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Te Mana Kounga Kai – Ahitereiria me Aotearoa

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Supporting document

Safety assessment - Application A1349

Food derived from insect-protected corn line COR121

Executive summary

Application A1349 seeks approval for the sale and use of food derived from corn line COR121 that has been genetically modified (GM) for protection against lepidopteran insect pests. Insect protection is conferred by the expression of the *ipd083Cb.1* gene encoding the insecticidal IPD083Cb protein. IPD083Cb is from the giant maidenhair fern, *Adiantum trapeziforme* var. *braziliense*. COR121 also expresses the phosphomannose isomerase (PMI) protein from *Escherichia coli* strain K-12, which was used as a selectable marker.

Food Standards Australia New Zealand (FSANZ) has previously assessed the IPD083Cb and PMI proteins.

This safety assessment addresses food safety and nutritional issues associated with the GM food. It therefore does not address:

- risks related to the environmental release of GM plants used in food production
- risks to animals that may consume feed derived from GM plants
- the safety of food derived from the non-GM (conventional) plant.

History of use

Corn has a long history of safe use in the food supply. Corn-derived products are routinely used in a large number and diverse range of foods e.g. cornflour, starch products, breakfast cereals and high fructose corn syrup.

Molecular characterisation

The genes encoding IPD083Cb (*ipd083Cb.1*) and PMI (*pmi*) were introduced into corn line COR121 via standard plant transformation techniques. Detailed molecular analyses indicate that a single copy of each of the linked *ipd083Cb.1* and *pmi* expression cassettes is present at a single insertion site in the COR121 genome. There are no extraneous plasmid sequences or antibiotic resistance marker genes present in this line.

The introduced genetic elements were shown by molecular techniques and phenotypic analyses to be present within a single locus and stably inherited across multiple generations.

Characterisation and safety assessment of new substances

Both IPD083Cb and PMI are expressed throughout COR121. Expression levels are low in grain.

Characterisation studies confirmed that the IPD083Cb and PMI proteins are identical to proteins previously assessed by FSANZ. Updated bioinformatic analyses for both IPD083Cb and PMI proteins are consistent with previous analyses showing these proteins have no significant homology with any known allergens or toxins.

Taken together, the evidence supports the conclusion that IPD083Cb and PMI are not toxic or allergenic to humans.

Compositional analyses

Detailed compositional analyses were performed on COR121. No statistically significant differences were found between grain from COR121 and the control for the 57 analytes evaluated. Grain from COR121 is therefore equivalent in composition to grain from conventional non-GM corn cultivars.

Conclusion

No public health and safety concerns have been identified in the assessment of insect-protected corn line COR121. Based on data provided in the present application and other available information, food derived from COR121 is as safe for human consumption as food derived from conventional non-GM corn cultivars.

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List of Abbreviations

Abbreviation	Description
ADF	acid detergent fibre
CCI	confidential commercial information
DNA	deoxyribonucleic acid
DW	dry weight
ELISA	enzyme-linked immunosorbent assay
FSANZ	Food Standards Australia New Zealand
g	gram
gDNA	genomic DNA
GM	genetically modified
HFCS	high fructose corn syrup
kDa	kilodalton
LLOQ	lower limit of quantitation
mg	milligram
Min	minutes
MT	million tons
NCBI	National Centre for Biotechnology Information
NDF	neutral detergent fibre
ng	nanogram
NGS	next generation sequencing
OECD	Organisation for Economic Co-operation and Development
PCR	polymerase chain reaction
PMI	phosphomannose isomerase
RF	reading frame
SDS-PAGE	sodium dodecyl sulphate polyacrylamide gel electrophoresis
µg	microgram
USDA	United States Department of Agriculture

1 Introduction

Food Standards Australia New Zealand (FSANZ) received an application from Corteva Agriscience Australia Proprietary Limited to vary Schedule 26 in the Australia New Zealand Food Standards Code. The variation is to include food from a new genetically modified (GM) corn line COR121, with the OECD Unique Identifier COR-ØØ121-4. This corn line has been modified for protection against lepidopteran insect pests.

