ANNEX I - ASSESSMENT OF ARTICLES CITED IN MEXICO'S INITIAL SUBMISSION CONCERNING ALLEGED ADVERSE HUMAN HEALTH EFFECTS FROM CONSUMING GE CORN[1]

PARAGRAPH	EXHBIT	SOURCE TITLE	ANALYSIS
130	MEX-118	Bernstein IL, Bernstein JA, Miller M, Tierzieva S, Bernstein DI, Lummus Z, Selgrade MK, Doerfler DL, Seligy VL. "*Immune responses in farm workers after exposure to Bacillus thuringiensis pesticides. Environ Health Perspect."*	This is a study of applicators of *Bt* sprays, not exposure to transgenic plants. This study is not relevant to *Bt* exposure through transgenic crops or food.
132	MEX-126	Séralini GE, Cellier D, de Vendomois JS. "*New analysis of a rat feeding study with a genetically modified maize reveals signs of*	This is just a statistical re-analysis of data from a biotechnology developer. This particular study is a whole-food animal feeding study, which is known to be difficult to interpret. Because these studies are so difficult to interpret, a comparative approach to safety assessment is used to specifically avoid having to rely on these kinds of studies.[2] This comparative approach is laid out in the

[1] To the extent the United States has not commented on a particular exhibit cited by Mexico in its Initial Submission, such an omission should not be interpreted as endorsement of the exhibit's credibility or relevance.

[2] In fact, directly responding to Séralini's work, the EU has dedicated three (multi-million euro) special projects to evaluate the need for such studies, and all three found that such studies were not ordinarily likely to provide useful information and did not meaningfully improve safety assessments for crops with agronomic input traits (*i.e.*, traits that affect yield, quality, and ability to resist biotic and abiotic stressors—the vast majority of GE crops on the market). D. Zeljenková et al., "Ninety-day oral toxicity studies on two genetically modified maize MON810 varieties in Wistar Han RCC rats (EU 7th Framework Programme project GRACE)," 88 ARCHIVES OF TOXICOLOGY 2289 (2014), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4247492/pdf/204_2014_Article_1374.pdf (total of 17 partners from 13 countries involved) (Exhibit USA-140); P. Steinberg et al., "Lack of adverse effects in subchronic and chronic toxicity/ carcinogenicity studies on the glyphosate-resistant genetically modified maize NK603 in Wistar Han RCC rats," 93 ARCHIVES OF TOXICOLOGY 1095 (2019), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7261740/pdf/204_2019_Article_2400.pdf ("In conclusion, in the European GRACE and G-TwYST projects a series of animal feeding trials were performed (Zeljenková et al. 2014, 2016; this study). This series of studies neither delivered a scientific basis for the 90-day animal feeding trial demanded by the European Commission to be performed for each new GM plant variety nor did it indicate that untargeted, extended feeding studies with rats fed GM plant material are of value for a final confirmation of safety. Thus, an added value of animal studies relative to the available nonanimal studies for the risk assessment of GM plants (EFSA Scientific Committee et al. 2017) was not substantiated.") (Exhibit USA-141); X. Coumoul et al., "The GMO901 Project: Absence of Evidence for Biologically Meaningful Effects of Genetically Modified Maize-based Diets on Wistar Rats After 6-Months Feeding Comparative Trial," 168 TOXICOLOGICAL SCIENCES 315 (2019), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6432862/pdf/kfy298.pdf (Exhibit USA-142); *see also* European Food Safety Authority, "Safety and Nutritional Assessment of GM Plants and Derived Food and Feed: The Role of Animal Feeding Trials," 46 FOOD & CHEMICAL TOXICOLOGY S2 (2008), https://www.sciencedirect.com/science/article/abs/pii/S0278691508000884 ("In the situation where molecular, compositional, phenotypic, agronomic and other analyses have demonstrated equivalence between the GM plant derived food and feed and their near isogenic counterpart, except for the inserted trait(s), and do not indicate the occurrence of unintended effects, experiences with GM plants modified for agronomic input

PARAGRAPH	EXHBIT	SOURCE TITLE	ANALYSIS
		hepatorenal toxicity". Arch Environ Contam Toxicol.	Codex *Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants* ("Codex Guidelines").[3] Mexico has effectively taken the least valuable study in the food safety assessment and re-evaluated it. The article does nothing to refute other data and information used in the process that are more routinely relied upon for safety assessment.
132	MEX-127	De Vendômois JS, Roullier F, Cellier D, Séralini GE. "*A comparison of the effects of three GM corn varieties on mammalian health"*. Int J Biol Sci. 2009.	This is also a re-analysis of a study conducted by a technology developer. Even if the authors' analysis were to be correct, this would only be one piece of data used in a safety assessment and typically at the exception to other more reliable studies. Moreover, Mexico's COFEPRIS already authorized the three GE corn events referenced here—MON810, MON863, and NK603—as have numerous other regulators around the world,[4] and Mexico has not offered any new analysis from COFEPRIS indicating a need to modify the original assessment, and the associated rationale.
132	MEX-128	El-Shamei, Z. S., A.A. Gab-Alla, A. A. Shatta, E. A. Moussa & A. M. Rayan. (2012). "*Histopathological Changes in Some Organs of Male Rats Fed on Genetically Modified Corn (Ajeeb YG*)". Journal of American Science.	This is only one part of a safety assessment and even the article acknowledges that point. This is a study done as part of a PhD thesis in Egypt, which approved this variety (MON810) for cultivation (and which Mexico has approved for consumption).

traits have demonstrated that the performance of 90-day feeding trials with rodents or feeding trials with target animal species have provided little if anything to the overall safety assessment (except for added confirmation of safety).") (Exhibit USA-143).

[3] Codex *Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants* ("Codex Guidelines"), sec. 3, paras. 11-12 (Exhibit USA-114).

[4] *See* COFEPRIS Safety Evaluation of MON863 (Sept. 29, 2003) (Exhibit USA-144); COFEPRIS Safety Evaluation of MON810 (Nov. 6, 2002) (Exhibit USA-145); COFEPRIS Safety Evaluation of NK603 (June 7, 2002) (Exhibit USA-146); Food and Agriculture Organization of the United Nations ("FAO") Genetically Modified ("GM") Foods Platform, MON810 (listing assessments and authorizations in Australia, Brazil, Canada, China, the EU, Indonesia, Kenya, Malaysia, Mexico, New Zealand, Paraguay, the Philippines, South Korea, Singapore, Thailand, Turkey, the United States, Uruguay, and Vietnam) (Exhibit USA-147); FAO GM Foods Platform, NK603 (listing assessments and authorizations in Australia, Brazil, Canada, Colombia, the EU, Indonesia, Iran, Japan, Malaysia, Mexico, New Zealand, Paraguay, the Philippines, South Korea, Russia, Singapore, Thailand, Turkey, the United States, and Uruguay) (Exhibit USA-148); FAO GM Foods Platform, MON863 (listing assessments and authorizations in Australia, Canada, China, Colombia, the EU, Japan, Malaysia, Mexico, New Zealand, South Korea, Russia, Singapore, Thailand, Turkey, and the United States) (Exhibit USA-149).

