Voluntary Premarket Consultation
On *Del/Ros1-N* tomato
(BNF 178)

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Background

• *Del/Ros1*-N tomato has increased levels of anthocyanins in the fruit
• Developed by Dr. Cathie Martin and Norfolk Plant Sciences (NPS)
• Submitted March 3, 2020; completed June 20, 2023
• Introduced proteins:
  – Delila and Rosea1 transcription factors from garden snapdragon
  – NPTII as a selectable marker from *E. coli* Tn5
The intended human food uses are the same as other tomatoes on the US market.

Tomato is consumed fresh, in salads, as well as a processed food.

NPS stated that the *Del/Ros1*-N tomato is not intended for use in animal food in the United States.
The Focus of FDA’s evaluation:

• Does human food from *Del/Ros1*-N tomato contain new proteins or other substances that require premarket approval as food additive?

• Is human food from *Del/Ros1*-N tomato as safe as human food from other tomato varieties?
Molecular Characterization

• *Agrobacterium*–mediated transformation
• Confirmation of a single insert
• Absence of vector backbone DNA
• Inheritance and stability
  – The DNA insertion is stable across generations and genetic background
  – The purple phenotype was inherited in a Mendelian segregation fashion
• Open reading frame analysis
  – No known tomato ORFs are disrupted; no evidence of new putative peptide
Safety of new proteins

• Delila and Rosea1 transcription factors
  – Donor organism – snapdragon (*Antirrhinum majus*)
    • Has been in human diet
  – History of safe consumption
    • Comparable to TFs that control anthocyanin biosynthesis in commonly consumed fruits and vegetables
  – Bioinformatic analysis
    • No sequence similarity to known allergens or toxins
  – Expression levels
    • Below the limit of detection in the fruit (0.5 ng Delila and 0.2 ng Rosea1 protein per mL juice)
  – Digestibility
    • Rapidly degraded by pepsin in simulated gastric fluid
Safety of new proteins

• NPTII
  • Presence/identity confirmed through genomic and phenotypic analysis
  • Expression levels:
    – Below the limit of detection (0.2 ng NPTII protein per mL juice)
  • Authorized for use as a food additive in tomato (21 CFR 173.170, NPTII is also referred to as aminoglycoside 3’ phosphotransferase II in FDA’s regulations)
Safety of new substance - anthocyanins

- **History of safe consumption**
  - Present in the skin of some purple-skinned tomato varieties, and in eggplant and purple-fleshed potatoes

- **Levels in the tomato fruit**
  - Undetectable in wild-type tomatoes
  - 0.4 mg per g fresh weight in *Del/Ros1-N* tomato (MoneyMaker genetic background)

- **Estimated dietary exposure**
  - 100 mg/day at the mean, and 225 mg/day at the 90th percentile
  - Comparable to consumption of high anthocyanin foods
NPS analyzed samples from *Del/Ros1*-N tomato and the control tomato.

Performed based on the principles outlined in OECD Consensus Document for tomato composition.

NPS analyzed and reported the levels of components, including proximates (protein, fat, carbohydrates, fiber, and ash), fatty acids, minerals (magnesium, potassium, and sodium), carotenoids (β-carotene and lycopene), vitamins (vitamin C, vitamin K1, and folate), and α-tomatine.

The levels of most components are similar; the levels of total folate, lycopene, β-carotene, and α-tomatine in the *Del/Ros1*-N tomato are 25% higher compared to the control.

The levels of all tested components in *Del/Ros1*-N tomato and the control are within the published literature ranges.
Conclusions

• Except for the intended anthocyanin change in *Del/Ros1-N* tomato, human food from *Del/Ros1-N* tomato is not materially different in composition, safety, and other relevant parameters from tomato-derived human food currently on the market.

• Use of genetically engineered *Del/Ros1-N* tomato in human food does not raise issues that would require premarket review or approval by FDA.
The increased levels of anthocyanins and therefore, purple colored-fruit may be considered material facts requiring disclosure under Sections 201(n) and 403(a)(1) of the FD&C Act [21 U.S.C. § 321(n) and 343(a)(1)].

Companies marketing food from *Del/Ros1*-N tomato are advised to consult with CFSAN’s Office of Nutrition and Food Labeling.
New Plant Variety Consultations

BNF No. 178
Tomato
*Del/Ros1-N*
*Del/Ros1-N*

Developer: Norfolk Plant Sciences John Innes Centre Norwich Research Park Norwich NR4 7UH United Kingdom

Trait(s): Increased levels of anthocyanins in the fruit

Submission Date: Mar 3, 2020

Introduced Protein: Delila *Antirrhinum majus*

Introduced Protein 2: Rosea1 *Antirrhinum majus*

Introduced Protein 3: Neomycin phosphotransferase II (NPTII) *Escherichia coli* transposon Tn5

Contains EPA-regulated trait: No

FDA’s Memo(s):
- Human Food Use - CFSAN (PDF, 1007 kB) Jun 13, 2023
- Animal Food Use - CVM (PDF, 137 kB) Jun 16, 2023

FDA’s letter: Human food only (PDF, 1.09 MB) Jun 20, 2023

Completed Consultation
Questions in the future?

Contact us at plantbiotech@fda.hhs.gov