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TMEC Secretariat
Mexican Section
Pachuca No. 189, 17th Floor
Colonia Condesa, Demarcación Territorial Cuauhtémoc
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Subject: Biotechnology Innovation Organization (BIO) Civil Society Participation in *Mexico - Measures concerning genetically engineered corn* (MEX-USA-2023-31-01).

Distinguished Members of the Panel,

BIO extends its gratitude to the Panel for its decision, dated December 15, 2023, granting the opportunity to submit written views aimed at assisting the Panel in evaluating the submissions and arguments put forth by the Parties in the ongoing dispute. At the outset, BIO and its member companies would like to emphasize that we recognize and respect Mexico's sovereign right to establish food safety standards and regulations in alignment with its unique cultural, economic, and environmental considerations. Nonetheless, as a member of the World Trade Organization, and a signatory to the U.S.-Mexico-Canada Agreement (USMCA), Mexico also bears a responsibility to establish food safety standards in a manner that is transparent, and grounded in sound scientific principles.[1][2] This commitment to sound science and transparency helps to ensure that national food safety standards are aligned with international obligations, thereby enabling agricultural trade, and incentivizing investment in new agricultural technologies designed to mitigate the impact of climate change and increase global food security.

The focus of our intervention centers specifically on safety considerations for food and feed derived from genetically engineered (GE) plants, specifically maize. This intervention does not address environmental risk assessment requirements, otherwise known as cultivation requirements, for GE crops. This distinction is important because Mexico currently does not have a functioning framework to allow for

[1] 28_Good_Regulatory_Practices.pdf (ustr.gov)
[2] https://www.wto.org/english/tratop_e/sps_e/spsagr_e.htm

the cultivation of GE corn, or any other GE crops, within its borders. Thus, BIO member companies do not sell, nor have they ever sold, GE corn seed for cultivation in Mexico. Furthermore, the focus of our intervention does not address the risk assessment standards and requirements for crop protection chemicals. We emphasize these points to avoid conflation of purposes of the risk assessments for GE food and feed use, environmental release of GE plants, and pesticide usage.

There are three facts that BIO wishes to call to the attention of the Panel:

1. **Mexico has well-established food and feed safety standards for the consumption and use of GE food and feed.** Mexico's regulatory requirements that allow for the consumption of GE products for use in food and feed, including maize, are outlined in the 2008 Regulations for the 2005 Law on Biosafety of Genetically Modified Organisms (the "2008 Regulations" and "2005 Biosafety Law").[3] The standards and evaluation procedures for GE food and feed, which were revised and codified in 2008, have been operational for nearly three decades, and provide a science-based framework for assessing the safety of GE products before they are introduced into the Mexican market.

   Prior to the current presidential administration in Mexico, GE food and feed safety assessments were conducted in a manner consistent with international guidelines and standards, as outlined in the 2003 CODEX Alimentarius[4] and by the Organization for Economic Cooperation and Development (OECD)[5]. In Mexico the GE food and feed safety assessment is conducted by the Federal Committee for Protection from Sanitary Risks (COFEPRIS), which is an independent regulatory agency responsible for safeguarding public health. This agency has a proven track record of thoroughly evaluating and verifying GE food and feed safety of new products. This is demonstrated by the fact that COFEPRIS has reviewed and authorized roughly 90 biotech gene traits (events) in maize between 2002 and 2019. It should be highlighted that COFEPRIS's dietary risk standards for GE foods are tailored specifically to typical Mexican diets, thus ensuring that GE products introduced to the Mexican market meet the standard of "substantial equivalence" when compared to their conventional counterparts.

2. **BIO member companies comply with the 2008 Biosafety Regulations.** In order to comply with the 2008 Regulations, seed technology companies employ a systematic approach to developing regulatory science data for GE seeds. The process of generating regulatory science data for submission to the competent Mexican authorities begins with a clear definition of risk assessment objectives and an in-depth review of existing scientific literature that may be relevant to the particular GE trait. Protocols are then validated and established for laboratory and field experiments, including for example the assessment of protein expression, composition, molecular characterization, and allergenicity and toxicity profiles.

