September 25, 2018

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

SUBMITTED ELECTRONICALLY VIA REGULATIONS.GOV

RE: Docket No. FDA-2018-N-2155 for Foods Produced Using Animal Cell Culture Technology; Public Meeting; Request for Comments

Thank you for the opportunity to submit comments on how the Food and Drug Administration (FDA) should evaluate the safety of clean meat (sometimes called cell-based meats or cultured meat).[1] We are grateful to FDA for engaging stakeholders in a robust and open dialogue on these important issues. We appreciate FDA's commitment to enabling innovation and technological advances in the food sector while ensuring the safety of the resulting food products. We also support the agency's commitment to clarify science- and risk-based regulatory policies to advance innovation and increase regulatory predictability.

We have come together to submit these comments to provide FDA with the best information available as the agency considers the appropriate regulation of clean meat and to demonstrate our desire to work with the agency and other stakeholders. Our organizations represent an array of interests united by the desire to see the safe and efficient introduction of clean meat to the U.S. marketplace.

We are heartened that FDA is considering a pathway for clean meat to come to market under the existing regulatory framework. The United States provides robust food regulatory oversight capable of ensuring safe and properly labeled clean meat.

Our comment first addresses the need for clean meat and the reasons that FDA is well situated to ensure its safety and then turns to the specific questions that FDA posed in its request for comments.

[1] Many companies in this space prefer the term "cell-based meats." The Good Food Institute has used the term "clean meat" for two years and continues to use the term for now, but is reevaluating the proper nomenclature for this kind of meat.

I. The Regulatory Path to Market Should Ensure Consumer Safety and Confidence Without Imposing Unnecessary Regulatory Burdens on Producers.

We support FDA's commitment to ensuring food safety while enabling technological advances in the food sector by, among other things, establishing a clear, risk-based, and predictable regulatory system.[2]

There is substantial consumer interest in clean meat[3] for numerous reasons, including lower environmental impacts and increased efficiency, which will enable the production of high-quality protein to feed a growing world population. In particular, clean meat converts inputs into meat much more efficiently than using livestock to convert feed crops into meat and thus requires significantly less land, water, fertilizer, herbicides, and pesticides. Because it does not produce manure, clean meat eliminates this source of air and water pollution (and its attendant harms to the local environment and communities). Clean meat production can be powered through renewable energy sources and is expected to produce lower emissions of greenhouse gasses. Moreover, clean meat requires less land than conventional meat production, and the land that is spared can be dedicated to the production of clean energy, which can power clean meat facilities — which could lead to meat that allows for the production of more energy than is required to produce it. Finally, clean meat will not require prophylactic antibiotics, so it will not drive the evolution of antibiotic-resistant superbugs.[4] Lastly, while clean meat is not substantially different from conventionally-produced meat in its basic nature and composition, it is produced in an aseptic or a sanitary/confined environment, which reduces the risk of microbial contamination.

For these reasons, over the past two years, "clean meat" has been the preferred nomenclature for this method of meat production;[5] however as indicated earlier, cell-based meats is the currently preferred term by many private companies that are operating in this sector. To be clear, we are not suggesting that this nomenclature be used in product labeling, but rather as a shorthand for describing the environmental and other factors that distinguish clean meat from conventional meat production. Individual producers will likely label their products with different terms based upon the composition of the finished product and other relevant product characteristics, working with the appropriate regulatory agency or agencies. This sector is committed to providing clear and truthful labeling that complies with regulatory requirements and addresses consumer interest.

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[2] *See, e.g.*, Transcript of FDA Public Meeting: Foods Produced Using Animal Cell Culture Technology, Docket No. FDA-2018-N-2155 at 14, 24 (July 12, 2018), https://bit.ly/2PI10XO (hereinafter "Transcript of July 12 FDA Meeting").

[3] *See generally* Faunalytics, *Messages to Overcome Naturalness Concerns in Clean Meat Acceptance: Primary Findings* (July 2018), https://bit.ly/2D6MW8Z (Appendix A).

