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

Human and animal food use

- 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

Compositional analysis

- 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.

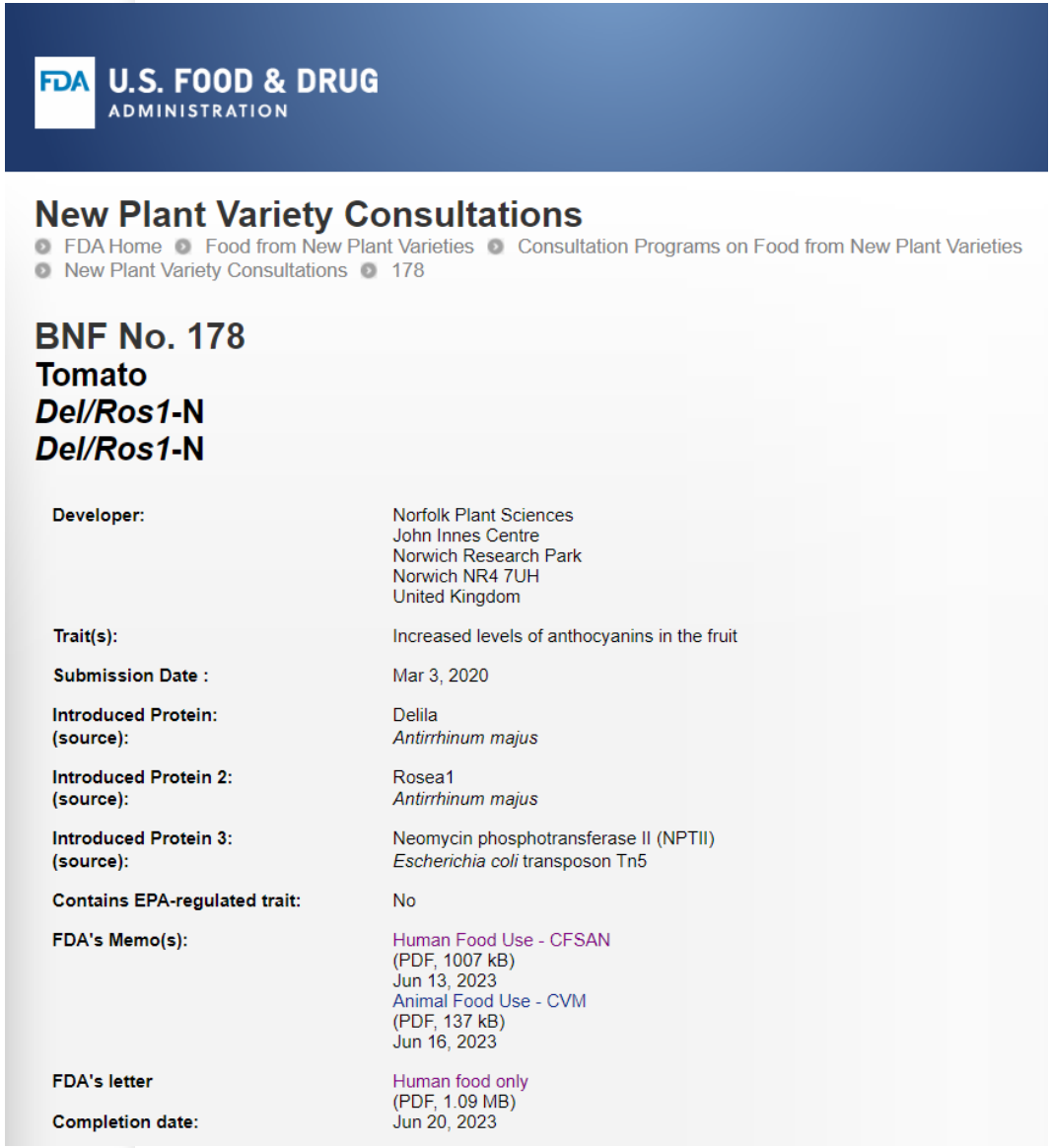
- Use of genetically engineered *Del/Ros1*-N tomato in human food does not raise issues that would require premarket review or approval by FDA.

Labeling considerations

- 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.

Completed Consultation



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New Plant Variety Consultations

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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: (source):	Delila *Antirrhinum majus*
Introduced Protein 2: (source):	Rosea1 *Antirrhinum majus*
Introduced Protein 3: (source):	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)
Completion date:	Jun 20, 2023

Questions in the future?

Contact us at
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