Insect protection is conferred by the expression of the *ipd083Cb.1* gene encoding the insecticidal IPD083Cb protein. IPD083Cb is an insecticidal protein from the giant maidenhair fern, *Adiantum trapeziforme* var. *braziliense*. COR121 also expresses the phosphomannose isomerase (PMI) protein from *Escherichia coli* strain K-12, which was used as a selectable marker.

Food Standards Australia New Zealand (FSANZ) has previously assessed the IPD083Cb and PMI proteins.

If approved, food derived from COR121 corn line may enter the Australian and New Zealand food supply as imported food products.

2 History of use

2.1 Host organism

The host organism is corn (*Zea mays*) which is also referred to as maize. The non-GM corn line PH184C was used as the parental variety for the genetic modification described in this application.

Corn was one of the first plants to be cultivated by humans (Ranum et al. 2014) and is now the world's dominant cereal crop, with a global production of 1,218 MT[1] in 2024/25, ahead of wheat (799 MT) and rice (820 MT) (FAOSTAT 2026). Due to its economic importance, corn has been the subject of extensive study.[2]

The United States is the world's largest producer of corn, producing 378 MT in 2024/25, while Canada produced 15.3 MT in the same period (FAOSTAT 2026). Of the corn grown in the United States and Canada, an estimated 94% and ~91%, respectively, is GM.[3,4] No GM corn is currently grown commercially in Australia or New Zealand.

Relatively small quantities of non-GM corn are grown in Australia and New Zealand. In 2024/25 these amounted to 0.447 and 0.244 MT respectively (FAOSTAT 2026). To supplement their limited local production of corn, Australia and New Zealand import both corn grain and processed corn products. For example, in 2024, imports of corn flour into Australia and New Zealand were 14,463 and 2,129 tonnes respectively, while imports of corn oil totalled 841 and 28 tonnes respectively (FAOSTAT 2026).

[1] million tons
[2] Refer to detailed reports published by the OECD (OECD 2002), the Grains Research and Development Corporation GRDC (2017) Maize Northern Region - GrowNotes: Grains Research and Development Corporation. Australia. and the Office of the Gene Technology Regulator OGTR (2008) The Biology of Zea mays L. ssp mays (maize or corn). Office of the Gene Technology Regulator. Australia..
[3] For more information please see USDA Economic Research Service – http://www.ers.usda.gov/data-products/adoption-of-genetically-engineered-crops-in-the-us.aspx
[4] Statistics Canada, 2024 – https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=3210004201

Corn has a long history of safe consumption by humans.[5] Food products derived from processing of corn kernels include corn flour, meal, oil, starch and sweeteners such as high fructose corn syrup (HFCS). In Australia and New Zealand, corn starch is used in dessert mixes and canned foods, and HFCS is used in breakfast cereals, baking products, corn chips and extruded confectionary.

2.2 Donor organisms

2.2.1 *Adiantum trapeziforme*

The source of the *ipd083Cb.1* gene is the giant maidenhair fern, *Adiantum trapeziforme* var. *braziliense*. Members of the maidenhair fern family and other non-seed plants have been used in traditional medicine for treating respiratory infections such as cough, colds and pneumonia (Rastogi et al. 2018). The applicant notes that there have been no reports of *A. trapeziforme* being poisonous to either humans or livestock.

2.2.2 *Escherichia coli*

The *pmi* gene is derived from *Escherichia coli*, a Gram-negative bacterium which is ubiquitous in the environment. *E. coli* strain K-12 is a non-pathogenic strain with a long history of use for laboratory and commercial applications. There are no toxicity or health concerns associated with the K-12 strain.

[5] A large proportion of corn produced is also used as animal feed

3 Molecular characterisation

Molecular characterisation is necessary to provide an understanding of the genetic material introduced into the host genome and helps to frame the subsequent parts of the safety assessment. The molecular characterisation addresses three main aspects:

- the transformation method together with a detailed description of the DNA sequences introduced to the host genome
- a characterisation of the inserted DNA, including any rearrangements that may have occurred as a consequence of the transformation
- the genetic stability of the inserted DNA and any accompanying expressed traits.