PARAGRAPH	EXHIBIT	SOURCE TITLE	ANALYSIS
132	MEX-129	Oraby, Hanaa; Kandil, Mahrousa; Shaffie, Nermeen; and Ghaly, Inas (2015) *"Biological impact of feeding rats with a genetically modified-based diet*" Turkish Journal of Biology: Vol. 39: No. 2, Article 11.	The test article in this study is not defined but rather is just listed as corn and soy without specifying which corn varieties. The study vaguely refers to "a laboratory diet of mainly 60% yellow maize and 34% soybeans," so it is impossible to attribute the effect seen to either corn or soy let alone a specific corn variety (none of which are defined).
132	MEX-131/132	M.A.A. Ibrahim, E.F. Okasha, "*Effect of genetically modified corn on the jejunal mucosa of adult male albino rat"*, Exp Toxicol Pathol.; Zdziarski, I.M., Carman, J.A. and Edwards, J.W. (2018) "*Histopathological Investigation of the Stomach of Rats Fed a 60% Genetically Modified Corn Diet"*, Food and Nutrition Sciences.	These are additional rat-feeding studies that are considered the least reliable information in assessing food safety of whole foods when compared to the internationally accepted approach that relies on a comparative assessment of the safety of the new food and its conventional counterpart.
132	MEX-133/134	Sagstad A, Sanden M, Haugland O, Hansen AC, Olsvik PA, Hemre GI. "*Evaluation of stress- and immune-response biomarkers in Atlantic salmon, Salmo salar L., fed different levels of genetically modified maize (Bt maize), compared with its near-isogenic parental line and a commercial suprex maize"*. J Fish Dis. 2007; Gu J, Krogdahl Å, Sissener NH, Kortner TM, Gelencser E, Hemre GI, Bakke AM. "*Effects of oral Btmaize (MON810) exposure on growth and health parameters in normal and sensitised Atlantic*	It is unclear how a study conducted on salmon, a non-mammalian animal, is relevant to human health in this dispute, nor does Mexico explain the significance of this study to human health.[5]

[5] Studies that are used to evaluate potential genotoxicity in humans are established assays using mammalian systems. Mammalian laboratory animals, such as rats, mice, and rabbits, are used given the closer biological similarities to humans. Assays using non-mammalian species are not established to inform genotoxic risk in humans.

PARAGRAPH	EXHBIT	SOURCE TITLE	ANALYSIS
		salmon, Salmo salar" L. Br J Nutr. 2013.	
132	MEX-135	Mesnage- Robin, Z-Sarah, Tenfen-Agapito, VilperteV-inicius, Renney-George, Ward- Malcolm, Séralini-Gilles Eric, O-Nodari Rubens and N-Antoniou, Michael (2016). "*An integrated multiomics analysis of the NK603 Roundup-tolerant GM maize reveals metabolism disturbances caused by the transformation process*". Nature.	This study looked at the metabolome of NK603 corn and reported: "The most pronounced metabolome differences between NK603 and its isogenic counterpart consisted of an increase in polyamines including N-acetyl-cadaverine (2.9-fold), N-acetylputrescine (1.8-fold), putrescine (2.7-fold) and cadaverine (28-fold), which depending on context can be either protective or a cause of toxicity." (p. 1). The paper also states, "Overall, whether the increased levels of cadaverine and putrescine found in the NK603 maize samples can account for the signs of potential negative health effects upon its consumption by rats, as implied by the blood/urine biochemical analysis, needs to be further analyzed in experiments using more quantitative methods." (p. 10). The author's conclusion that NK603 and its isogenic control are not substantially equivalent does not seem to be based on any objective standard as the analysis of N-acetyl-cadaverine, N-acetylputrescine, putrescine, or cadaverine is not recommended by the Organisation for Economic Co-operation and Development ("OECD") Consensus Document on the compositional analysis of corn, which provides guidance on what analytes should be measured when evaluating the food and feed safety of GE corn.[6] Of the thousands of chemicals present in corn only a few are likely to be meaningful in terms of food safety if their levels were to be changed.[7] Finally, as with other studies of this type, changes in molecular markers such as of oxidative stress, do not necessarily indicate that plant health is negatively affected.[8]

[6] OECD, "Consensus Document on Compositional Considerations for New Varieties of Maize (Zea Mays): Key Food and Feed Nutrients, Anti-Nutrients and Secondary Plant Metabolites," Table 14 (Aug. 20, 2002), https://one.oecd.org/document/env/jm/mono(2002)25/en/pdf (Exhibit USA-150).

[7] Moreover, cadavarine is often associated with rotting tissue, meaning that the increase in cadavarine could be a sign that the sample was not in good condition. This is yet another example of Mexico alleging issues but not actually taking subsequent steps to confirm that these are, in fact, food safety issues.

[8] J.E. Chambers et al., "Biomarkers as Predictors in Health and Ecological Risk Assessment," 8 HUMAN AND ECOLOGICAL RISK ASSESSMENT: AN INTERNATIONAL JOURNAL 165 (June 2010) ("[T]he degree of inhibition can be readily influenced by endogenous (*e.g.*, age) and exogenous (*e.g.*, chemical exposures) factors, and [] the degree of inhibition is not readily correlated with toxicological effects. Caution is urged, therefore, in an attempt to utilize biomarkers in the risk assessment process until more complete documentation is available on the specificity, sensitivity, and time course of changes, and on the impact of multiple exposures or the time of exposures.") (Exhibit USA-151).

PARAGRAPH	EXHBIT	SOURCE TITLE	ANALYSIS
132	MEX-136	Walsh MC, Buzoianu SG, Gardiner GE, Rea MC, Ross RP, Cassidy JP, Lawlor PG. "*Effects of shortterm feeding of Bt MON810 maize on growth performance, organ morphology and function in pigs".* Br J Nutr. 2012.	"Higher feed intake" is not necessarily an adverse health outcome. Feed conversion rates are a measure of growth performance and not necessarily safety.
132	MEX-137	Carman, J. A., et al. (2013). "*A long-term toxicology study on pigs fed a combined genetically modified (GM) soy and GM maize diet. Journal of Organic Systems."*	This study used a mixture of GE corn varieties and GE soy, and thus attributing any effects seen would be very challenging. One would not expect a credible food safety study to be performed this way with a diet that is so ill-defined with multiple variables.
132	MEX-138	Glöckner, G. & G-É. Séralini. (2016). "*Pathology reports on the first cows fed with Bt176 maize"* (1997–2002). Scholarly J. Agric. Sci.	This anecdotal paper expressly states that "it was not designed as a scientific experiment." It reports observations that can be useful in forming hypotheses, which can be further tested scientifically, but as observations do not, in and of themselves, demonstrate a safety concern.[9]
133	MEX-139	Mesnage R, Clair E, Gress S, Then C, Székács A, Séralini GE. "*Cytotoxicity on human cells of Cry1Ab and Cry1Ac Bt insecticidal toxins alone or with a glyphosate-based herbicide".* J Appl Toxicol.	This is an in vitro study in which the Cry1Ab protein was presented to cells in culture. This has limited applicability to human health because one would expect the Cry1Ab protein to be digested and broken down to its component amino acids well before it reached the kidney. This is not the type of study that would be useful to a safety assessment of a *Bt* corn variety. This study admits: "The exposure during consumption can appear low enough to avoid side effects, and whether this occurs in vivo remains to be checked." (p. 3). Cells in real life are never exposed at these concentration levels.
134	MEX-140	Monica Andreassen, Elena Rocca, Thomas Bøhn, Odd-Gunnar	This study states the opposite of what Mexico asserts.[10] In any event, the fact that pollen, plant debris, or even Cry1Ab protein may be an inhalant allergen

[9] Furthermore, contrary to what Mexico states, the referenced paper was not why Bt176 was withdrawn; the reason was the presence of an ampicillin-resistance selection marker, and ampicillin is one of the antibiotic resistance issues the EU wanted to manage. However, studies found no horizontal gene transfer to infectious bacteria from Bt176 corn. *See, e.g.*, E. Badosa et al., "Lack of detection of ampicillin resistance gene transfer from Bt176 transgenic corn to culturable bacteria under field conditions," 48 FEMS MICROBIOLOGY ECOLOGY 169 (May 2004), https://onlinelUSAibrary.wiley.com/doi/epdf/10.1016/j.femsec.2004.01.005 (Exhibit USA-152).