[4] *See* Liz Specht and Christie Lagally, GFI, *Mapping Emerging Industries: Opportunities in Clean Meat* at 2 (June 6, 2017), https://bit.ly/2QCQdPZ (Appendix B).

[5] *See* Bruce Friedrich, GFI, *"Clean Meat" Is Catching On: A Reflection on Nomenclature* (May 24, 2018), https://bit.ly/2NiDBzr (Appendix C).

Producers will have a vested interest in communicating the nature of the product to consumers for a range of reasons, including growing consumer interest in food production and sustainability and explaining differences in price, given that clean meat products likely will be introduced at a higher price than conventional meat. Accordingly, clean meat companies will have every reason to ensure that their marketing materials provide clear and accurate information to consumers so they know exactly what they are buying when they buy clean meat.[6]

In a report published last year, the National Academies of Sciences, Engineering, and Medicine (National Academies) recommended that regulatory agencies develop a single point of entry into the regulatory system to streamline the regulatory approval process for clean meat and other products like it.[7]

FDA is well situated to implement National Academies' recommendation for clean meat products. As FDA explained in its public meeting on July 12, 2018, and in its meeting materials, the agency has the expertise to evaluate the safety of clean meat under its existing authorities. Clean meat facilities resemble food production facilities currently under FDA's oversight and, as the agency has pointed out, it has extensive experience evaluating microbial, algal, and fungal cells generated by large-scale culture that are used as food ingredients or in food production.[8] The agency also manages safety issues associated with animal cell culture manufacturing for therapeutic applications and, therefore, understands issues relating to cell and tissue development.[9]

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[6] Whether clean meat is "meat" comes up in two contexts: whether USDA has regulatory oversight authority based on the agency's regulatory definition of meat and the statutory definition of poultry, and whether clean meat will be able to use meat terms on labels. The disposition of the first issue does not determine the second: that is, clean meat could fall under FDA's purview rather than USDA's and still use meat terminology on the label. Plant-based meats, which are regulated by FDA, already lawfully use meat terms on their labels (with qualifiers or other disclosures).

[7] National Academies of Sciences, Engineering, and Medicine, *Preparing for Future Products of Biotechnology* at 9, 141-144 (2017), https://bit.ly/2MG2Jes (Appendix D).

[8] *See, e.g.*, Transcript of July 12 FDA Meeting at 23 ("For example, FDA has evaluated a variety of foods produced by cell culture, including microbial products such as probiotics, algal products such as spirulina and fungal products or the mycoprotein products as well."); FDA, Notice of Public Meeting; Request for Comments, 83 Fed. Reg. at 28238, 28239 (June 18, 2018) ("FDA will be involved in the regulation of foods generated by animal cell culture technology in light of our broad statutory authority and our extensive expertise and experience in relevant scientific areas. Currently, FDA evaluates microbial, algal, and fungal cells generated by large-scale culture and used as direct food ingredients . . . .").

[9] *See, e.g.*, 83 Fed. Reg. at 28239 (stating that FDA "manages safety issues associated with animal cell culture technology in therapeutic settings"); *see also* Transcript of July 12 FDA Meeting at 21-22.

II. Potential Hazards Associated with Production of Foods Using Animal Cell Culture Technology Are Comparable to Those Associated with Other Forms of Food Production and Processing that FDA Regulates.

In its request for comments, FDA asks what considerations specific to animal cell culture technology would be appropriate to include in evaluating food produced by this method of manufacturing. Fundamentally, our position is that the safety of the final product as consumed — the clean beef, poultry, chicken, seafood, or other meat — is the relevant consideration. As FDA explains in its guidance regarding assessment of the potential effects of changes in food manufacturing, safety evaluations should focus on assessing the identity, intended use, technical effect, and anticipated exposure of a food substance. Further, "[t]he manufacturing process of a food substance is considered for the purposes of safety assessment only insofar as it may affect the properties and safety of the finished product."[10]

Nonetheless, understanding the process by which clean meat is produced and the substances that are expected to be used in the production process should help FDA ensure that the final product is safe. Here, we answer the specific questions that FDA posed in its request for written comments.

