U.S. FOOD & DRUG ADMINISTRATION
Human Foods Program

Terry Reyes, Ph.D.
Senior Manager, Global Regulatory and Public Policy
UPSIDE Foods, Inc.
804 Heinz Ave.
Berkeley, CA 94710

Re: Cell Culture Consultation Notification File: CCC 000002

Dear Dr. Reyes:

This letter is in response to supplemental information provided by UPSIDE Foods, Inc. (UPSIDE, the firm) regarding the firm's consultation with the Food and Drug Administration (FDA, we) regarding a cultured animal cell food product and associated production process, designated as CCC 000002. We received the supplement on October 5, 2023. The supplement describes revised heavy metal specifications for UPSIDE's food product. On December 1, 2023, April 11, 2024, June 25, 2024, and August 1, 2024, UPSIDE submitted clarifying information regarding the specification for lead, including a revised lead specification for both the serum-containing and serum-free cell culture media formulations, the batch analyses, and copies of the certificates of analyses.

We previously responded to CCC 000002 on November 16, 2022. The subject of CCC 000002 is cultured chicken (*Gallus gallus*) cells with characteristics of muscle and connective tissue, produced by the method described in CCC 000002, and harvested as multicellular tissue for use as human food. Based on FDA's evaluation of the information UPSIDE presented to FDA, as well as other information available to the agency, we concluded in our response letter that we did not have any questions at that time regarding UPSIDE's conclusion that foods comprised of or containing the cultured cellular material resulting from the production process defined in CCC 000002 are as safe as comparable foods produced by other methods and would not contain substances that adulterate the food.

On April 13, 2023, FDA responded to a supplement dated February 17, 2023, that described two additional substances used during production of its cultured cellular material. Based on the information UPSIDE presented to FDA, we responded that we had no questions at that time regarding UPSIDE's conclusion that foods comprised of or containing cultured chicken cell material resulting from the production process defined in CCC 000002 are as safe as comparable foods produced by other methods.

In the supplement dated October 5, 2023, UPSIDE provides revised heavy metal specifications for arsenic (lowered from <1000 ppb to <20 ppb), cadmium (lowered from <2000 ppb to <20 ppb), and mercury (lowered from <2000 ppb to <10 ppb).

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For lead, UPSIDE presents the results of three non-consecutive batches, produced using serum-containing and serum-free cell culture media, demonstrating that the average result of the batch analysis is 13.3 ppb and 47.6 ppb, respectively. For the serum-containing process, UPSIDE lowered the specification for lead from <100 ppb to <75 ppb. For the serum-free process, UPSIDE is maintaining its lead specification at 100 ppb.[1] We note that the specification limit of 100 ppb for lead is consistent with the Codex Alimentarius maximum level of lead for meat and fat of poultry (see General Standard for Contaminants and Toxins in Food and Feed).

Based on the information UPSIDE has presented to FDA, we continue to have no questions at this time regarding UPSIDE's conclusion that foods comprised of or containing cultured chicken cell material resulting from the production process defined in CCC 000002 are as safe as comparable foods produced by other methods. FDA will continue to work with the firm to further refine heavy metal specifications as the production process evolves.

We have added the supplement provided by UPSIDE, and all applicable amendments to the supplement, to the safety narrative submitted by UPSIDE. A copy of the supplement, all applicable amendments, as well as a copy of this letter responding to the supplemental information regarding CCC 000002 are available to the public at https://www.cfsanappsexternal.fda.gov/scripts/fdcc/?set=AnimalCellCultureFoods.

Sincerely,

Andrew J. Zajac -S

Digitally signed by Andrew J. Zajac -S
Date: 2024.11.14 12:49:57 -05'00'

Andrew J. Zajac
Staff Director
Innovative Foods Staff
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cc: Melissa Hammar
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[1] UPSIDE clarified that currently, the cultured chicken cell material is produced using serum-containing cell culture media. UPSIDE stated that the specification for the maximum level of lead remains 100 ppb for the cultured chicken cell material produced using serum-free cell culture media, to ensure that the firm has flexibility in conforming to the set specification as it continues to optimize the production process. UPSIDE stated that it will notify FDA when it begins producing cultured chicken cell material using the serum-free cell culture media. In a meeting with FDA on October 30, 2024, UPSIDE committed to further tighten the specifications based on results obtained from future batch analyses and continued optimization of its process.