[10] Mexico's Initial Submission alleges "[i]mmunogenicity and allergenicity from inhalation of pollen and plant debris from GM Bt corn (MON810), as well as exposure to purified Cry1Ab proteins." Mexico's Initial Submission, para. 134 (citing MEX-140). MEX-140 states: "No anti-Cry1Ab antibodies were detected following exposure to the plant materials." (p. 521).

PARAGRAPH	EXHBIT	SOURCE TITLE	ANALYSIS
		Wikmark, Johnnie van den Berg, Martinus Løvik, Terje Traavik & Unni Cecilie Nygaard (2015) "*Humoral and cellular immune responses in mice after airway administration of Bacillus thuringiensis Cry1Ab and MON810 cry1Ab-transgenic maize"*, Food and Agricultural Immunology.	does not mean that it is unsafe when present in food. Mexico's measures focus on food, not aeroallergens. This is not the type of test typically considered in the internationally accepted Codex Guidelines.
135	MEX-141	Shen, C., Yin, XC., Jiao, BY. et al. "*Evaluation of adverse effects/events of genetically modified food consumption: a systematic review of animal and human studies"*. Environ Sci Eur 34, 8 (2022).	This is a literature review of published studies. The only human data reported was from one crossover study that is not relevant to corn because the test article was camelina.
137	MEX-142	Futuyma, D. J. (2013). "*Evolution"*. Third edition. Sunderland, Massachusetts U.S.A, Sinauer Associates, Inc. Publishers.	Mexico states: "There are mechanisms that can modify the evolutionary structure of individuals within a population, such as gene flow, which is the transfer of genes from one population to another." The United States does not dispute this statement. This is true and it is a natural phenomenon that occurs absent of genetic engineering.
138	MEX-143/144	Herrero, M., E. Ibañez, P. J. Martín-Álvarez and A. Cifuentes (2007). "A*nalysis of Chiral Amino Acids in Conventional and Transgenic Maize*" Anal. Chem; Levandi, T., C. Leon, M. Kaljurand, V. García-Cañas and A. Cifuentes (2008). "*Capillary Electrophoresis Time-of-Flight Mass Spectrometry for Comparative Metabolomics of Transgenic versus Conventional Maize*". Anal. Chem.	These phenomena—disparities in the content and chirality of amino acids and differences in the production of metabolites—typically are not themselves safety concerns.
138	MEX-145	Agapito-Tenfen, S.Z., M.P. Guerra, R.O. Nodari & O. Wikmark. (2020*). "Untargeted Proteomics-Based Approach to Investigate Unintended Changes in Genetically*	This paper identifies a potential allergenic protein in its sample set, and does not determine that the protein is an allergenic protein, contrary to what Mexico states in paragraph 138 of its Initial Submission.

PARAGRAPH	EXHBIT	SOURCE TITLE	ANALYSIS
		Modified Maize Used for Food and Feed Purposes". Preprints.	
138	MEX-146	Benevenuto, R. F., H. J. Venter, C. B. Zanatta, R. O. Nodari & S. Z. Agapito-Tenfen. (2022). "*Alterations in genetically modified crops assessed by omics studies: Systematic review and meta-analysis"*. Trends in Food Science & Technology.	This article does not present any adverse effects on plant health or food safety but rather just proposes that omics could be incorporated into a risk assessment process.
139	MEX-147	Giraldo, P. A., Shinozuka, H., Spangenberg, G. C., Smith, K. F., & Cogan, N. O. I. (2021). "*Rapid and Detailed Characterization of Transgene Insertion Sites in Genetically Modified Plants via Nanopore Sequencing"*. Frontiers in plant science.	Mexico's claim that "any modification of the genetic material of any species, have an enormous and possibly irreversible effect on the way it evolves" also applies to corn bred through traditional breeding, including native Mexican varieties. This phenomenon is not unique to GE corn.
139	MEX-148	Bushey DF, Bannon GA, Delaney BF, Graser G, Hefford M, Jiang X, Lee TC, Madduri KM, Pariza M, Privalle LS, Ranjan R, Saab-Rincon G, Schafer BW, Thelen JJ, Zhang JX, Harper MS. "*Characteristics and safety assessment of intractable proteins in genetically modified crops"*. Regul Toxicol Pharmacol, 2014.	This paper shows the exact opposite of what Mexico is arguing. Mexico alleges that "the expression of new proteins can trigger allergic reactions whose effects are not estimated in comparative analysis." The paper shows the diligence that scientists are taking to consider how to assess the potential allergenicity of proteins that may have physical characteristics that make them hard to assess by the typical processes. There is an entire annex to the Codex Guidelines that explains how to perform an allergenicity assessment.[11]
144	MEX-155	Oraby HA, Kandil MH, Hassan AAM, Al-Sharawi HA. 2014. "*Addressing the issue of horizontal gene transfer from a diet containing genetically modified components into rats tissues"*. Afr J Biotechnol.	This is a poorly performed study that lacked controls investigating whether components in common between the test and control diet would each appear in these tissues. The researchers sampled tissues of liver and brain, but did not show that the DNA was in the cells (as opposed to blood or fluid) such that when new cells were produced the new cells also had the DNA. Presence of antibiotic resistance genes in blood and fluid is not a hazard. What could possibly start to be a hazard were if it were incorporated into certain cells of the body, but the study did not show that. Further, this article vaguely refers to "laboratory chow

[11] *See* Codex Guidelines, Annex 1 ("Assessment of Possible Allergenicity") (Exhibit USA-153).

PARAGRAPH	EXHBIT	SOURCE TITLE	ANALYSIS
			containing mainly 60% of yellow maize and 34% of soybeans," so it is impossible to attribute the effect seen to either corn or soy let alone a specific corn variety.
144	MEX-156	Oraby, H.AS., Aboul-Maaty, N.AF., Al-Sharawi, H.A. et al. 2022. "*Horizontal transfer of antibiotic resistance genes into microflora and blood cells in rats fed on GM-diet"*. Bull Natl Res Cent.	This study states that "[n]one of these animal diets were labeled as genetically modified" (p. 2) but purports to show that the diets contain genetic elements often used in genetic engineering. The article states: "Animal feed samples were obtained from different animal feed suppliers in Cairo." As a result, it is not clear (i) what the test article was; (ii) whether it was, in fact, genetically engineered or how much of it was genetically engineered; (iii) where the researchers actually purchased the food; or (iv) how someone could repeat the study. A scientific study should be well-documented so that others can perform the same study and confirm the results. Given that the test material was not generally well characterized, it is very difficult to interpret this study. The study also should have had a control group that received diet without the genetic elements to show that what the authors were measuring was not an artifact of something other than the diet. The paper also does not say how the researchers chose which bacterial colonies to study after culturing 24-48 hours, or what kinds of bacteria were present. For example, it is possible that some of the bacteria could have naturally contained the antibiotic resistance markers, as some bacteria naturally contain the genes that the researchers looked for. It would have been important to rule out that the bacteria the researchers found did not naturally have the genes they were intending to detect.
145	MEX-157	ISAAA. (s/f). "*GM Events with Antibiotic resistance. International Service for the Acquisition of Agribiotech Applications.*	As Mexico notes: "At the international level, there is a record of 161 approved GM events with antibiotic resistance, several of which are edible plants, including corn with 34 events." Rather than supporting Mexico's position, these data just reinforce how inconsistent Mexico's views are compared to other regulators around the world. By Mexico's own language, regulators chose to approve events with antibiotic resistance markers more than 34 times based on scientific evidence of safety. The Codex Guidelines address how to assess the safety of antibiotic resistance markers.[12] Moreover, these antibiotic resistance markers are just "selection markers," which are tools developers use in the process of developing the transgenic crop, and not intended to confer resistance to antibiotics in the field.

[12] Codex Guidelines, sec. 5, paras. 55-58 (Exhibit USA-114).

