</p> <p>Loss of biodiversity, negative impact on pollination and an imbalance in the ecosystem.</p>	Acceptable, because the risk is negligible	None

			<p>organisms. (Romeis, J., <i>et al.</i>, 2019, Lövei, G. L., & Arpaia, S. 2005)</p> <p>Maize with events MON87460 and MON810 is an agriculturally beneficial product with pesticide activity against only lepidopteran pests of maize, and no potentially adverse effects on non-target organisms or threatened species were observed based on extensive characterization of maize with events MON87460 and MON89034.</p> <p>Maize with events MON87460 and MON89034 expresses the introduced <i>Cry1Ab</i>, <i>Cry2Ab2</i> and <i>Cry1A</i>, <i>CspB</i> proteins, which protects plants against attack of maize by stalk caterpillar pests. The Cry protein exhibits selective toxicity against certain <i>lepidopteran</i> pests, but not against other insect orders. This specificity in mode of action is consistent with findings reported in published literature demonstrating that proteins of the Cry1A class exhibit selective toxicity to Lepidoptera Whiteley <i>et al.</i>, 1986; Crickmore <i>et al.</i>, 1998; Mendelsohn <i>et al.</i>, 2003; Romeis <i>et al.</i>, 2004; Romeis <i>et al.</i>, 2006).</p>			
5.	Potential to be invasive of natural habitats	Increased Fitness resulting in increased competitive advantage leading to disruption of agricultural system	<p>Highly Unlikely</p> <p>Maize plants are non-invasive in natural habitats (Gould, 1968). Based on centuries of experience with conventional domesticated maize, there is no potential for maize to be invasive in natural habitats or to persist in the agronomic environment without human intervention. Corn is a poor competitor, which outside of cultivation has no significant impact on biodiversity or the environment.</p> <p>Volunteer maize is not found growing along fences, ditches, roads, nor in natural habitats that are outside of cultivated agricultural farms.</p> <p>TELA maize stacked event has no invasiveness potential compared to currently commercialized varieties</p>	<p>Minor</p> <p>Loss of genetic diversity</p>	Acceptable, because the risk is negligible.	None

6.	Potential impact on Soil Microorganisms	Unintended adverse effects on nutrient cycles in soil, resulting from the effect of newly expressed proteins on target or non-target organisms involved in biochemical processes	<p>Unlikely</p> <p>Maize production, in general, is known to have indirect impacts on biogeochemical processes, through tillage, application of fertilizers and establishment of a monoculture (where grown as the only crop) in a defined area. Since maize with events MON87460 and MON89034 was found to be compositionally equivalent to conventional maize and did not differ in morphology, development, yield, dissemination, susceptibility to stress, plant health and survival characteristics, there is no evidence that it is different to conventional maize in relation to its direct influence on nutrient levels in the soil.</p> <p>The expression of CspB, Cry1Ab, Cry2Ab2, Cry1A and NPTII proteins is a characteristic of genetically modified maize that could potentially cause an adverse environmental effect on biogeochemical processes. However, the proteins are expressed in very minute quantities and are readily degraded once exposed to the environment. (Ferré, J., and Van Rie, J. 2002; Bravo, A., <i>et al</i>/2007). Furthermore, these proteins are not novel to the environment as they naturally occur in soil microorganisms from which they were originally obtained. (Höfte, H., & Whiteley, H. R. 1989) (Bravo, A., & Soberón, M. 2008)</p> <p>The extensive experience with the commercialization of various insect resistant crops expressing CspB and Cry proteins have not revealed any adverse effects till date. As with conventional maize, it is highly unlikely that there would be any significant immediate or delayed adverse effects of maize events MON87460 and MON89034 on biogeochemical processes in soil.</p>	Marginal Soil degradation, reduction in crop yield, adverse impact on the phenotype of the crop cultivated	Acceptable, because the risk is negligible.	None
7.	Potential to Develop Resistant Insect Population	Development of resistant insect populations due to reemergence of crop susceptibility	<p>Likely</p> <p>The development of resistance is a naturally occurring process unique to evolution and may occur over time.</p> <p>The rate at which resistant insect populations develop are generally dependent on factors such</p>	Major The integrity of the technology of the crop will	Although the Risk of developing resistance to traits is high,	Implement an insect resistance management (IRM) plan