- **What kinds of variations in manufacturing methods would be relevant to safety for foods produced by animal cell culture technology?**

The safety of the final product should be assessed in ways that are similar to other foods produced from (non-animal) cell cultures. While there may be variations in production methods or processes that may introduce, for example, different points of potential entry for contaminants, the relevant metric for consumer safety is whether the final product is free from contaminants under applicable standards and the production process otherwise meets good manufacturing practice and other applicable food safety requirements.

In some cases, the types of contaminants that are identified as potential hazards and for which controls are put in place may vary depending on the species or type of cell being cultivated or the conditions of the production environment. The most notable potential variations from a safety perspective involve the types of substances in which the cells will come in contact (see question below). For example, if a company is producing cells that will be used as an ingredient in downstream processes (to make a product like a sausage, for instance), there may not be any scaffolding material involved. Another example is that some production methods may involve microcarriers to which the cells adhere during the proliferation phase, whereas other methods

[10] FDA, Guidance for Industry, *Assessing the Effects of Significant Manufacturing Process Changes, Including Emerging Technologies, on the Safety and Regulatory Status of Food Ingredients and Food Contact Substances, Including Food Ingredients that are Color Additives* at 13 (June 2014), https://bit.ly/2OxQzWP.

may use cells that naturally grow in suspension. If microcarriers are involved, their safety as an edible component of the final product should be demonstrated, unless they are not present in the final product and this can be sufficiently demonstrated (either because they are degraded during or after harvesting, or because the separation technique to harvest the cells from the microcarriers is sufficiently selective).

- **What kinds of substances would be used in the manufacture of foods produced using animal cell culture technology and what considerations would be appropriate in evaluating the safety of these uses?**

Clean meat production will require up to three main material inputs: the cells, the cell culture medium, and the scaffold. Because the cells are derived directly from species and breeds that are routinely farmed for meat, they will physiologically mimic cells within animal muscle tissue. Thus, the final products should not have a substantially different safety or nutritional profile than conventional meat from the same species.[11] A cell culture medium will be required for all clean meat production, as it supplies nutrients to the animal cells to enable the cells to reproduce and create the biomass that will eventually be consumed. Scaffolds, which provide a support structure to help the cells create a desirable, meat-like texture, will be used by some companies for certain types of products, but are not as a rule required in clean meat production.[12]

The cell culture medium used by producers to date contains ingredients that are frequently used in food and for which food-grade suppliers are available. These ingredients include salts, sugars, and amino acids. These materials are already widely used in the food industry, and their safety is well understood and documented.[13]

The medium may also contain recombinant proteins and/or small molecules present at low concentrations. The recombinant proteins would be produced through methods currently used to make enzymes and other food processing aids routinely used in the food industry. In addition, the same host strains that are widely used to make such food enzymes likely will be used to manufacture recombinant proteins for use in the production of clean meat. While these proteins or molecules could be present in the final product at very low levels, FDA could require that any trace levels are not biologically active or are below a certain threshold that would ensure safety. As such, the methods for evaluating the safety of recombinant proteins should be the same as

[11] Although not required for clean meat production, some companies may opt for genetic engineering, including recombinant engineering, of cell lines used in clean meat production or acquire cell lines derived from genetically engineered animals.

[12] *See* Elizabeth Specht et al., *Opportunities for Applying Biomedical Production and Manufacturing Methods to the Development of the Clean Meat Industry*, 132 Biochem. Eng. J. 161-168 (Apr. 15, 2018), https://bit.ly/2NkHC6s (Appendix E).

[13] *See generally* 21 C.F.R. parts 182, 184.

those used to evaluate recombinant proteins used in other food products, such as chymosin for cheese or pectinase for fruit juice clarification.[14]

Scaffolds for clean meat will be comprised of edible materials that may or may not biodegrade — and thus may or may not be present at detectable levels in the final product — during the manufacture of clean meat. These may include polysaccharides like alginate (derived from seaweed),[15] cellulose derived from plants,[16] or textured proteins derived from plant protein isolates, among other materials. These materials are already widely used in the food industry, and their safety is well documented.