PARAGRAPH	EXHBIT	SOURCE TITLE	ANALYSIS
146	No citation	N/A	Mexico claims, citing nothing, that "[s]ince 2013, robust scientific evidence (over 1000 human samples from four independent studies) have shown that DNA fragments large enough to carry genes from food can avoid degradation and enter the human circulatory system." This statement appears to refer to MEX-158 (below). This study does not mention that the DNA obtained from food was stably integrated into the human DNA, let alone expressing any proteins. The presence of food-origin DNA in the blood stream is not harmful, and MEX-158 does not distinguish transgene DNA from any other DNA that was present in the plant.
146	MEX-158	Spisák S, Solymosi N, Ittzés P, Bodor A, Kondor D, Vattay G, Barták BK, Sipos F, Galamb O, Tulassay Z, Szállási Z, Rasmussen S, Sicheritz-Ponten T, Brunak S, Molnár B, Csabai I. *"Complete genes may pass from food to human blood"*. PLoS One. 2013.	Mexico claims that "[S]tudies in animals (trout, goats, pigs and mice) fed GMO diets support this idea [that DNA fragments from food can enter the human circulatory system], which means that these fragments have been found in the digestive tract and leukocytes." The studies cited in this article do not appear to address consumption of GE corn (and nonmammalian trout are irrelevant as it relates to adverse effects in humans in this case). This article also did not report or evaluate stable integration into the DNA of the organism consuming it.
147-148	MEX-044	Chávez, C., Virgen-Ortiz, J. J., Serrano-Rubio, L. E., Martínez-Téllez, M. A., & Astier, M., "*Comparison of nutritional properties and bioactive compounds between industrial and artisan fresh tortillas from corn landraces*", 2020, Current Research in Food Science.	Mexico claims that "GM corn has reduced levels of protein, fiber and antioxidants compared to native corn varieties." The cited article does not even address GE corn. The article discusses blue tortillas, white tortillas, and industry-made tortillas. The "BT" referred to in this article refers to blue tortillas. Similarly, Mexico claims: "GM corn has demonstrated marked disparities in its levels of macronutrients, micronutrients and essential minerals compared to native corn," citing this article. Again, this article does not investigate GE corn, but rather it focuses on nutritional value of tortillas made from blue corn, white corn, or industrial corn. The article provides no evidence to indicate where the corn is sourced from or whether any of the corn is GE.
148	MEX-049	De la Parra, C., Serna Saldivar, S. O., & Liu, R. H. "*Effect of processing on the phytochemical profiles and antioxidant activity of corn for production of masa, tortillas, and tortilla chips*, 2007,	Mexico alleges that "[s]ince [GE corn] come[s] mostly from commercial hybrid lines of corn, they have a lower amount of phenolic compounds and anthocyanins and, therefore, a lower antioxidant capacity," citing this article. This article is about the processing of corn in general and is not specific to GE corn. Whether GE or not, most commercialized corn varieties are hybrid varieties.

PARAGRAPH	EXHBIT	SOURCE TITLE	ANALYSIS
		Journal of Agricultural and Food Chemistry.	
149	MEX-068	Steven A. Abrams, Jaclyn Lewis Albin, Philip J. Landrigan. Committee on nutrition, council on environmental health and climate change. (2023). "*Use of Genetically Modified Organism (GMO)-Containing Food Products in Children. Pediatrics."*	Mexico cites this article as support for the contention that GE foods are used to produce large quantities of nutritionally-deficient "ultra-processed foods." This article suffers from numerous deficiencies. Although the article claims "widespread use of GMO ingredients in food, including nearly all ultra-processed foods in the United States," there is not a clear equivalency to the use of GE-derived ingredients and "ultra-processed" foods, and the article does not cite any scientific studies to support such equivalency. In addition, this paper places undue emphasis on the International Agency for Research on Cancer ("IARC") classification of glyphosate as "probably carcinogenic to humans" in 2015 (*see also* analysis of this IARC classification in MEX-301, below). The article does not acknowledge that IARC did not assess the risks of glyphosate residues on or in food but simply identified the hazards potentially associated with glyphosate in general, without consideration of exposure levels. Nor does the article acknowledge that subsequent to the IARC classification, the joint Food & Agriculture Organization of the United Nations ("FAO")/World Health Organization ("WHO") Meeting on Pesticide Residues ("JMPR") considered the body of evidence for cancer outcomes for glyphosate, including the studies reviewed by the IARC and additional relevant studies, and still concluded that glyphosate "is unlikely to pose a carcinogenic risk to humans via exposure from the diet."[13] This article also does not acknowledge the conclusions of multiple global regulatory authorities and experts that glyphosate is not likely to be carcinogenic to humans (*see* analysis of MEX-301, below). Finally, the article implies that consumption of GE products is inherently associated with increased pesticide exposures and that exposure to pesticide residues inherently means there is increased risk. These implications relate to a misunderstanding, or lack of awareness, of pesticide tolerances and the rigorous assessments that support those determinations. The article also ignores that pesticides may be used on both GE and non-GE crops (*see* Annex II, concerning agrochemical usage and GE crops). The risk of an exposure depends on the toxicity of the compound and the type and amount of exposure. It is not accurate

[13] Joint FAO/WHO Meeting on Pesticide Residues ("JMPR"), "Pesticide Residues in Food – 2016: Toxicological Evaluations," at 257 (May 2016) (Exhibit USA-154). When glyphosate was last evaluated by JMPR in 2019, the Meeting concluded that acute and long-term dietary exposures to residues of glyphosate are unlikely to present a public health concern for the uses considered by JMPR. Extra Joint FAO/WHO Meeting on Pesticide Residues, "2019 Report – Pesticide Residues in Food," at 81 (2019) (Exhibit USA-155).

PARAGRAPH	EXHBIT	SOURCE TITLE	ANALYSIS
			to imply that any exposure to glyphosate residues in one's diet necessarily results in an increase in risk of adverse health effects, as the United States further explains in Section IV.A of its Rebuttal.
150	MEX-160	Matos, R.A., Adams, M., Sabaté J. (2021). "*Review: The consumption of ultra-processed foods and noncommunicable diseases in Latin America"*. Frontiers in Nutrition.	Mexico asserts that "[t]he impact of these ultra-processed foods on the Mexican diet is alarming." Genetic engineering has nothing to do with ultra-processed foods, to the extent the latter is even a health issue. Foods well beyond corn can be used as ingredients in ultra-processed products, such as wheat, canola, cottonseed, and even sugar, and is not something unique or specific to genetic engineering. This article does not discuss information about corn, let alone GE corn.
181	MEX-217	Krimsky, S. (2015). "*An Illusory Consensus behind GMO Health Assessment."* Science, Technology & Human Values.	Mexico, in claiming that "[t]he safety of GMOs is completely illusory," is simply reiterating the title of the paper, which is emotive. The author provides a review of the literature, much of which has shown no negative health impacts of GE foods and feed, and uses a methodology that is ill-defined but appears to be the result of keyword searches.
181	MEX-218	Hilbeck, A., Binimelis, R., Defarge, N. et al. "*No scientific consensus on GMO safety"*. Environ Sci Eur 27, 4 (2015).	This is a statement purportedly signed by 300 researchers (who are not listed in this paper); it is not a research article. The main point of this paper is that a blanket statement of food and environmental safety for all GMOs cannot be made and thus the Cartagena Protocol on Biosafety and Codex advocate for reviews on a case-by-case basis. If Mexico agrees with this statement, then Mexico should conduct a case-by-case risk assessment, as the United States argued in its Initial Submission and this Rebuttal. The statement relies on multiple Séralini studies (*see* Section II.A of U.S. Rebuttal) and also cites blog posts, some of which no longer exist, as well as Wikipedia.
185	MEX-225	Séralini GE, Clair E, Mesnage R, Gress S, Defarge N, Malatesta M, Hennequin D, de Vendômois JS. Republished study: "*long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified corn"*. Environ Sci Eur. 2014.	This is a republication of Séralini's retracted 2012 study (*see* Section II.A of U.S. Rebuttal). The study concludes: "Our findings imply that long-term (2 year) feeding trials need to be conducted to thoroughly evaluate the safety of GM foods and pesticides in their full commercial formulations." The EU has thoroughly evaluated the need for such feeding trials and has uniformly concluded across three comprehensive studies that they are not routinely warranted.[14] The value of long-term studies has also been refuted by Codex since 2003.[15]

[14] *See supra* Analysis of MEX-128.