Some of the information in this section was provided in the application as Confidential Commercial Information (CCI). While full details of CCI cannot be provided in this public report, FSANZ has had regard to this information in its assessment.

3.1 Transformation method

The DNA was inserted in to the corn genome using CRISPR-Cas9 mediated site-specific integration (Gao et al. 2020). This involved 2 sequential transformation steps using 2 transformation plasmids.

In the first transformation step, a landing pad plasmid was used to insert the landing pad sequence at a targeted site within the genome of non-GM corn line PH184C. Additional helper plasmids were used to facilitate regeneration of corn plants following transformation. No elements from these helper plasmids were integrated into the corn genome.

In the second transformation step, a trait plasmid was used to exchange a portion of the landing pad sequence for the *ipd083Cb.1* and *pmi* expression cassettes. This plasmid also contained additional cassettes to facilitate the transformation process. These cassettes were not integrated into the corn genome. The final insertion in corn line COR121 comprises sequences from both the landing pad plasmid and the trait plasmid, incorporating the intended *ipd083Cb.1* and *pmi* expression cassettes.

Only plants with the intended insertion and no unintended DNA sequences were selected for further development. Following evaluation of trait efficacy and agronomic performance, corn line COR121 was selected.

3.2 Detailed description of inserted DNA

Corn line COR121 contains the *ipd083Cb.1* and *pmi* gene expression cassettes as well as some residual DNA sequences derived from the landing pad plasmid.

Further details of the inserted DNA are CCI.

3.3 Development of the corn line from the original transformant

A breeding programme was undertaken for the purposes of:

- obtaining generations suitable for analysing the characteristics of COR121
- ensuring that the COR121 event is incorporated into elite lines for commercialisation.

Details of the breeding history depicting how COR121 was derived from the original

transformant and the specific generations used in the molecular characterisation studies are CCI.

3.4 Characterisation of the inserted DNA and site(s) of insertion

A range of analyses were undertaken to characterise the genetic modification in COR121. These analyses focused on the nature and stability of the insertion and whether any unintended re-arrangements or products may have occurred because of the transformation procedure.

Next generation sequencing (NGS) was used to characterise the number of integration sites, insert integrity, absence of extraneous sequences and genetic stability.

Leaf-derived genomic DNA (gDNA) from COR121 (5 generations) and the non-GM parental line PH184C (control) were sequenced. Additionally, positive control samples were generated using the control genomic DNA spiked with the transformation and helper plasmids. One copy of plasmid per copy of the corn genome was spiked. Sufficient sequence reads were obtained to cover the entire genomes of COR121 and the control, with an average depth of coverage ranging from 153x to 259x.

3.4.1 Insert integrity and site of integration

NGS reads from a single generation of COR121 were mapped to the intended insertion sequence and the control genome. Two unique insert-flank junction sites were identified. Each junction sequence comprised the inserted T-DNA sequence joined to a flanking sequence in the corn genome. This indicates that a single copy of the intended insertion has been integrated into the genome of COR121. Further examination of the sequencing results confirmed the organisation of the insert in COR121 is as expected.

Although some sequencing reads from the control aligned to the intended insertion sequence[6], these were endogenous genetic elements present in the corn genome. No junction sequences were detected in the control.

3.4.2 Absence of backbone and other sequences

Alignment of NGS reads from the controls or COR121 to the transformation and helper plasmids confirmed there was no integration of backbone sequences into COR121, including any antibiotic resistance genes.

3.4.3 Stability of the genetic changes in corn line COR121

The concept of stability encompasses both the genetic and phenotypic stability of the introduced trait over several generations. Genetic stability refers to maintenance of the modification (as produced in the initial transformation events) over successive generations. Phenotypic stability refers to the expressed trait remaining unchanged over successive generations.

3.4.3.1 Genetic stability

NGS was used to show the genetic stability of the inserted DNA in COR121 by evaluating leaf-derived gDNA from 5 generations of COR121. Genomic DNA from the control served as a negative control, and the control DNA spiked with the transformation plasmids served as a

[6] Several genetic elements found in the intended insertion sequence are derived from corn.

positive control.

