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IPA Meeting with FDA
Wednesday February 19 2020 (All day)

IPA Team in attendance;
Solange Henoud Lallemand Health Solutions and IPA Regulatory Committee Chair
Dr. Amy Smith, DuPont and IPA Codex Task Force Chair
Dr. Corey Hilmas, KGK Science and IPA Americas Task Force Leader
Ivan Wassermann, Amin Talati Wasserman and IPA Counsel
George Paraskevakos, IPA Executive Director.

We met with the following offices and people;

1. OFAS - Office of Food Additive Safety (OFAS), Division of Food Ingredients (DFI)
   Dr. Negash Belay; Regulatory Review Team Lead
   Dr. Stephanie Hice; Staff Fellow (Regulatory Review Scientist/Microbiologist)
   Dr. Lane Highbarger; Regulatory Review Scientist/Microbiologist
   Dr. Mical Honigfort; Regulatory Review Branch Chief
   Dr. Lauren VieBrock; Regulatory Review Scientist/Microbiologist
2. CFSAN Codex focal point representative
   Dr Douglas Balentine - Senior Science Advisor for Global Nutrition Policy
3. CFSAN – Office of Dietary Supplements Program
   Steven Tave – Acting Director ODSP
   Dr. Cara Welch – Deputy Director ODSP
   Dr. Haijing Hu – Director Regulatory Implementation Staff ODSP
   Dr. Ali Abdel Rahman – Director Evaluation and Research Staff ODSP

A) OFAS

1. GRAS Guidance proposal.
   a. A proposal for a Microbial food culture list has been put forth from the industry supported by both IPA and IFAC (initiated by Kevin Gillies). The goal, in essence, is to expand the scope of FDA prior sanctions to include lactic acid bacteria in certain fermented foods. This comprehensive list can include the IDF list of microbial cultures with a demonstrated safe history of use in food of genus and species that are considered GRAS for conventional use in food by the general population. It appears that the request has been well received by the office and the letter and request is being reviewed. No timeline has been disclosed for this. IPA suggested to OFAS to reach out if any assistance is needed for the establishment of the right mechanism to help enable this list.
   b. Such a list could be publically available on the FDA website under the GRAS Inventory or as an update to the partial list of microorganisms used in food.
2. GRAS Notifications.
   a. We brought up the concerns of timeline and backlogs that may in part be due to unnecessary applications. OFAS replied that while there was a backlog after the government shutdown, they are more or less “caught up” and the perception of a backlog is likely due to delays in updating the website that lists the notifications. Nevertheless, we insisted on the fact that species with a long history of use and well established safety are unnecessary when no vulnerable population such as

infants for example are involved or a particular use outside the conventional addition of probiotics into foods, thus previously proposed approach can be considered. (As an example mirroring the EU QPS list).
    b. OFAS brought to our attention that, unlike ODSP processes, the use of master files is contradictory to the GRAS approach.
3. Extending the use of GRAS notifications
    a. FDA is open to the idea of extending the GRAS use of a substance at higher dosages or to other food matrices without the need of resubmitting a full GRAS notification. A "supplemental notification" is all that is needed.
4. OTHER GRAS TOPICS
    a. FDA stressed that GRAS notifications are voluntary. Also indicated that dietary supplements uses are generally not appropriate evidence of safety for a GRAS notification.
    b. IPA challenged FDA's statement that they would reject GRAS notifications for ingredients in "dietary supplement form" (caps, tabs etc.) We pointed out that in the preamble to the Final Rule on Statements of Identity for dietary supplements (p.49837 see attached) Based upon the preamble language in that final rule, FDA was clear that conventional foods CAN BE in tablet, capsule form. The mere fact that an ingredient is in that form should not be the basis for rejecting a GRAS notification, in instances where the notification does not include the ingredient's use as a dietary supplement. We are following up with FDA on this ruling topic.
    c. FDA commented on the use of trade names or designations of strains, concluding that they use the deposit designation in the GRAS notices and letters of no questions.
    d. When asked about common problems they experience when reviewing notifications, they stated (1) submitting efficacy studies as evidence of safety; and (2) not sharing "confidential" data reviewed by the company's independent GRAS panel.
    e. They stressed that a report from an expert panel is not needed as part of a GRAS notification.
    f. They welcome pre-submission meetings with companies, either in-person of by phone.
5. Creation of a Probiotic Safety Consortium.
    a. This request to engage with experts from industry was well received. OFAS would consider and welcome exchange on these topics (safety of probiotics and how to interpret some sensitive parameters such as resistance genes, etc.)
6. Invite to the next IPA World Congress in DC and IPA's regulatory workshop to exchange on the previous topics – well noted and availabilities are possible.