[15] Codex Guidelines, sec. 3, para. 11-12 (reflecting consensus that animal studies, including long-term animal studies, are not widely accepted to assess the safety of whole foods and are extremely difficult to interpret) (Exhibit USA-114). As of March 2024, the United States has completed more than 200 evaluations of food from genetically engineered or genome edited plants and has not yet seen a need to request such a study.

PARAGRAPH	EXHBIT	SOURCE TITLE	ANALYSIS
			Moreover, the journal provides a disclaimer that it is republishing the study for transparency but disclaims its contents: "ESEU aims to enable rational discussions dealing with the article from G.-E. Séralini et al. (Food Chem. Toxicol. 2012, 50:4221–4231) by re-publishing it. By doing so, any kind of appraisal of the paper's content should not be connoted. The only aim is to enable scientific transparency and, based on this, a discussion which does not hide but aims to focus methodological controversies." (p. 2).
193	MEX-085 (citing MEX-125)	CONAHCYT, "*Scientific Record on Glyphosate and GM Crops*", 2020 (in turn citing González-Ortega, E., Piñeyro-Nelson, A., Gómez-Hernández, E., Monterrubio-Vázquez, E., Arleo, M., Dávila-Velderrain, J., Martínez-Debat C. y Álvarez-Buylla E. R., "*Pervasive presence of transgenes and glyphosate in corn-derived food in Mexico*", 2017).	MEX-125 is not a risk assessment of glyphosate (or of dietary exposure to glyphosate) but rather focuses on identifying transgenes and glyphosate in Mexico. This paper is a snapshot in time at a specific location of a limited number of processed maize-based food samples (as opposed to raw agricultural commodity samples) pulled from a marketplace and tested for the presence of transgenes and glyphosate residues. Due to the methods used, the presence of glyphosate cannot be conclusively connected to the application of glyphosate to glyphosate-tolerant corn. Glyphosate is used extensively, and there are many potential sources along the value chain. The glyphosate residues detected are well below the trade standard maximum residue limits ("MRLs"). The majority of the transgene-containing samples contained no detectable glyphosate residues at all, according to the analytical methods in the study. Risk is a function of exposure and toxicity, and the presence of residues alone does not equate to risks.

ANNEX II - ASSESSMENT OF STATEMENTS IN MEXICO'S INITIAL SUBMISSION CONCERNING AGROCHEMICAL USAGE AND GE CROPS[16]

PARAGRAPH	ALLEGATION	ANALYSIS
92	"A systemic herbicide (and the contaminants or toxins into which it can be broken down within the plant) cannot be 'washed out' because it accumulates within the plant itself."	This is not accurate. Glyphosate is rapidly metabolized in plants and does not persist in the organism.[17]
93	"GMO do not reduce the amount of agrochemicals."	This is a highly nuanced space, and context is key. Studies have actually found that herbicide use has risen more quickly with non-GE crops than GE crops.[18] However, usage alone is not a good measure, because the toxicity of each pesticide is not directly related to the amount (weight) applied and there is no consideration of how the active ingredients disperse into the environment.[19] When the environmental impact quotients ("EIQ") are calculated—a measure incorporating the amounts applied and their relative toxicity to particular environmental indicators such as fish or pollinators—there is a net decrease in the EIQ with GE crops.[20] The chronic toxicity for herbicides used in maize remained unchanged between 1990 and 2015 (even while acre treatments increased), and acute toxicity for herbicides used in maize fell 88% over this same time period, largely because glyphosate replaced older and more toxic herbicides previously used more widely.[21]

[16] To the extent the United States has not commented on a particular statement by Mexico in its Initial Submission, such an omission does not imply an endorsement of the statement's credibility or accuracy.

[17] *See, e.g.*, S. Duke, "Enhanced Metabolic Degradation: The Last Evolved Glyphosate Resistance Mechanism of Weeds?," 181 PLANT PHYSIOLOGY 1401 (2019) (Exhibit USA-156).

[18] *See, e.g.*, A. Kniss, "Long-term Trends in the Intensity and Relative Toxicity of Herbicide Use," NATURE COMMUNICATIONS (Apr. 2017) (Exhibit USA-157).

[19] *See* G. Brookes, "Genetically Modified (GM) Crop Use 1996–2020: Environmental Impacts Associated with Pesticide Use Change," 13 GM CROPS & FOOD – BIOTECHNOLOGY IN AGRICULTURE AND THE FOOD CHAIN 262, 264 (2022), https://www.tandfonline.com/doi/epdf/10.1080/21645698.2022.2118497?needAccess=true&role=button (Exhibit USA-46).

[20] *Id.* at 277 (finding that, between 1996 and 2020, the widespread use of insect-resistant and herbicide-tolerant seed technology reduced pesticide application by 748.6 million kilograms (-7.2 percent) and, as a result, decreased the environmental impact associated with insecticide and herbicide use on these crops by 17.3 percent) (Exhibit USA-46).

[21] A. Kniss, "Long-term Trends in the Intensity and Relative Toxicity of Herbicide Use," NATURE COMMUNICATIONS, at 3 (Apr. 2017) (Exhibit USA-157).

PARAGRAPH	ALLEGATION	ANALYSIS
94	"Bt technology has also failed to reduce the use of insecticides."	Mexico cites nothing to support this statement, and it is simply not true.[22]
94	"[T]he insecticidal toxins produced by GM plants have led to the development of resistance in pest insects, which would indicate that Bt technology is environmentally and agronomically unsustainable."	The scientific community has always known that *Bt* resistance was going to occur. Resistance to *Bt* powders in diamondback moth was first reported in 1990, and resistance management has always been part of GE corn and cotton production.[23]
158	"[G]lyphosate is a highly dangerous pesticide and this is irrefutable."	Mexico cites the U.S. Environmental Protection Agency's ("EPA") "Draft National Level Listed Species Biological Evaluation for Glyphosate," which does not lead to the conclusion that Mexico alleges. EPA submitted a "Final National Level Listed Species Biological Evaluation for Glyphosate" to the U.S. Fish and Wildlife Service and National Marine Fisheries Service to initiate formal consultation under section 7 of the Endangered Species Act. This document is not relevant for a human health risk assessment and is limited in scope to potential impacts on endangered and threatened animal and plant species and their critical habitats from the application of glyphosate and subsequent exposure to non-target wildlife and plants within the United States. The purpose of this document was not to determine if glyphosate is "dangerous" for purposes of a human health risk assessment.[24]
161	"[T]he main function of GM corn is to tolerate greater amounts of herbicides, specifically glyphosate. This means that direct consumption of GM corn results in	It is incorrect to assume that plants that are tolerant to glyphosate automatically will have higher residues of glyphosate in the edible plant parts. The amount of pesticide applied, and the timing of application both impact residue levels. An example of this can be seen in the glyphosate residue data that the JMPR

[22] *See, e.g.*, E. D. Perry et al., "Genetically Engineered Crops and Pesticide Use in U.S. Maize and Soybeans," 2 SCIENCE ADVANCES 1 (Aug. 2016), https://www.science.org/doi/pdf/10.1126/sciadv.1600850 (finding that adopters of GE insect-resistant (Bt) maize used 11.2 percent (0.013 kilogram per hectare) less insecticide than nonadopters) (Exhibit USA-47).