The analysis showed the 2 insert-flank junction sequences present in all 5 generations were identical. No other junction sequences were present. The consistency of these results confirmed the intended insertion sequence is stably maintained in corn line COR121.

3.4.3.2 Phenotypic stability

Mendelian inheritance

Since the inserted DNA is at a single locus within the COR121 genome, it would be inherited according to Mendelian principles. Quantitative digital polymerase chain reaction (dPCR) was used on seed chip samples to determine the presence or absence of the COR121 insertion. Based on Mendelian inheritance principles, the expected segregation ratios were 3:1 in 2 of the 5 generations tested (generations 1 and 5), while the remaining 3 generations were homozygous (generations 2 – 4).

A chi-square test was performed at the 0.05 significance level to compare the observed segregation ratios for the 2 segregating generations of COR121 corn. A chi-square test was not performed for the remaining 3 generations as all plants were positive, as expected for homozygous generations.

The results demonstrated the expected segregation ratio for each generation (Table 1), indicating the inserted DNA is present at a single locus in COR121 and is inherited predictably according to Mendelian principles.

Table 1: Segregation results in five generations of COR121

Generation	Expected segregation ratio (positive:negative)	Observed number of plants			Statistical analysis	
		Positive	Negative	Total	χ^2	P-value
1	3:1	76	20	96	0.89	0.3458
2	Homozygous positive	95	0	95	-	-
3	Homozygous positive	96	0	96	-	-
4	Homozygous positive	96	0	96	-	-
5	3:1	71	25	96	0.06	0.8137

Expressed phenotype over several generations

Expression levels of IPD083Cb and PMI were evaluated in an outcrossed generation derived from COR121 and demonstrated the expected protein expression profile in field studies (refer to section 4.3). These findings are consistent with the Mendelian inheritance analysis.

Taken together, FSANZ is satisfied that IPD083Cb and PMI are stably expressed over multiple generations.

3.4.4 Reading frame analysis

A bioinformatic analysis of the COR121 insert, as well as the flanking DNA regions, was undertaken to identify whether any novel reading frames (RFs) had been created by the DNA insertion in COR121, and whether any putative peptides encoded by the identified RFs have

the potential for allergenicity or toxicity.

Sequences of ≥ 8 amino acids (aa) in COR121 within the insertion or spanning the boundary between the insertion and its flanking genomic regions were translated *in silico* from stop codon to stop codon (TGA, TAG, TAA) in all 6 reading frames.[7] Novel RFs were identified from the COR121 insert including the flanking DNA regions that corresponded to putative peptides of 8 amino acids or greater in length. These putative peptides were investigated further to determine whether their amino acid sequences showed similarity with known allergen and toxin peptide sequences in established databases.

Details of allergenicity and toxicity analysis were provided as CCI and considered by FSANZ. The analysis did not identify any biologically significant similarities to known allergens or protein toxins.

These analyses are theoretical only, as it is highly unlikely that any of the identified RFs would be expressed *in planta*.

3.5 Conclusion

Corn line COR121 contains a single copy of the inserted DNA at a specific locus in the corn genome. Sequencing results confirmed the *ipd083Cb.1* and *pmi* expression cassettes were inserted with the expected organisation. No plasmid backbone sequences, including any antibiotic resistance genes from the plasmid used in the transformation, are present.

The inserted DNA is stably inherited and expressed across several breeding generations of COR121. Bioinformatic analyses of the novel RFs created by the insertion did not raise any allergenicity or toxicity concerns.

[7] Evaluation of sequences stop-to-stop codon is a more conservative approach compared to the evaluation of start-to-stop codon sequences.

4 Characterisation and safety assessment of novel substances

In considering the safety of newly expressed substances it is important to note that a large and diverse range of proteins are ingested as part of the normal human diet without any adverse effects. Only a small number of dietary proteins have the potential to impair health, because they have anti-nutrient properties or they can cause allergies in some consumers (Delaney et al. 2008).

To identify potential hazards, a detailed understanding of the biochemical function and phenotypic effects and concentration levels of the newly expressed protein in the edible part of the plant is required. It is also important to determine if the protein is expressed in the plant as expected, including whether any post-translational modifications have occurred.

