Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004
T +1 202 637 5600
F +1 202 637 5910
www.hoganlovells.com

MEMORANDUM

From: Gary Jay Kushner
Brian D. Eyink

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Re: USDA and FDA Settle Jurisdiction over Products Derived from Livestock and Poultry Cell Lines

The U.S. Department of Agriculture's (USDA's) Food Safety and Inspection Service (FSIS) and the Food and Drug Administration (FDA) announced today a formal agreement coordinating joint jurisdiction over the production of products derived from cell lines of livestock and poultry.[1] This agreement marks the next significant step in establishing the regulatory framework for these products and delineates the general roles that FSIS and FDA will play in regulating the developing of cell lines, culturing cells, harvesting cells, processing products from those cell cultures, labeling, and post-market enforcement. It builds on a November 2018 joint statement by USDA Secretary Perdue and FDA Commissioner Gottlieb last Fall, in which they announced that the agencies would establish a coordinated framework for regulating these products working within their existing statutory authorities. [2] Although today's formal agreement establishes a general regulatory framework, additional work remains, as both agencies will have to review and possibly update regulations, develop more specific regulatory guidance for these products, and resolve a number of important questions.

In general, the formal agreement adopts a "pre-harvest" and "post-harvest" approach, with FDA asserting oversight "through the time of harvest" and FSIS assuming jurisdiction over harvested cells that are intended for use in meat or poultry products. The agreement leaves jurisdiction at the point of "harvest" unresolved, with the agreement apparently contemplating both agencies having a role. The agreement calls for information sharing and coordination between FDA and FSIS, and the agencies have committed to a collaborative process for fleshing out the regulatory process moving forward.

Importantly, this agreement focuses on cell cultures derived from the cells of livestock and poultry, which traditionally are subject to FSIS jurisdiction.[3] The agreement does not address cell cultures derived from other species, such as fish, which traditionally fall under FDA jurisdiction, although

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[1] *Formal Agreement Between the U.S. Department of Health and Human Services Food and Drug Administration and U.S. Department of Agriculture Office of Food Safety*, March 7, 2019, https://www.fsis.usda.gov/wps/wcm/connect/0d2d644a-9a65-43c6-944f-ea598aacdec1/Formal-Agreement-FSIS-FDA.pdf?MOD=AJPERES. A copy of the agreement it attached to this memorandum.

[2] *See* HL Memo, USDA and FDA Announce Joint Oversight Over Cell Cultured Products (Nov. 20, 2018).

[3] Unless otherwise specified, references in this memorandum to "cells" or "cell cultures" refer to cell lines of livestock and poultry.

FDA's approach toward cell culture technologies under this agreement is likely instructive for those product categories as well.

FDA Jurisdiction and Responsibilities

Under the agreement, FDA will generally assert jurisdiction over all steps of the process "through the time of harvest" of cultured cells, at which point FDA will "help coordinate the transfer of regulatory oversight" to FSIS. Specifically, under the agreement, FDA will assert jurisdiction over the following steps:

- Initial evaluation of materials, processes, and manufacturing controls for cell culture technologies, through "premarket consultation processes." This will include oversight of tissue collection, cell lines and cell banks, and components and inputs to the cell culture process. FDA will consult with FSIS as part of the premarket consultation process.
- Initial cell collection and the development and maintenance of cell banks.
- Proliferation and differentiation of cells through the time of harvest.

The agreement contemplates that cell culturing operations will be required to register with FDA, which triggers FDA's suite of food safety regulations, including Current Good Manufacturing Practices (CGMPs) and Preventive Controls requirements. Cell culturing operations would also be subject to FDA inspections and FDA enforcement action. FDA would coordinate its efforts with FSIS, but FDA is not to inspect "activities solely regulated by" FSIS.

The agreement contemplates that FDA would retain jurisdiction over the cell culturing process "through the time of harvest" and that "at harvest," FDA would "help coordinate the transfer of regulatory oversight" to FSIS, including "providing information necessary for USDA to determine whether harvested cells are eligible to be processed into meat or poultry products that bear the USDA mark of inspection."

FSIS Jurisdiction and Responsibilities

Although FSIS would be consulted during FDA's premarket consultation process, FSIS's in-plant jurisdiction under the agreement would begin "at harvest," when it would work with FDA to "help coordinate the transfer of regulatory oversight" from FDA to FSIS. FSIS would then oversee the processing, packaging, and labeling of cultured cells used in meat or poultry products under its existing authorities under the Federal Meat Inspection Act and Poultry Products Inspection Act. Specifically, FSIS would have jurisdiction over several key steps:

- Harvesting of cells cultured from livestock or poultry for the purpose of producing meat or poultry products.
- Processing and packaging cultured cells into meat or poultry products.
- Labeling of meat or poultry products made from cultured cells.
- Post-market enforcement, including product recalls.

The agreement contemplates that FSIS would apply its existing food safety frameworks to the processing steps under its jurisdiction, including its sanitation requirements and Hazard Analysis and Critical Control Point (HACCP) framework. Labels for meat or poultry products made using cultured cells would require FSIS label approval, as is the case with other products under FSIS's jurisdiction, and the labels would bear the USDA mark of inspection. FSIS would coordinate its efforts with FDA and share information as needed, including notifying FDA "if objectionable conditions are identified" and working "collaboratively with" FDA to address objectionable conditions "with respect to harvesting" and relying on FDA to address issues related to pre-harvest activities.

Shared Responsibilities for Next Steps

The agreement sketches out the general contours of FSIS-FDA regulation of cell cultured products, but the details remain to be worked out. The agreement specifically contemplates that FSIS and FDA will work together to develop a more detailed "joint framework or standard operating procedure" to "facilitate coordination of shared regulatory oversight related to the harvest of biological material." The agencies will also jointly review their regulatory and statutory frameworks to determine whether any changes are required to implement the joint framework. Further, the agencies will develop "joint principles" for product labeling claims "to ensure that products are labeled consistently and transparently."

The agreement does not place a timeframe around these next steps.

Key Open Questions

The agreement establishes a joint framework and sheds much-needed light on how FDA and FSIS plan to jointly regulate livestock and poultry products derived from cell lines of livestock and poultry. In doing so, however, the agreement leaves unanswered several key questions for these types of products, and raises more still. For example:

- What will FDA's premarket consultation process look like, and how generalizable will any individual determination be?
- The agreement appears to contemplate both FDA and FSIS having jurisdiction at the time of "harvest." How will the agencies define "harvest," how precisely will they coordinate jurisdiction, and how will they fit "harvesting" into their respective food safety regulatory frameworks?
- How specifically will product names, standards, and claims be regulated, and what will FDA and FSIS coordination look like in practice?
- How will importation of these products be regulated, how will FDA oversee the importation of "pre-harvest" cell lines, and will foreign countries be able to meet FSIS's equivalency standards for "harvest" or "post-harvest" activities?

As the agencies move forward with implementing the joint framework agreement, interested companies should follow the process closely, consider how the answers to these and other questions may affect their businesses, and look for opportunities to engage in developing this regulatory framework.

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We will continue to monitor this and other developments related to the use of cell culture technology. In the meantime, please do not hesitate to contact us if you have any questions.