- **Are the potential hazards associated with production of foods using animal cell culture technology different from those associated with traditional food production/processing? Is there a need for unique control measures to address potential hazards associated with production of foods using animal cell culture technology?**

FDA is well positioned to require that adequate preventative controls are in place to mitigate potential hazards and thereby ensure that clean meat is safe. As discussed during the FDA public meeting, the hazards and controls related to clean meat production are not substantially different from other foods developed using cell culture technology. These hazards and controls are well established and understood. Moreover, FDA has extensive experience evaluating products produced using cell culture technology, as well as inspecting the facilities in which these products are manufactured.

The primary hazards could include the introduction of contaminants at various stages in the production process, similar to other cell culture and fermentation technologies, and the introduction of unintended substances through food packaging, which is a common hazard in food production generally. Contamination should be monitored for each batch to ensure that adventitious agents are not present in the final product at harmful levels, as with any food product. Closed-containment bioprocess designs developed elsewhere in biopharma and other industrial biotechnology applications (including those for producing food processing aids like

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[14] *See, e.g.*, 21 C.F.R. § 184.1685 (FDA's regulation listing chymosin as generally recognized as safe); FDA, Substances Added to Food (formerly EAFUS), Pectinase from *Bacillus Subtilis*, https://bit.ly/2NXh5fa (last accessed Sept. 20, 2018); FDA, Substances Added to Food (formerly EAFUS), Pectinase from *Aspergillus Niger*, https://bit.ly/2MPuP6X (last accessed Sept. 20, 2018); *see also, e.g.*, FDA, Response Letter GRAS Notice No. GRN 000089 (Apr. 3, 2002), https://bit.ly/2xAF7T1.

[15] *See, e.g.*, 21 C.F.R. §§ 184.1187, 184.1724 (FDA's regulations listing calcium alginate and sodium alginate as generally recognized as safe).

[16] *See, e.g.*, 21 C.F.R. §§ 182.1480, 182.1745 (FDA's regulations listing methylcellulose and sodium carboxymethylcellulose as generally recognized as safe).

recombinant enzymes), in conjunction with stringent operational protocols, could be used to minimize the risk of contamination.

The animal cells will not be viable when they are sold in supermarkets or restaurants because animal cells have a very short period of viability when removed from culture. Therefore, there is no need to evaluate proliferation capacity or other living traits of the cells at the time of harvest or at point of purchase by a consumer. This is no different from meat derived from animal slaughter, where the animal cells themselves are non-viable at the point of consumption even if consumed raw.[17]

Finally, the materials that come into contact with the cells during cultivation should be evaluated for suitability for food, just like any other processing aid or packaging material used in the food industry. For example, it is possible that the early stages of the seed train will be cultivated in single-use polymer bags. These materials should be evaluated for leaching in the same way that food packaging is evaluated, with consideration given to the duration and conditions (such as temperature and pH) of contact with the material.

Conclusion

Cell culture technology will enable the production of high-quality protein foods without posing risks that cannot be managed effectively by responsible producers. FDA can regulate this industry by using science- and risk-based regulatory approaches under its existing authorities as well as its extensive experience to help ensure the safe production of clean meat.

This industry is committed to cooperation and transparency. We are excited about the opportunity to produce safe, efficient, and delicious foods for American consumers, and we look forward to continued collaboration with FDA as we prepare to bring our foods to market.

Thank you for the opportunity to submit these comments. We look forward to continued dialogue.

Sincerely,

Lou Cooperhouse, President & CEO, BlueNalu, Inc.
Peter Verstrate, CEO, Mosa Meat
Darren Henry Ph.D., Founder, Seafuture
Ido Savir, Co-Founder & CEO, SuperMeat
Jessica Almy, Director of Policy, The Good Food Institute
Liz Specht, Ph.D., Senior Scientist, The Good Food Institute

[17] The danger associated with raw conventional meat consumption is due to the presence of live bacterial contaminants, not from the animal cells themselves; clean meat will be devoid of these bacterial contaminants.