Two proteins are expressed in COR121: the IPD083Cb insecticidal protein, which provides protection against lepidopteran pests; and the PMI protein which allows for growth on media containing mannose and acts as a selectable marker during the transformation process.

4.1 IPD083Cb

IPD083Cb, isolated from the giant maidenhair fern (*Adiantum trapeziforme* var. *braziliense*), is an 853 amino acid, ~95 kDa protein encoded by the *ipd083Cb.1* gene. The IPD083Cb protein, when expressed *in planta*, provides protection from certain lepidopteran pests by disrupting their midgut epithelium, similar to Cry proteins from *B. thuringiensis*. However, the midgut receptor sites are different to those bound by *Bt*-derived insecticidal proteins (including Cry2A.127, Vip3Aa, or a variant of Cry1Ab). This suggests that IPD083Cb is unlikely to share cross-resistance with insects resistant to Cry proteins (Liu et al. 2019).

4.1.2 Safety of the introduced IPD083Cb

FSANZ has previously assessed the IPD083Cb protein in soybean line COR23134 (Application A1323). The full safety assessment report for Application A1323 is publicly available on the FSANZ website[8].

Since the IPD083Cb protein expressed in COR121 is identical in amino acid sequence to the IPD083Cb protein expressed in COR23134 soybean, no further safety evaluation is required. FSANZ did however review updated bioinformatic studies[9] for IPD083Cb protein that looked for amino acid sequence similarity to known protein allergens and toxins. Results from the updated studies do not alter the previous conclusions.

4.1.3 Conclusion

IPD083Cb expressed in COR121 is identical to the one previously assessed in Application A1323. Updated bioinformatic analyses confirmed IPD083Cb has no similarity with known allergens or toxins. The IPD083Cb protein is therefore unlikely to be toxic or allergenic to humans.

[8] Application A1323 webpage – https://www.foodstandards.gov.au/food-standards-code/applications/a1323-food-derived-insect-protected-soybean-line-cor23134

[9] The bioinformatic analysis for A1349 was conducted in January 2025, reflecting an updated assessment relative to A1323, for which the analysis was completed in January 2023.

4.2 PMI

The *pmi* gene in COR121 encodes the enzyme PMI, which catalyses the interconversion of mannose 6-phosphate and fructose 6-phosphate. Expression of PMI protein allows plant cells to use mannose as a source of carbon, which assists with the identification of transformed cells (Negrotto et al. 2000).

The *pmi* gene encodes a 391 amino acid protein with a calculated molecular weight of ~43 kDa. PMI has been assessed by FSANZ as a novel protein in numerous previous applications.

4.2.1 Safety of the introduced PMI

The PMI protein has been previously assessed by FSANZ in 9 corn lines,[10] as well as in rice line GR2E.[11] These previous assessments did not raise any safety concerns and there are no credible reports of adverse health effects in humans. Since the PMI protein expressed in COR121 is identical in amino acid sequence to the PMI proteins expressed in previously assessed corn and rice lines, no further safety evaluation is required. FSANZ did however review updated bioinformatics studies (February 2024) for PMI that looked for amino acid sequence similarity to known protein allergens and toxins. The results from the updated studies do not alter the previous conclusions.

4.2.2 Conclusion

PMI expressed in COR121 is identical to previously assessed PMI proteins. Updated bioinformatic analyses confirm that PMI has no similarity with known allergens or toxins. The PMI protein is therefore unlikely to be toxic or allergenic to humans.

4.3 Protein expression levels in COR121

For analysis of the expression levels of the IPD083Cb and PMI proteins in COR121, tissues were collected from 4 replicate plots at 6 field-trial sites. These sites were in representative corn-producing regions in the United States and Canada during the 2024 growing season.[12] Tissues were collected at varying stages of growth: leaf (V6, V9, R1 and R4), root (V9, R1 and R4), pollen (R1), forage (R4) and grain (R6). See Figure 1 for a summary of corn growth stages. Tissues were lyophilised, homogenised (except pollen samples) and stored frozen until analysis.