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[3] https://conahcyt.mx/cibiogem/images/cibiogem/eng/Docs/Ing_RLBOGMs_P.pdf

[4] https://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXG%2B44-2003%252FCXG_044e.pdf

[5] OECD (1993) "Safety Evaluation of Foods derived by Modern Biotechnology" https://www.oecd.org/science/biotrack/41036698.pdf.

To enable trade within North America BIO members prepare regulatory submissions in accordance with standards set forth by the Mexican authorities. That information is rigorously analyzed by the Mexican authorities to assess the overall food and feed safety of the GE event. Under normal circumstances BIO members routinely engage with the relevant regulatory agencies in Mexico to ensure that regulatory data and information is being submitted in a manner that complies with the 2005 Biosafety Law and 2008 Regulations. Submissions to COFEPRIS requesting food and feed authorization are typically 300 pages long and include addendums of 20-40 full-length reports with additional details on the conduct of the safety studies. Post-approval, BIO members continue monitoring for any new safety information relevant to the risk assessment and report any unexpected findings relevant to safety to competent authorities in Mexico and around the world in compliance with local laws and regulations. The process is iterative, with continuous learning and improvement to align with evolving regulatory requirements and scientific advancements, ensuring the responsible deployment of GE food and feed in Mexico and around the world.

3. **The Government of Mexico has not amended or altered in any way its existing GE regulations, laws, or standards, nor has it issued new guidance related to the assessment of GE products in the context of dietary risk.** The absence of changes or additional guidance confirms that the existing GE regulatory framework and standards for evaluating the safety of GE food and feed products remains consistent with the 2008 Regulations. Moreover, the Government of Mexico has not conducted a new risk assessment, nor produced any new scientific evidence, that would justify a change to the 2008 regulations.

In an effort to facilitate a clear understanding of the scope and breadth of information requested from applicants undergoing GE food and feed safety assessments in Mexico, BIO has outlined the data and study requirements, along with brief explanations of their intended purposes (refer to Addendum 1). These are the requirements that are listed in the 2008 Regulations developed in accordance with the 2005 Biosafety Law. [6]

One important element of the data provided to COFEPRIS is a Mexico-specific dietary exposure risk assessment. Mexican human consumption data for corn and other crops comes directly from La Alimentacion de los Mexicanos [7]. Dietary assessments are extremely conservative, in that they assume that the new GE corn product alone makes up 100 percent of the corn consumed by an individual, and that there is no degradation of the newly expressed protein. It is highly unlikely that a single GE product would comprise all consumed corn foodstuffs, as many different corn sources are utilized in Mexico. In addition, preparing corn products for human consumption typically involves a processing step such as cooking or denaturing.[8] Such processing would result in proteins present in corn to be denatured or degraded, further decreasing potential exposure.

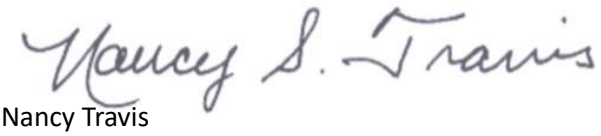
[6] https://conahcyt.mx/cibiogem/images/cibiogem/eng/Docs/Ing_LBOGM_P.pdf
[7] la_alimentacion_de_los_mexicanos_-_pedro_garcia_uriguen.pdf (jalisco.gob.mx)
[8] https://www.sciencedirect.com/science/article/abs/pii/S0278691510007398

From BIO's perspective, the primary issue at hand is that there is no scientific justification for the Mexican government to prohibit the use of GE corn in tortillas, or, for that matter in any other food or feed product. The facts are as follows: In 2008, Mexico put in place regulations consistent with international safety standards and risk assessment paradigms for GE food and feed. This system functioned in a relatively predictable and science-based manner, and was protective of Mexican consumers, for over two decades. Shortly after the current administration took office, the process for GE food and feed safety risk assessments - as implemented by COFEPRIS - became non-functional in that it ceased to perform its core duties associated with GE food and feed risk assessments. This cessation in activity was not a function of new information relevant to the safety of GE traits in corn, nor the specific use of GE corn in the making of tortillas. Indeed, Mexico has not conducted any risk assessment to justify a deviation from the existing regulations. The *Decree Establishing Various Actions Regarding Glyphosate and Genetically Modified Corn*, issued on February 13, 2023, which outlines a ban on GE products for specific food uses, and an eventual phase-out of imported corn with GE traits entirely, is therefore inconsistent with the 2008 Regulations, as it is not supported by any new scientific evidence. Given these facts, it is our conclusion that the presidential decree was not motivated based on scientific evidence, old or new.