[23] *See, e.g.*, B. Tabashnik, "Evolution of Resistance to *Bacillus Thuringiensis*," 39 ANNUAL REVIEW OF ENTOMOLOGY 47 (1994) (Exhibit USA-158).

[24] For additional context, EPA's Biological Evaluations are by design very conservative in nature and rely on the worst-case exposure scenarios (maximum application rates, shortest application intervals, maximum number of applications per year). The objective of a Biological Evaluation is to make the determination as to whether use of glyphosate is Not Likely to Adversely Affect or Likely to Adversely Affect each of the 1,795 threatened and endangered species in the United States. EPA's threshold for this determination is effects to a single individual of a given population of threatened or endangered species. Separate analyses are then carried out to determine if there are likely to be population-level effects. The exposure assumptions are very high, because the evaluation uses extremely conservative model inputs, and the bar for effects to threatened and endangered species is extremely low. This document does not have anything to do with glyphosate exposure from human dietary consumption (or any other form of human exposure), let alone human health risk from consuming GE corn.

PARAGRAPH	ALLEGATION	ANALYSIS
	consuming a product that has been exposed to a greater amount of an herbicide[.]"	reviewed in 2005 (concerning conventional and glyphosate-tolerant maize) and 2011 (glyphosate-tolerant maize only). In 2005, the recommended MRL of 5.0 ppm was based on the conventional maize data. The 2011 meeting reconfirmed the previous MRL recommendation of 5.0 ppm because the dataset of conventional maize actually gave rise to a higher maximum residue level.[25] Residue levels are primarily a function of how glyphosate is used and not whether the crop is glyphosate-tolerant. From a dietary exposure and risk perspective, what matters is the potential residue level at the consumption point, not how much was applied in the field, and both GE and conventional corn can be treated with glyphosate.
182	"GBHs of commercial brands such as *Roundup* contain toxic agents such as petroleum derivatives and heavy metals."	The cited studies (MEX-219 & MEX-220) do not demonstrate actual risk upon consumption of the food products at biologically relevant levels.
191	"[A]pplication of glyphosate causes native corn to become even more exposed to insect pests."	The cited study (MEX-234) merely postulated this and did not present data.

[25] JMPR, "Pesticide Residues in Food 2005," at 129-130, 144 (2005) (Exhibit USA-159); JMPR, "Pesticide Residues in Food 2011," at 155, 159 (2011) (Exhibit USA-160).

ANNEX III - ASSESSMENT OF EXHIBITS IN MEXICO'S INITIAL SUBMISSION ALLEGING GLYPHOSATE EXPOSURE[26]

PARAGRAPH	EXHIBIT	SOURCE TITLE	ANALYSIS
165	MEX-183/184	Krüger. M. et. al. (2014). "*Detection of Glyphosate Residues in Animals and Humans".* Environ Anal Toxicol 2014/ Krüger. M. et. al. (2013). "*Field Investigations of Glyphosate in Urine of Danish Dairy Cows"*. Environ Anal Toxicol 2013.	The presence of glyphosate in excreta does not mean there is an adverse health effect; elimination is expected.[27] To the extent residues appear in animal tissue, Codex and the United States (as well as other countries) have set MRLs for residues of glyphosate in meat byproducts (including liver and kidney). Neither MEX-183 nor MEX-184 analyzed samples of food or feed for residues of glyphosate or provided information how much (or the types) of food/feed was consumed by the livestock. Additionally, there are other limitations to the utility of these studies including that not all of the data were shown and the data were presented graphically. MEX-183 provided limited information (a graph) about residues observed in several livestock tissue samples. The highest levels were in lung tissue and were well below the Mexican and U.S. tolerance levels for residues of glyphosate in meat byproducts (1 ng/g = 0.001 ppm) and therefore would not be considered a risk of concern.
406	MEX-301	IARC, "*Monograph on Glyphosate*", 2015.	The IARC report is not a risk assessment. The IARC is a cancer agency within the WHO whose purpose is to "identif[y] and classif[y] hazards," *i.e.*, to assesses whether a chemical product is capable of producing harm and what harm it may produce.[28] The IARC's work constitutes "hazard identification"—

[26] To the extent the United States has not commented on a particular exhibit cited by Mexico in its Initial Submission, such an omission does not imply an endorsement of the exhibit's credibility or accuracy. As noted in the U.S. Rebuttal Submission, Mexico cited a large volume of studies that have nothing to do with glyphosate exposure through dietary consumption, let alone through consumption of GE corn. *See, e.g.*, Sections V.D.1.c, V.D.2.a, V.D.2.b.1, V.D.2.c. Nevertheless, in the interest of reinforcing the lack of relevance of Mexico's cited support, the United States will address certain exhibits that Mexico cited in relation to its Article 9.6.8(a) arguments, concerning its "risk assessment." *See* Mexico's Initial Submission, Section VII.E.4.

[27] A common, but erroneous, conclusion from biomonitoring data is that low levels of a chemical in a biological sample (*e.g.*, urine, blood) will be harmful to humans; however, detection is not equivalent to risk. Biomonitoring data requires conversion to estimated external dose levels in order to evaluate whether potential risks may exist. For instance, urinary glyphosate levels have been reported by several organizations and research groups, including the U.S. Centers for Disease Control and Prevention. Detection is expected given how glyphosate enters, distributes, breaks down, and exits the body. When converted to external doses, the estimated doses associated with these urinary levels are orders of magnitude lower than the current dietary reference dose (*i.e.*, the maximum acceptable oral dose of a substance, below which no adverse health effects should result from a lifetime of exposure).

[28] *See* Pan American Health Organization ("PAHO"), "Questions and Answers on the Use Diazinon, Malathion and Glyphosate" (Sept. 2015), https://www.paho.org/en/documents/questions-and-answers-use-diazinon-malathion-and-glyphosate-2015 (Exhibit USA-161).

PARAGRAPH	EXHIBIT	SOURCE TITLE	ANALYSIS
			the first step in a "risk assessment."[29] A "risk assessment" would go on to evaluate exposure and characterize the overall level of risk.[30] The FAO/WHO JMPR is responsible for these subsequent steps and assesses the risk of pesticide residues in and on food.[31] The IARC did not assess the exposure and risks associated with glyphosate residues in or on food; instead, it identified and characterized the hazards potentially associated with glyphosate exposure, without consideration of exposure levels. The IARC report simply found that, at some level of exposure, glyphosate probably had the potential to increase the risk of a particular type of cancer (non-Hodgkin's lymphoma) in humans. The release of the IARC report expressly indicated that the IARC findings were neither a risk assessment nor a modification of the technical instructions for glyphosate.[32] Subsequently, the JMPR (the FAO/WHO pesticide risk assessment body) considered the body of evidence for cancer outcomes for glyphosate, including the studies reviewed by the IARC and additional relevant studies, and concluded that glyphosate "is unlikely to pose a carcinogenic risk to humans via exposure from the diet."[33] International expert panels and regulatory authorities—including the U.S. EPA[34], Australian Pesticide and

[29] *See id.* at 3 (Exhibit USA-161); *see also* Panel Report, *European Communities – Measures Concerning Meat and Meat Products (Hormones), Complaint by the United States*, WT/DS26/R/USA, para. 8.103 (adopted Feb. 13, 1998) (Exhibit USA-162).

[30] *Id.* (Exhibits USA-161 & USA-162).

[31] PAHO, "Questions and Answers on the Use Diazinon, Malathion and Glyphosate," at 1 (Sept. 2015), https://www.paho.org/en/documents/questions-and-answers-use-diazinon-malathion-and-glyphosate-2015 ("JMPR is an international scientific group of experts administered jointly by the Food and Agriculture Organization of the United Nations (FAO) and WHO, tasked with evaluating the risk associated with pesticide residues in food and elsewhere. It is also known as the Joint FAO/WHO Meeting.") (Exhibit USA-161).