		to the controlled insect or pest of concern and associated yield losses	<p>as the biology and ecology of the insect species; the genetics of resistance; the insecticidal properties of the crop; and the characteristics of the agricultural production system.</p> <p>The evolution of resistance in targeted lepidopteran pests is a potential concern that could arise from the widespread cultivation of TELA maize with MON89034 and MON87460 traits.</p> <p>However, in countries where maize with event MON89034 and MON8760 have been planted, insect resistance management (IRM) plans have been implemented to minimize the risk of insect resistance evolving to the Cry proteins. This will continue to be the case where TELA maize is grown in Nigeria. Therefore, following the deployment of maize with events MON87460 and MON89034 in Nigeria, an Insect Resistance Management (IRM) plan will be implemented. Therefore, the risk of target pests evolving resistance to the Cry proteins with the use is expected to be minimal.</p>	be compromised. Yield loss from resistance to conferred traits.	it is deemed Acceptable , if Insect Resistance Management (IRM) measures are complied with.	with an effective communication component. Follow responsible product stewardship principles for the events.
Food safety Assessment						
8.	Human & Livestock Health & Nutrition	Altered nutritional composition of the events	<p>Highly unlikely</p> <p>Information on differences in proximate content, moisture, calories, minerals or phytic acid, between grain samples collected from the event and control shows the following;</p> <p>The statistical analysis reviewed did not highlight consistent differences between sites in nutrient component levels of MON 87460, MON 89034, and controls. The limited number of differences observed in this study reflected natural variation in conventional maize and supported the equivalence in composition of MON 87460 and MON89034 proteins to conventional maize. Similarly, the statistical analysis of anti-nutrients and main secondary metabolites did not highlight consistent differences between sites in their levels in MON 87460, MON 89034, and the control. Thus, a comprehensive evaluation of the antinutrient components and major secondary metabolites</p>	<p>Minor</p> <p>Change in nutritional profile that could impact human & livestock health</p>	Acceptable, because the risk is negligible .	None

			<p>supported the compositional equivalence of MON 87460 and MON 89034 to conventional maize.</p> <p>Therefore, maize grains and forages derived from MON 87460 and MON 89034 and consequently, foods and feeds derived from MON 87460 and MON 89034, can be considered, in terms of composition, equivalent to those derived from conventional corn with a history of safe use.</p>			
9.	Potential for toxicity and allergenicity	Unsafe foods arising from consuming TELA maize	<p>Highly Unlikely</p> <p>Mice acute oral toxicity studies demonstrated that the two proteins are not acutely toxic and do not cause any adverse effects even at the highest dose levels test, which are 2072 and 2198 mg/kg body weight for Cry1A.105 and Cry2Ab2 proteins, respectively.</p> <p>Cry1A.105 and Cry2Ab2 proteins are rapidly digestible (95-99% digested in 30 seconds) in simulated gastric fluids. Proteins that are rapidly digestible in mammalian gastrointestinal systems are unlikely to be allergens when consumed.</p> <p>Cry1A.105 and Cry2Ab2 proteins do not share any amino acid sequence similarities with known allergens, gliadins, glutenins, or protein toxins which have adverse effects to mammals. Using the guidance provided by the FDA, a conclusion of “no concern” was reached for the donor organisms and the Cry1A.105 and Cry2Ab2 proteins.</p> <p>CspB is derived from <i>Bacillus subtilis</i>, a soil microorganism with a history of safe use in fermented foods and probiotics (de Boer and Diderichsen 1991; Hosoi, <i>et al.</i> 2003). <i>B. subtilis</i> is also Generally Recognized as Safe (GRAS) for use in the manufacturing</p>	<p>Marginal</p> <p>Increased toxicity levels and allergenic reactions</p>	Acceptable, because the risk is negligible.	None