IPD083Cb and PMI were extracted from tissues using standard methods and their expression levels quantified in each tissue using quantitative ELISA.

[10] 5307 (Application A1060; FSANZ 2012), MIR162 (Application A1001; FSANZ 2008a), 3272 (Application A580; FSANZ 2008b), MIR604 (Application A564; FSANZ 2006), DP23211 (A1202; FSANZ 2020), DP51291 (Application A1270; FSANZ 2023), DP915635 (Application A1272; FSANZ 2024) and DP910521 (A1281; FSANZ 2024), MZIR260 (A1302; FSANZ 2025).

[11] Rice line GR2E - Application A1138; FSANZ 2017.

[12] The location of the 6 field trial sites: US – one site in Pennsylvania, Nebraska, Minnesota, Wisconsin and Iowa; Canada – one site in Ontario.

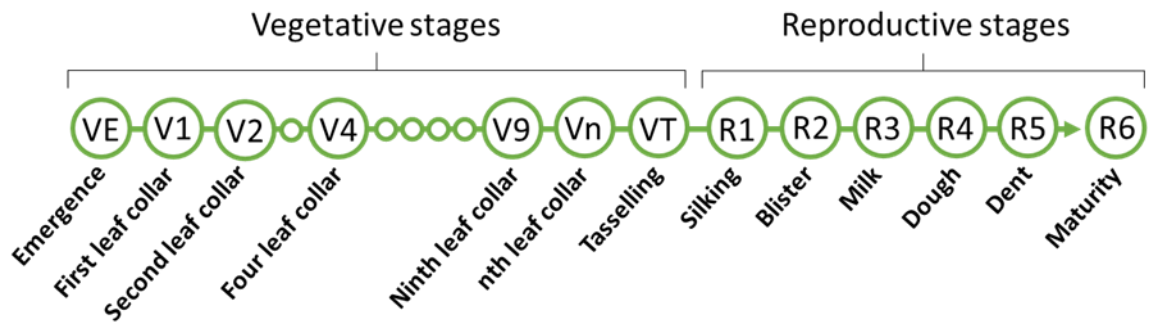

Figure 1. *Stages of corn growth. Grain is harvested at maturity (R6).*

ELISA results for IPD083Cb showed highest expression at the R6 stage in leaf tissue (290 – 720 ng/mg DW[13]) with the lowest in pollen (<0.48 – 1.3 ng/mg DW). Expression remained low in grain (0.66 – 1.4 ng/mg DW).

For PMI, highest expression was at the R4 stage in leaf tissue (28 – 60 ng/mg DW), with the lowest in grain (2.4 – 6.0 ng/mg DW).

For the full set of expression data, including standard deviations and ranges, refer to the Application dossier[14] (page 83).

[13] Dry Weight
[14] Application dossier – https://www.foodstandards.gov.au/food-standards-code/applications/a1349-food-derived-insect-protected-corn-line-cor121

5 Compositional analyses

The main purpose of compositional analyses is to determine if the genetic modification has resulted in any unexpected compositional change to the food. Compositional analyses are also important for evaluating the intended effect where there has been a deliberate change to the composition of the food.

The aim of the compositional analysis is to measure only those constituents most relevant to the safety of the food or that may have an impact on the whole diet. Important analytes therefore include the key nutrients, toxicants and anti-nutrients for the food in question. The key nutrients and anti-nutrients are those components in a particular food that may have a substantial impact in the overall diet. They may be major constituents (fats, proteins, carbohydrates or enzyme inhibitors such as anti-nutrients) or minor constituents (minerals, vitamins). Key toxicants are those toxicologically significant compounds known to be inherently present in an organism, such as compounds whose toxic potency and level may be significant to health.

5.1 Key components

The key components to be analysed for the comparison of transgenic and conventional corn are outlined in the OECD Consensus Document on Compositional Considerations for New Varieties of Maize (OECD 2002), and include: proximates (protein, fat, fibre, ash, carbohydrates), amino acids, fatty acids, minerals, vitamins and the anti-nutrients phytic acid, raffinose, furfural and the phenolic acids ferulic acid and *p*-coumaric acid.