Agricultural technologies, particularly genetic engineering, are essential to farmers' ability to meet ever-increasing global food demand, which is driven by expanding populations and changing consumer preferences. New and existing GE technologies contribute to environmental sustainability by protecting crops from disease, insects, and extreme weather conditions, while simultaneously reducing the need for fuel and chemical inputs per ton of corn produced. For society to continue to benefit from agricultural production technologies, trading partners - particularly ones bound under the standards and principles of a free trade agreement - must maintain science-based and non-trade-distorting GE policies.

We appreciate the opportunity to provide information and look forward to the Panel's decision on this critical issue.

Sincerely,



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ADDENDUM

Mexico's Food Products and Animal Feed Biosafety Regulations

Mexico mandates the submission of precise and detailed information deemed necessary for evaluating the potential risks associated with the importation and consumption of GE food and feed. The requirements for the risk assessment are described in Title Three, Chapter II of the 2008 Biosafety Regulations. This data is considered essential for evaluating the potential risks posed to human or animal health through the consumption of the genetically engineered trait being reviewed. The specific requirements of the Mexican government (**in bold**), along with brief descriptions *(in italics*) of their intended purposes, is as follows:

A) Recipient Organism (vegetal, animal or microorganism):

1. Identification – *Applicants are required to provide a clear identification of the biological entity under evaluation.*

2. Most recent taxonomic designation – *Applicants are required to provide the latest classification or categorization of the organism within the taxonomic system.*

3. Origin, history of safe use in foods, previous experience in use or consumption – *This section would ideally include details about the origin of the organism and its historical usage in food, emphasizing any established record of safe consumption.*

4. Pathogenicity associated to genders and species, any suitable evidence of the production potential of toxic compounds or anti-nutrients – *Applicants are to provide an examination of the potential harm caused by the organism, considering gender and species differences, and assessing evidence of its capability to produce harmful substances or substances that could hinder nutrition.*

5. Indication on the presence of plasmids, transposons and integrons containing antimicrobial-resistant genes- *These requirements specifically emphasize whether these elements contain genes associated with antimicrobial resistance. In the context of safety assessments, this information is important because the presence of antimicrobial-resistant genes in genetic elements is essential to evaluate the potential environmental and health risks associated with the release of GE plants. Assessing the likelihood and consequences of gene transfer events helps ensure the responsible development and deployment of biotechnological products.*

B) Information on Each Donor Organism: *This section of the assessment covers taxonomic classification, historical use, origin, and a focus on genetic elements related to antimicrobial resistance for each gene donor organism.*

1. **Most Recent Taxonomic Classification:** *Information about the most up-to-date categorization or classification of the gene donor organism within the taxonomic system.*
2. **History of Use:** *Details regarding the historical utilization of the gene donor organism, providing insights into its previous applications or consumption.*
3. **Origin:** *Information on the origin of the gene donor organism, helping to understand its natural habitat and characteristics.*
4. **Indication on the Presence of Plasmids, Transposons, and Integrons Containing Antimicrobial-Resistant Genes:** *Insight into whether the gene donor organism possesses*

specific genetic elements, such as plasmids, transposons, or integrons, which may carry genes associated with antimicrobial resistance.

C) Considerations for genetically modified microorganisms, **whether they are donors or recipients:** *This section is not applicable for Genetically Modified Organism (GMO) crops. (Note that the acronym GMO is used in this appendix, whereas GE and GM are used in other official filings.)*

D) Introduction of Genetic material: *An evaluation of introduced genetic material involves understanding its function, location, arrangement, sequence details, transformation method, regulation of gene expression, and the stability of the modification.*