B) CFSAN - CODEX representative Dr. Doug Balantine

1. Met with US FDA Codex Focal Point.
    a. Discussion revolved around the last CCNFSDU meet in Dusseldorf. Discussed the importance of prioritization (agenda item 10) and how Argentina and Malaysia need to make the case for probiotic harmonization, remaining on agenda and the start for new work.
    b. Other and more important discussion revolved around how the WHO definition for probiotics might better serve the industry if we revisited it. Specifically the last clause 'conferring a health benefit to the host.' The discussion revolved around a

revision of the text looking at a more functional approach/definition, without the requirement to show a specific health benefit. If the "health benefit" provision remains part of the standard, how is it to be determined? A possible "model" proposed for this is FDA's current evaluation of what ingredients meet the definition of "fiber," which also has a health benefit component.

2. Invite to the next IPA World Congress in DC and IPA's regulatory workshop to exchange on the previous topics – well noted and availabilities are possible.

C) CFSAN – Office of Dietary Supplements Program

1. Probiotics within any DSHEA revisions or addendum.
   The comment which came back from FDA regarding any DSHEA revision was that this was never stated or considered from their perspective. This was more buzz created from industry. The discussion then to add a specific consideration for probiotics within DSHEA was short lived.
2. Probiotic Master Files and Grandfathered list of species.
   FDA is open to the use of Master Files but reiterated that their interest from meeting IPA is to understand what is currently not being allowed by FDA that could benefit industry if taken up. FDA explained that currently an ingredient company can submit an NDIN and designate certain information, including fermentation medium and cryoprotectants, as "commercial confidential information" and therefore (likely) exempt from public disclosure under FOIA. Finished product companies submitting NDINs for products containing the ingredient can "reference" the NDIN with the ingredient company's permission. IPA explained that the use of a master file would show to FDA safety of the strain (i.e. minimum safety requirements within the dossier) which would be in the context of building a grandfathered list of species. Dr. Hu brought up the topic of plasmids. She was under the impression that plasmids provide *strain* ID and the chromosome provides *species* ID. We explained that this is not the case, and plasmids are extrachromosomal and do not define a strain vs a species. Instead it is the comprehensive analysis of the genome plus any plasmids (which may or may not be present) that provide the basis for identification and characterization.
3. Probiotic Safety Consortium
   IPA had requested this at last year's public stakeholder meet in May, and items such as the previous discussion regarding strain safety and others can be addressed and qualified. The FDA mentioned that this can be an industry led initiative, i.e. IPA can initiate and then invite other industry stakeholders including governments.
4. Taxonomy change of Lactobacillus species (IPA brought this to FDA's attention Oct 2018).
   We explained the importance of having harmonization when applying the change to the lactobacillus with other countries, especially at borders. FDA explained that there are no updates to be done from their side (it will not mandate by when (or even if) the names will have to change on product labels), but said it will be cooperative with labelling resulting complications if any. FDA appreciated we are bringing this to their attention beforehand. IPA stressed that any transition period to changes would be significant in allowing industry to adapt. Consequently we reported that IPA has begun a campaign to advise all probiotic stakeholders of what is coming, what to look for and how to address this change.
5. CFU and Mg discretionary guidance

We repeated our concerns of mandating both of CFU and Mg and suggested to the FDA to redraft the enforcement discretion on the use of CFU without enforcing the Mg other than in specific cases such as batch fermentation. They suggested that consumers will not be deceived by weight declarations if CFUs are also declared. We disagreed. FDA explained that a regulatory amendment is not practical in matter of timelines therefore IPA suggested the above amendment, which is not unprecedented where FDA has issued enforcement discretion on a regulatory requirement.

6. Education
   IPA mentioned previous discussion for a special project, regarding collaboration with FDA to provide outward facing content for probiotic education to consumers. Other than a reporting web link on the FDA web site such a web page does not exist and no plans at this time exist to create this stating resource constraints as the reason.
7. Invite to the next IPA World Congress in DC and IPA's regulatory workshop to exchange on the previous topics – well noted and availabilities are possible.

End of the Meetings