5.2 Study design

COR121, the non-GM control corn line PH184C, and 4 non-GM reference corn lines were grown and harvested from 8 field trial sites in the United States and Canada during the 2024 growing season.[15] The sites were representative of corn growing regions suitable for commercial production. The field sites were established in a randomised complete block design with 4 replicates per site. Each block contained COR121, control, and 4 reference lines. Plants were grown under agronomic field conditions typical for each growing region.

Grains from COR121, the control and reference lines, were harvested at typical maturity (R6 growth stage) from all plots. Control and reference samples were collected prior to the collection of COR121 samples to minimize the potential for contamination. Samples were chilled before being transferred to a freezer (≤ -10ºC) or placed on dry ice within 3 hours of collection and shipped frozen to an analytical laboratory.

Compositional analyses were performed based on internationally recognised procedures including official methods specified by the Association of Official Analytical Chemists (AOAC), the American Association of Cereal Chemists (AACC), and the American Oil Chemists' Society (AOCS), methods specified by the manufacturer of the equipment used for analysis, or other published scientific methods.

A total of 62 analytes in grain were assessed (see Figure 2 for a complete list). Of these, 5 analytes gave results below the assay lower limit of quantification (LLOQ) and were excluded from the statistical analyses (lauric acid, myristic acid, eicosadienoic acid, vitamin B2 and furfural; listed in grey in Figure 2).

[15] The location of the 8 field trial sites: US - one site in Pennsylvania, Nebraska, Wisconsin, Illinois and Minnesota; 2 sites in Iowa and Canada – one site in Ontario

For the remaining 57 analytes, ‘descriptive statistics’ (mean, range and 95% confidence interval) were generated. Statistical analyses were performed using Statistical Analysis Software (SAS) 9.4 (SAS Institute, Cary, North Carolina 2012).

For 55 of the 57 analytes, both COR121 and the control corn had <50% of samples below the LLOQ. A mixed model analysis of variance was applied for combined data and locations, covering the eight replicated field trial sites. The across-site mixed model analysis included the fixed effect of entry and was adjusted by the random effects of the site, the replicate nested within the site, and the interaction between the site and the entry.

For 2 of the 57 analytes (heptadecenoic acid and heptadecanoic acid) >50% of either COR121 or the control corn samples were below the LLOQ. For these analytes, Fisher’s exact test was used to assess whether there was a significant difference in the proportion of samples below the LLOQ between the two corn lines across sites for combined data and locations, covering the eight replicated field trial sites.

In assessing the statistical significance of any difference between COR121 and the control, a P-value of 0.05 was used. A further adjusted P-value was determined using the false discovery rate (FDR) method, as a consideration of the chance of false positives being observed with the testing due to the multiple analytes being analysed. In cases where the raw P-value was <0.05 but the FDR-adjusted P-value was >0.05, the difference was considered likely to be a false positive. In cases where a given sample was below the LLOQ for an individual analyte, a value of half the LLOQ was assigned for statistical analysis.

Any statistically significant differences were evaluated further to assess whether they were likely to be biologically meaningful. Three ranges were used:

1. Compositional data from the non-GM reference lines grown concurrently in the same trial as COR121 and the control were combined across all sites and used to calculate an in-study reference range for each analyte. This defines the variability in corn cultivars grown under the same agronomic conditions.
2. A literature range based on the natural variation of analytes from publicly available data was also considered (AFSI 2022). This defines the variability in additional non-GM commercial corn cultivars grown in a wider range of agronomic conditions.
3. Any statistically significant differences between COR121 and the control were compared to *tolerance intervals* derived from an in-house database containing compositional analyses from 206 non-GM commercial corn lines cultivated across 214 unique environments in North and South America, from 2003 – 2021. Tolerance intervals are expected (with 95% confidence) to contain at least 99% of the values for corresponding analytes of the conventional corn population (Hong et al. 2014). This defines the variability in corn cultivars grown under a wide variety of agronomical conditions.

Key analyte levels (proximates and minerals) were also analysed in forage. The results were unremarkable and have not been included in this report.