1. **Function of Introduced DNA**: *Applicants are required to provide an explanation of the role and purpose of the introduced DNA in the genetically modified organism.*
2. **Location and Arrangement of Genetic Material**: *Details on where the genetic material is situated and its specific arrangement within the organism.*
3. **For every DNA that is introduced, the following shall be described: DNA sequence or restriction map, characterization of each genetic component including marking genes regulating elements, promoters, terminators and others having an effect on DNA function;** *Essentially this section requires applicants to describe the analysis of a DNA sequence or restriction map. This involves understanding and identifying different genetic components within the DNA, such as genes, regulating elements, promoters, terminators, and other elements that influence how the DNA functions. The end goal is to study the various parts of the genetic code to better comprehend how they contribute to the overall functioning of DNA.*
4. **Transformation Method and Amount of Codifier Sequences:** *A detailed account of the method used for transformation and the quantity of codifier sequences employed.*
5. **Regulation of Gene Expression:** *Information on how gene expression is regulated, including the identification of any reading frames within the inserted DNA or those created by alterations in adjacent DNA on the chromosome.*
6. **Stability of Modification:** *Assessment of the stability of the genetic modification over multiple generations.*
7. **Intermediary Host Organisms:** *Details regarding any intermediary host organisms involved in the process.*

E) Marker Gene used as an element for Organism Selection: *This section outlines considerations when a marker gene is employed for organism selection. When utilizing a marker gene for organism selection, the assessment requires an explanation for the chosen marker gene and, if it imparts antimicrobial resistance, a substantiation for its use, along with reasons for not opting for a different marker gene.*

1. **Reasons for Marker Selection:** *Explanation of the rationale behind choosing a specific marker gene for organism selection.*
2. **Use of Antimicrobial Resistance Gene as a Marker -** *If the marker gene imparts antimicrobial resistance, there must be a justification provided. Additionally, the documentation should establish the basis for not choosing an alternative marker gene.*

F) The Genetically Modified Organism (GMO): *The assessment of the GMO involves understanding the organization of inserted genetic material, characterization methods, the impact of truncated portions, analysis of genetic products or transcription, stability under processing conditions, and the characterization of designated actions on expression products. This requires applicants to provide the following data and analysis:*

1. **Organization of Inserted Genetic Material and Characterization Methods** - *Information about how the inserted genetic material is organized within the GMO and the methods employed for its characterization.*
2. **If truncated portions are inserted, details about their size and the action mechanism of the expression product for the inserted genes must be established.**
3. **Genetic products or transcription analysis or analysis of expressed products to identify any new substance that may be present in the relevant food; or in the case of organisms intended for bioremediation in the environment or public health, any side effect in GMO's biochemistry, physiology and metabolism -** *Essentially this section is aimed at checking if there are any unexpected or unknown elements in the genetic makeup or activities of these modified organisms or foods.*
4. **Stability of Genetic Construction and Expression Under Processing Conditions** - *Assessment of the stability of the genetic construction under various processing conditions and the expression of new materials or changes in native materials.*
5. **Characterization, Sensitivity, and Specificity of Designated Action on Expression Products** - *Examination of the characterization, sensitivity, and specificity of designated actions on the expression products of inserted transgenes.*

G) Whenever genetic modifications change the expression of natural constituents or metabolites, information shall be provided as to the potential side effects on the related metabolic paths: *This requirement calls for the provision of information whenever genetic modifications alter the expression of natural components or metabolites within an organism. The goal is to understand and disclose potential side effects on related metabolic pathways. The requirement of applicants is to provide information on the potential side effects that may occur in the metabolic pathways when genetic modifications lead to changes in the expression of natural constituents or metabolites within an organism.*

H) Expression of Transgenes: *This section focuses on understanding the dynamics of gene expression, the influence of genetic modifications on different plant structures, verifying the achieved effects and stability of inheritance, assessing potential effects on recipient organism genes, and detailing the size and number of detectable insertions. Data requirements include:*

1. **Gene Expression Kinetics** - *Evaluation of the kinetics of gene expression in the modified organism, understanding the patterns and dynamics based on tissues collected from GMO plants grown in multiple replicated field trials.*
2. **Expression Level in Different Plant Structures (for Vegetables)** - *Specifically for vegetables, information on the expression level at various plant structures, providing insights into how the modification influences different parts of the plant.*
3. **Demonstration whether or not the effects sought with such modification have been accomplished, and if every expressed characteristic is inherited with stability in the dissemination amount needed for their use in food production, bioremediation or public health and if they are in agreement with inheritance laws;**
4. **State if there is information suggesting that one or more genes in the recipient organism has been affected by such changes or by the genetic exchange procedure, and**
5. **Size and number of copies of all detectable insertions, both those complete and truncated insertions.**