[32] *Id.* (Exhibit USA-161).

[33] JMPR, "Pesticide Residues in Food – 2016: Toxicological Evaluations," at 257 (May 2016) (Exhibit USA-154).

[34] U.S. Environmental Protection Agency ("EPA"), "Human Health Risk Assessment in Support of Registration Review" (Dec. 12, 2017) (Exhibit USA-164); EPA Office of Pesticide Programs, "Revised Glyphosate Issue Paper: Evaluation of Carcinogenic Potential" (Dec. 12, 2017) (Exhibit USA-173). In the United States, existing pesticides must be re-evaluated periodically to ensure that they continue to meet the appropriate safety standard, a process known as registration review. In December 2017, as part of glyphosate's ongoing registration review, EPA conducted a comprehensive human health risk assessment of glyphosate that considered hazard and exposure data, including an in-depth review of all relevant animal carcinogenicity and genotoxicity studies for the active ingredient glyphosate, as well as epidemiological studies that investigated potential cancer outcomes from using pesticide products containing glyphosate. EPA's risk assessment process combines hazard, dose-response, and exposure assessments to describe the overall risk from glyphosate. EPA's independent evaluation of the available scientific data for glyphosate found no risks of concern to human health when used in accordance with the current label instructions; found no indication that children are more sensitive to glyphosate; concluded that glyphosate is "not likely to be carcinogenic" to humans; and concluded that glyphosate

PARAGRAPH	EXHIBIT	SOURCE TITLE	ANALYSIS
			Veterinary Medicines Authority[35], Canadian Pest Management Regulatory Agency[36], European Food Safety Authority[37], European Chemicals Agency[38], German Federal Institute for Risk Assessment[39], New Zealand Environmental Protection Authority[40], and the Food Safety Commission of Japan[41]—have all found the available data on glyphosate sufficiently robust for deciding that there is no basis for human hazard concern with respect to this herbicide. The IARC Monograph's conclusion is not consistent with any other international organization or regulatory authority that has evaluated the carcinogenic potential of glyphosate.
406	MEX-305	Martin, E., "*Glyphosate Toxicological Anthology*", 2020.	This is simply an annotated bibliography based on keyword searches of several databases of scientific journals. This is not a risk assessment nor do any of the listed titles present an appropriate assessment of risk from consuming GE corn that may have glyphosate residues.
407	MEX-304	ATSDR U.S. Department of Health and Human Services. "*Agency for*	Mexico incorrectly states that the ATSDR toxicological profile makes findings that are consistent with the IARC Monograph (*see* analysis of MEX-301

does not interact with the thyroid, estrogen, or androgen signaling pathways based on a weight-of-evidence review. EPA anticipates issuing its final registration review decision on glyphosate in 2026. As part of registration review, EPA intends to revisit and further explain its evaluation of the carcinogenic potential of glyphosate, but the underlying scientific findings regarding glyphosate, including its finding that glyphosate is not likely to be carcinogenic to humans, currently remain the same. *See* EPA, "Glyphosate" (Sept. 2023), https://www.epa.gov/ingredients-used-pesticide-products/glyphosate (Exhibit USA-174).

[35] Australian Pesticides & Veterinary Medicines Authority, "Final Regulatory Position: Consideration of the Evidence for a Formal Reconsideration of Glyphosate" (Mar. 2017), https://www.apvma.gov.au/sites/default/files/publication/26561-glyphosate-final-regulatory-position-report-final_0.pdf (Exhibit USA-175); *see also* Australian Pesticides & Veterinary Medicines Authority, "Glyphosate" (last updated Oct. 2023), https://www.apvma.gov.au/resources/chemicals-news/glyphosate ("Glyphosate has also been assessed by other government regulators and independent scientists around the world. These assessments consistently found that glyphosate has low toxicity for humans, animals, fish, insects (including bees) and other invertebrates.") (Exhibit USA-176).

[36] Canada Pest Management Regulatory Agency, "Glyphosate – Re-evaluation Decision" (Apr. 2017), https://publications.gc.ca/collections/collection_2017/sc-hc/H113-28/H113-28-2017-1-eng.pdf (Exhibit USA-177).

[37] European Food Safety Authority ("EFSA"), "EFSA Explains the Scientific Assessment of Glyphosate" (July 2023), https://www.efsa.europa.eu/sites/default/files/2023-07/glyphosate_factsheet.pdf (Exhibit USA-178).

[38] European Chemicals Agency, "EU Glyphosate Renewal - Risk Assessment Committee opinion" (May 30, 2023), https://www.glyphosate.eu/grg/whatsnew/eu-glyphosate-renewal-risk-assessment-committee-opinion/ (Exhibit USA-179).

[39] German Federal Institute for Risk Assessment, "WHO/FAO committee (JMPR) re-assesses glyphosate and confirms the BfR and EFSA conclusion that a carcinogenic risk is not to be expected" (May 2016), https://www.bfr.bund.de/cm/349/who-fao-committee-jmpr-re-assesses-glyphosate-and-confirms-the-bfr-and-efsa-conclusion-that-a-carcinogenic-risk-is-not-to-be-expected.pdf (Exhibit USA-180).

[40] New Zealand Environmental Protection Authority, "Review of the Evidence Relating to Glyphosate and Carcinogenicity" (Aug. 2016), https://www.epa.govt.nz/assets/Uploads/Documents/Everyday-Environment/Publications/EPA-glyphosate-review.pdf (Exhibit USA-181).

[41] Food Safety Commission of Japan, "Glyphosate – Summary" (Sept. 2016), https://www.jstage.jst.go.jp/article/foodsafetyfscj/4/3/4_2016014s/_pdf/-char/en ("Glyphosate had no neurotoxicity, carcinogenicity, reproductive toxicity, teratogenicity, and genotoxicity.") (Exhibit USA-182).

PARAGRAPH	EXHIBIT	SOURCE TITLE	ANALYSIS
		Toxic Substances and Disease Registry. Toxicological Profile for Glyphosate", 2020.	above). Although the glyphosate ATSDR toxicological profile summarizes current studies and conclusions from other organizations and regulatory authorities related to carcinogenic potential, ATSDR did not conduct an independent cancer evaluation and merely referenced the IARC classification alongside summarizing other studies. Mexico similarly alleges that the ATSDR shows a "strong correlation between exposure" and certain adverse effects (Mexico's Initial Submission, para. 406) without any consideration of the doses where the effects were observed.
408	MEX-306	Vandenberg, L.N., Colborn, T., Hayes, T.B., Heindel, J.J., Jacobs, Jr., D.R., Lee, D.H., Shioda, T., Soto, A.M., vom Saal, F.S., Welshons, W.V., Zoeller, R.T. y Peterson Myers, J. "*Hormones and Endocrine-Disrupting Chemicals: Low-Dose Effects and Nonmonotonic Dose Responses*" 2012.	This study does not have anything to do with GE corn. Mexico claims: "Data and information from animal studies and human cell studies suggest that exposure to low doses of glyphosate effects hormone levels and reproductive systems, leading to endocrine disruption." The cited study does not describe glyphosate in depth, and only mentions it among others in Table 6 (where it is erroneously referred to as "glyphosphate"). It is unclear what methods or levels of exposure are being addressed, or the details of the alleged findings.
408	MEX-307	Ingaramo, P., "*Are glyphosate and glyphosate-based herbicides endocrine disruptors that alter female fertility*?".	This study does not have anything to do with GE corn. This is a review article, with no new data presented. The overall conclusions of this article are unclear.[42]
408	MEX-308	Davico, C. E, Pereira, A.G., Nezzi, L., Jaramillo, M.L., de Melo, M.S., Müller, Y.M.R., y Nazari, E.M., "*Reproductive toxicity of Roundup WG® herbicide: impairments in ovarian follicles of model organism Danio rerio*".	This study used a formulated product (Roundup WG® (RWG)), and dose concentrations appear to be based on the formulated product, as opposed to glyphosate. As such, potential effects cannot be attributed to glyphosate exposure.
408	MEX-431	Masood, M.I, Mahrukh Naseem, S., Warda, A., Tapia-Laliena, M.A., ur Rehman, H., Nasim, M.J. and	The study examined isolated stem cells from animals not exposed to the compound. The cells were exposed in vitro in a petri dish. The test compound was the technical grade material, and not the formulated product. This is not a

[42] In addition to the lack of relevance, this study discusses reproductive effects observed in a study by Almeida et al. (2017) where rodents were exposed to 500 mg/kg of a glyphosate-containing product, which is considered relatively high for mammalian toxicological studies and would not typically be considered relevant for a human health risk assessment. This study does not report effects at doses that would be considered "low levels," contrary to what Mexico asserts. *See* Mexico's Initial Submission, para. 408.