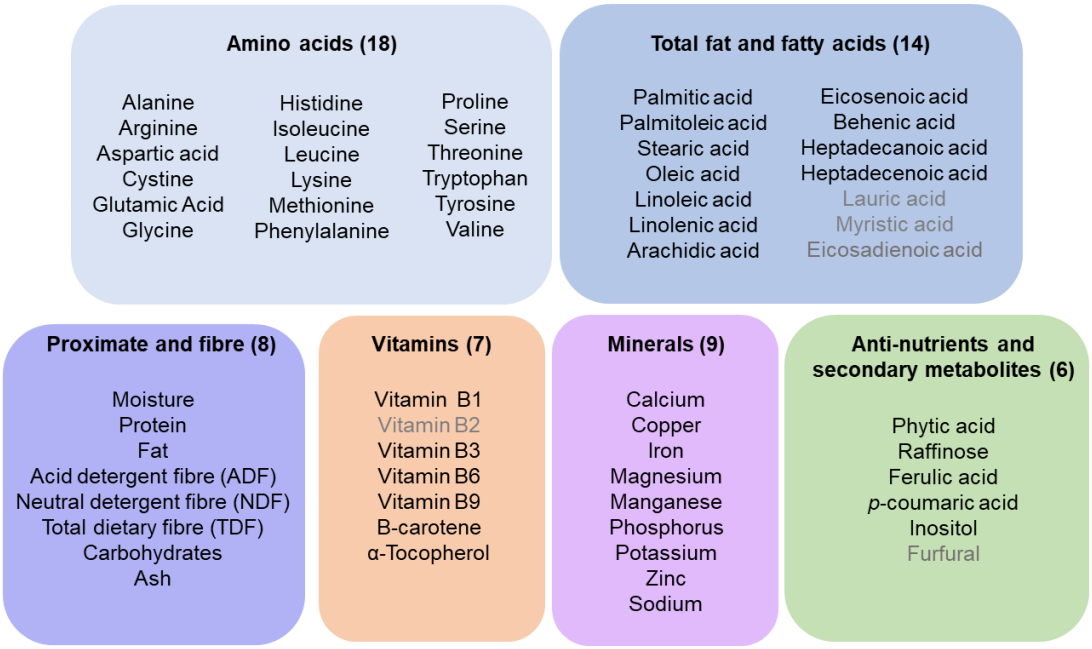

Figure 2. *Analytes measured in COR121 grain samples.*

5.3 Analyses of key components in grain

Of the 57 analytes for which mean values were provided, there were 7 analytes for which there was a statistically significant difference ($p < 0.05$) between COR121 and the non-GM control: moisture, oleic acid, eicosenoic acid, calcium, copper, iron and inositol. All 7 analytes had FDR-adjusted P-value of >0.05, suggesting that the differences in these analytes were likely to be false positives. As such, no further analysis is required.

For the complete data set refer to the Application dossier (pages 87 – 106).

The compositional data support the conclusion that no statistically or biologically significant differences exist in the levels of key constituents in COR121. Grain from COR121 can therefore be regarded as equivalent in composition to grain from conventional non-GM corn.

6 Nutritional impact

In most cases, an assessment of nutritional impact can be achieved through a detailed understanding of the genetic modification and its consequences, together with an extensive compositional analysis of the food, such as that presented in section 5.

Where a GM food has been shown to be compositionally equivalent to conventional cultivars, the evidence to date indicates that feeding studies using target livestock or other animal species will add little to the safety assessment (OECD 2003; Bartholomaeus et al. 2013). If the compositional analysis indicates biologically significant changes, either intended or unintended, to the levels of certain nutrients in the GM food, additional nutritional studies may be necessary to assess the potential impact of the changes on the whole diet.

COR121 is the result of a genetic modification for protection against insect pests, with no intention to significantly alter nutritional parameters in the food. The compositional analyses have demonstrated that the genetic modification has not altered the nutrient composition of COR121 compared with conventional non-GM corn cultivars. The introduction of food derived from COR121 into the food supply is therefore expected to have negligible nutritional impact.

7 References

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