(I) Comprehensive overview of the detection and identification methods for the GMO - *This section calls for a thorough explanation of GMO detection methods, covering infrastructure, adjuvants, primer sequences, probes, antibodies, reliability levels, and controls.*

1. **Detection and Identification Methods**- *Provide detailed information on the methods employed to detect and identify the GMO.*
2. **Infrastructure Requirements** - *Include information about the necessary infrastructure needed for accurate GMO identification.*
3. **Adjuvants for Extraction, Purification, and Material Detection** - *Specify any adjuvants required during extraction, purification, and material detection processes.*
4. **Primer Sequences and Specific Event Probes**- *Detail primer sequences and specific event probes used for detecting transgenic DNA, emphasizing sequences of at least 300 base pairs from the insertion site.*
5. **Specific Antibodies for Exogenous Protein** - *Include information on specific antibodies used to detect exogenous proteins in the GMO.*
6. **Reliability Level for Each Method** - *Describe the reliability level associated with each detection method employed.*
7. **Samples of Positive and Negative Controls** - *Samples of both positive and negative controls used in the detection process.*
8. **Genetically Modified Microorganisms**- *For genetically modified microorganisms, provide a detailed description of the identification method, ensuring clarity and grounding the selection in sensitivity, specificity, and reproducibility.*

(J) GMO as a foodstuff or intended for food processing - *Necessary information and studies required when using GMOs in food or food processing, covering product description, proposed use, changes in interaction, transgene expression, and substantial equivalence studies specific to consumption conditions in Mexico.*

1. **Product Description** - *Provide a detailed description of the GMO product.*
2. **Proposed Use and Processing Information**- *Clearly state the proposed use of the GMO, including detailed information about its processing.*
3. **Detail any changes introduced into the GMO that may alter its interaction with the alimentary matrix, the intestinal lumen, and microorganisms coexisting in the intestinal lumen.**
4. **Describe the development of transgene expression throughout the life cycle of the plant, specifying sections where the insertion is expressed**.
5. **Substantial Equivalence Studies for Use and Consumption in Mexico**- *Conduct studies to demonstrate substantial equivalence under conditions of use and consumption in Mexico. Note that a key component of Mexico's food/feed requirements is this dietary risk assessment. The concept of substantial equivalence is a key principle in the assessment of genetically modified organisms (GMO) products, particularly in the context of evaluating their safety for human consumption and the environment. Substantial equivalence suggests that a genetically modified organism and its traditionally bred counterpart are essentially similar in composition and characteristics, with no significant differences that would raise safety concerns. The concept of substantial equivalence does not imply absolute identicalness but rather a level of similarity that is deemed acceptable for safety. It provides a practical framework for risk assessment and regulatory decision-making by focusing on*

relevant characteristics and ensuring that any observed differences are scientifically justified and within the range of variations commonly found in traditionally bred organisms that have a long history of safe use.

This dietary risk assessment for corn is completed using Mexico-specific chronic consumption data obtained from La Alimentacion de los Mexicanos.[9] *The following elements are included in this assessment:*

a. **Content of true protein, non-protein nitrogen, amino acids profile.**
b. **If a new protein is introduced: presence and level at different sections of the plant, in the proposed food, consumption evidence in other foods, processing effects, biological function, digestibility.**
c. **Qualitative and quantitative composition of total lipids.**
d. **Composition of the carbohydrate fraction.**
e. **Qualitative and quantitative composition of vitamins.**
f. **Presence of antinutritional constituents.**
g. **Stability during storage, with a focus on nutrient degradation and nutriments bioavailability.**
h. **For each case, determine the impact of changes on nutritional constituents that might affect the global profile of nutrients.**

(K) Genetically Modified Microorganisms - *This section is not applicable for GMO crops.*