			<p>of enzyme preparations to be used in food (FDA 1999). CspB homologues are also present in Bt, a soil bacterium utilized safely in protection against insect pests in food crops and in potable water (Betz, <i>et al.</i> 2000). No adverse effects were noted in a number of safety studies conducted with Bt-based pesticides, including 90-day and 2-year chronic feeding studies (McClintock <i>et al.</i> 1995; Wang, <i>et al.</i> 2015).</p> <p>The NPTII has an extensive history of safe use for biotechnology-derived crops, as demonstrated by Fuchs, <i>et al.</i> 1993. The U.S. Food and Drug Administration (FDA) considers the NPTII protein to be GRAS for use in biotechnology-derived crops (Bradford, <i>et al.</i> 2005) and has also approved its use as a food additive (FDA 1994). In addition, EPA has established an exemption from the requirement of a tolerance for NPTII and the genetic material necessary for its expression in or on raw agricultural commodities (EPA 1994). DNA is often released from plant material by normal digestion process in the gastrointestinal tract or by activities of nucleases in various organisms in the environment the probability of an organism to be exposed to DNA stretches long enough to contain intact NPTII is very low because of the abovementioned digestion and degradation processes.</p> <p>Bioinformatic evaluations of MON 87460 and MON 89034 have been conducted several times, with all reports concluding that the CspB, NPTII, Cry1A.105 and Cry2Ab2 proteins are not similar to known allergens, toxins, or other biologically active proteins; the T-DNA inserts in MON 87460 and MON 89034 do not encode amino acid sequences with similarity to known allergens, toxins, or other biologically active proteins; and any putative polypeptides at the MON 87460 and MON 89034 insert</p>			
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			junctions were not similar to known allergens, toxins, or other biologically active proteins. The food and feed products containing maize with event MON 89034 and MON 87460 are safe for human and animal consumption.			
Processing						
10.	Potential impact of the event on workers and processors	Unintended adverse effects on humans and livestock resulting from the introduction of new toxins or allergens into the food and/or feed chain	Highly Unlikely Maize with events MON87460 and MON89034 is substantially equivalent to its conventional counterpart, except for the introduced traits of drought tolerance and lepidopteran insect resistance, maize with events MON87460 and MON89034 is therefore as safe as its conventional counterpart and does not require any special handling measures. It will, therefore, be handled like any other maize because there is no potential impact on workers and processors when compared to its conventional counterpart.	Marginal, Adverse health impacts to workers/processors from exposure to Cry proteins.	Acceptable, because the risk is negligible .	None

CONCLUSION:

In summary, the review of the information submitted by the applicant and the available literature, the National Biosafety Committee (NBC) has **confirmed** that the modified traits do not confer any characteristics that will result in unintended environmental effects following environmental release.

The review also concludes that the modified events and food and feed products derived from it are as safe and nutritious for human and livestock consumption as its conventional maize varieties.

RECOMMENDATIONS:

In view of the conclusion drawn from the review above, the National Biosafety Committee (NBC) finds the intended environmental release and placing on the market of TELA maize with stacked event MON 89034 and MON 87460 as having been substantially equivalent to its non-transgenic counterpart in terms of their potential environmental impact and food and feed safety. The Committee further recommends that any *Zea mays* progeny lines derived from maize event MON 89034 and MON 87460 may also be grown and used for food, feed and processing, provided that: no maize products resulting from intra / inter-specific crosses of event MON 89034 and MON 87460 with other genetically modified (GM) events are commercialized without prior approval of the individual GM maize events; the intended uses are in line with the terms and conditions guiding the permit and it is known that these plants do not display any additional non-authorized GM traits and as a consequence, the events, MON 89034 and MON 87460 are therefore recommended for approval.

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Commented [MA1]: Similar comment as provided for Cowpea

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