PARAGRAPH	EXHIBIT	SOURCE TITLE	ANALYSIS
		Schäfer, K.H., "*Environment permissible concentrations of glyphosate in drinking water can influence the fate of neural stem cells from the subventricular zone of the postnatal mouse*".	risk assessment of dietary exposure to glyphosate, nor does this study have anything to do with GE corn.
408	MEX-310	Kubsad, D., Nilsson, E.E., King, S.E., Sadler-Riggleman, I., Beck, D. and Skinner, M.K., "*Assessment of Glyphosate Induced Epigenetic Transgenerational Inheritance of Pathologies and Sperm Epimutations: Generational Toxicology*," in "*Scientific Reports."*	This study found no effects in the parental or first generation following intraperitoneal (gut) injections to gestating rats, but effects on the second and third generations in terms of ≥1 disease at one year of age—however, there was no clear pattern when looking at any one disease. This is not a risk assessment of dietary exposure to glyphosate through dietary consumption of GE corn.
408	MEX-311	Wilson, VS, Bobseine, K, Lambright, CR, Gray, LE Jr., "*A novel cell line, MDA-kb2, that stably expresses an androgen- and glucocorticoid-responsive reporter for the detection of hormone receptor agonists and antagonists."*	Mexico falsely alleges that "[t]he endocrine involvement of exposure to low doses of glyphosate in humans was demonstrated by assays in MDA-kb2 cell lines that allow the detection of hormone receptor antagonists, and in placental JEG3 cell lines." The cited study (MEX-311) does not even mention glyphosate. This study also does not reference GE corn.
408	MEX-312/207/193	Richard S., Moslemi S., Sipahutar H., Benachour N., Séralini G-E., "*Differential effects of glyphosate and roundup on human placental cells and aromatase*", 2005/Mesnage, R., Bernay, B., Séralini, G.E. (2013). "*Ethoxylated adjuvants of glyphosate-based herbicides are active principles of human cell toxicity"*. Toxicology/ Benachour, N. y Séralini, G.E. "*Glyphosate Formulations Induce Apoptosis and Necrosis in Human*	These studies expose isolated cells to technical grade glyphosate and formulated RoundUp. There is no discussion if the concentrations tested are likely to be relevant to circulating levels of glyphosate within an organism. Ingested or absorbed pesticides do not circulate within the organism at the concentration they are exposed to; rather, the concentration is usually significantly less. These studies are not a dietary risk assessment, nor do they have anything to do with consumption of GE corn. In fact, none of the articles Mexico has cited has had a comparison of the concentrations causing effects on cells in a petri dish to what concentrations are circulating in the body following exposure. Without that information, one cannot say if the tested concentrations have any relevance to real-world exposures or not.[43]

[43] These studies have several limitations that have been previously identified that would limit their ability to be used in a risk assessment context. *See* EPA, "Glyphosate - Systematic Review of Open Literature" (2017), https://www.regulations.gov/document/EPA-HQ-OPP-2009-0361-0067 (Exhibit USA-163). For

PARAGRAPH	EXHIBIT	SOURCE TITLE	ANALYSIS
		Umbilical, Embyonic, and Placental Cells".	
410	MEX-139	Mesnage R, *et al*., "*Cytotoxicity on human cells of Cry1Ab and Cry1Ac Bt insecticidal toxins alone or with a glyphosate-based herbicide."*	This section of Mexico's Initial Submission refers to "the presence of GMOs and glyphosate residues," but this study does not even study the amount of glyphosate residues on plants, much less GE corn.
410	MEX-208	Xu, J., Smith, S., Smith, G., Wang, W. y Li, Y. "*Glyphosate contamination in grains and foods: An overview*".	This is a review of glyphosate generally, and corn grain is not listed in the table of glyphosate residues.[44]
410	MEX-313	LEISA. *"Glyphosate in wheat, oats and beans."*	This short web article is highly emotive and displays significant bias. For example, this article uses words such as "food soaked in poison," "silent genocide," "accomplices" such as Argentine government agencies "turn[ing] a blind eye," and use of glyphosate "for greed and to sell more and faster." This article does not follow any standard journal practices and does not include proper citations to other research.
410	MEX-314	Rubio, F., Guo, E., & Kamp, L., "*Survey of glyphosate residues in honey, corn and soy products."*	This study expressly says that glyphosate residues were <u>not</u> detected on the corn (syrup) samples. (p. 7). No other type of corn sample was tested.

MEX-312, major limitations include not characterizing the test substance properly, and experiments focused more on the formulation as opposed to the active ingredient. *Id.* at 27, 149-150 (Exhibit USA-163). For MEX-207, major limitations include a focus on adjuvants, as opposed to the active ingredient, and deficiencies in reporting of study data. *Id.* at 26, 141-142 (Exhibit USA-163). For MEX-193, major limitations include incomplete characterization of the test substances and unknown relevance of in vitro effects to in vivo effects. *Id.* at 21, 100-102 (Exhibit USA-163).

[44] This study, and other studies cited by Mexico, also reference the glyphosate degradate, aminomethylphosphonic acid ("AMPA"). AMPA has a lower toxicity profile than that of glyphosate, with any observed effects associated with AMPA exposure occurring at doses much higher than glyphosate, even well above maximum dose levels set for guideline studies known as limit doses that are typically too large to be considered relevant for human health risk assessment. *See, e.g.*, EPA, "Human Health Risk Assessment in Support of Registration Review," at 30 (Dec. 12, 2017) (reflecting 90-day rodent study of AMPA (MRID 00241351) where effects seen at 1200 mg/kg/day, which is above the limit dose of 1000 mg/kg/day, and 90-day non-rodent study (MRID 43334702), with no effects up to the highest dose tested (~300 mg/kg/day)) (Exhibit USA-164). Residues of AMPA in both wild-type and GE crops are consistently less than residues of glyphosate. As both toxicity and magnitude of residues of AMPA are less than those for glyphosate, any risk assessment for glyphosate is protective of AMPA exposures.

PARAGRAPH	EXHIBIT	SOURCE TITLE	ANALYSIS
		Journal of Environmental & Analytical Toxicology.	
N/A	MEX-085, at 15-16 (citing Swanson et al. (2014))	Swanson, NL, A. Leu, J. Abrahamson & B. Wallet. (2014). "Genetically Engineered Crops, Glyphosate and the Deterioration of Health in the United States of America," *Journal of Organic Systems*. 9(2): 6-37).	Mexico's "risk assessment" (MEX-085) presents an adaptation and modification of the information presented in Swanson et al. (2014) and purports to show a correlation between an increased incidence of certain diseases as reported in data from the U.S. Centers for Disease Control and Prevention against survey data on the planting of GE crops. However, the Swanson et al. report lacks any data that demonstrate that the people that reported these diseases also were exposed to glyphosate (*e.g.*, in proximity to areas during glyphosate applications, from exposure to food, et cetera).