(L) Complete toxicity studies - *Mexico requires a comprehensive set of toxicity studies, covering severe toxicity, sub-chronic toxicity, chronic toxicity, specific studies for GMOs intended for food, and verification of transgenic proteins when utilized for bioassays. These studies are essential for evaluating potential health risks and ensuring the safety of the GMO in various contexts.*

1. **Severe Toxicity** – *Conduct and supply studies to assess severe toxicity, providing a thorough evaluation of potential adverse effects.*
2. **Subchronic Toxicity** - *Perform subchronic toxicity studies to examine the impact of the GMO over a specific period, identifying any potential subacute health risks.*
3. **Undertake chronic toxicity studies, particularly if subchronic toxicity findings indicate or suggest long-term risks associated with the expression products of transgenes. This assessment is contingent upon the intended use of the GMO, whether for human consumption, bioremediation, or public health.**
4. **In cases where GMOs are intended for food or food processing, conduct studies specifically on food constituents or any specific components that may undergo changes due to genetic modification.**
5. **Whenever transgenic protein obtained from bacterial cultures is utilized for bioassay purposes, establish proof that the protein expressed in the GMO possesses the same molecular weight and immunoreactivity as the microbial protein.**

(M) Allergenicity Studies – *Mexico requires a thorough examination of allergenicity, considering various factors such as the origin of genetic material, homology with known allergens, effects of pH and enzymatic digestion, stability against temperature, post-transduction modifications, and cross IgE*

[9] https://apiperiodico.jalisco.gob.mx/api/sites/periodicooficial.jalisco.gob.mx/files/la_alimentacion_de_los_mexicanos_-_pedro_garcia_uriguen.pdf

reactivity analysis when potential allergenicity is indicated. These studies are crucial for assessing and mitigating potential allergic risks associated with the GMO. This section outlines the requirements for comprehensive allergenicity studies associated with GMOs. The criteria used for these studies include:

1. **Origin of Transferred Genetic Material** - *Investigate the origin of the transferred genetic material to assess potential allergenicity.*
2. **Homology of Amino Acid Sequences**- *Examine the homology of amino acid sequences between the new protein and known allergens to identify any similarities that may trigger allergic reactions.*
3. **pH and Enzymatic Digestion Effects** - *Study the effects of pH and enzymatic digestion on the new protein to understand how these factors may influence allergenic potential.*
4. **Stability Against Temperature or Elaboration** - *Assess the stability of the protein against temperature or processing conditions, considering potential changes in allergenicity.*
5. **Post-Transduction Modifications**- *Investigate post-transduction modifications to understand their impact on allergenicity.*
6. **In cases where there is no homology between the transgenic protein and known allergens, but tests for enzymatic digestion, pH, and temperature stability indicate allergenic potential, provide information on cross IgE reactivity analysis between the new expression protein and a known allergen.**

(N) Events with combinations of genes: *Mexico requires information for the authorization of GMOs with combinations of genes, covering parental categorization, the procedure for obtaining the gene combination event, and importation authorization requirements, ensuring compliance with relevant laws and regulations. Key points include:*

1. **Specification of Parental Categories**-*Categorize parental events involved in the production of combinations of genes, specifying:*
    a. **Category 1: Parentals with non-related phenotypic characteristics.**
    b. **Category 2: Parentals with related characteristics but derived from different pathways or ways of action.**
    c. **Category 3: Parentals with characteristics related to the same metabolic or biosynthetic pathway.**
2. **Procedure applied to obtain the event with a combination of genes, including:**
    a. **Metabolic pathways where each codified transgenic protein acts in conjunction with the gene combination.**
    b. **Studies on the stability of inserted genes.**
    c. **Substantial equivalence studies.**

B) In the event of applications to authorize the importation of a GMO for the purposes referred to in Article 91 of the Law, the information and document evidencing that the GMO is authorized according to the laws in the country of origin, or failing which, the statement by the interested party about the nonexistence of such condition and the submittal of evidencing element supporting that the

SECRETARIAT OF HEALTH may resolve the application for authorization; *In short, the applicant is required to submit information and documents demonstrating that the GMO is authorized according to the laws in the country of origin. For BIO members, this means that an approval or authorization for food and feed use from the regulatory body in their country of origin is a pre-condition for the approval in Mexico.*