FDA U.S. FOOD & DRUG ADMINISTRATION

May 27, 2024

[redacted]

Sent via email to: [redacted]

Re: Citizen Petition – Docket Number FDA-2022-P-2724

Dear [redacted],

This letter responds to your citizen petition, dated September 29, 2022, and filed with the Food and Drug Administration (FDA, the Agency, or we) on November 1, 2022. In the petition, you requested FDA "immediately revoke the medical device classification of [Poly(4-Hydroxybutyrate)] P4HB based products from Becton Dickinson and reclassify these to 'Biologicals' – in order to ensure stringent clinical safety and efficacy testing of this material – most notably in cancer patients."

We have carefully considered the issues raised in your petition and other information before the Agency, and for the reasons described below, we are denying your request.

I. Request for Action

In the petition, you requested FDA "immediately revoke the medical device classification of P4HB based products from Becton Dickinson and reclassify these to 'Biologicals' – in order to ensure stringent clinical safety and efficacy testing of this material – most notably in cancer patients." We are aware of several clearances for P4HB based surgical meshes under 21 CFR 878.3300 (product codes OOD, FTL, OWT, OWZ, and OXC) and interpret your request to apply to these products. These products are intended to reinforce soft tissue and are classified as Class II devices under 21 CFR 878.3300. We interpret this as a request that FDA change the classification of these P4HB based surgical mesh products from devices as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) [1] to biological products as

[1] Section 201(h)(1) of the FD&C Act provides that the term "device" means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is –(A) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them, (B) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or (C) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

defined in section 351(i)(1) of the Public Health Service Act (PHS Act). [2]

II. Decision

For the reasons discussed further below, we believe the P4HB products cited are properly classified as devices pursuant to the statutory definition set forth in section 201(h) of the FD&C Act. As rationale for why you believe the cited P4HB products do not meet the device definition, you assert three primary reasons:

1. Transgenic production of P4HB in bacteria
2. Active metabolism of P4HB by mammalian cells
3. Immunological bioactivity of P4HB in polarizing a potentially oncogenic M2 macrophage inflammatory response in vivo

However, these reasons are not determinative as to whether a product meets the device definition. Instead, a product may be a device if it does "not achieve its primary intended purposes through chemical action within or on the body" and meets the other elements of the device definition.[3] Even if a product has chemical action, it could be a device as long as the primary intended purpose is not achieved through chemical action. Likewise, "chemical action" is not independent; it must be read within the entire context of the definition of device. With regard to the cited P4HB products, we have determined these products are appropriately classified as devices because the information before the Agency shows that the products are intended to affect the structure or any function of the body of man and do not achieve their primary intended purpose—the reinforcement of soft tissue—through chemical action. Instead, these products provide a physical structure that supports soft tissue where weakness exists.

Moreover, you do not provide a rationale for your claim that the products cited meet the definition of a biological product under section 351(i)(1) of the PHS Act. Classification of a biological product is determined based on the statutory definition. Even though this material is produced in bacteria, the cited P4HB surgical mesh products do not appear to be a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound) as described in section 351(i)(1) of the PHS Act.

III. Recent Actions Regarding the Cited Products

In your petition you cite safety concerns, including the "potentially unsafe introduction into the oncology space," and "that the FDA is permitting the non-stringent and unproven use of a potentially hazardous biochemical material in cancer patients." FDA takes these risks to patient safety very seriously and is committed to addressing these safety concerns. Since the filing of

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[2]Under section 351 of the Public Health Service Act (PHSA), the term "biological product" means "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound) applicable to the prevention, treatment, or cure of a disease or condition of human beings."

[3] See the guidance "Classification of Products as Drugs and Devices and Additional Product Classification Issues," available at https://www.fda.gov/media/80384/download

your Petition, BD has updated its labeling for the cited products, including updated warnings and precautions, to state that "The safety and effectiveness of Poly-4-hydroxybutyrate (P4HB) (product name), in breast surgery, including in augmentation and reconstruction of the breast, has not been determined by FDA." On November 9, 2023, FDA issued a safety communication to ensure that health care providers are aware of these labeling updates, and are aware that surgical mesh products, including BD's mesh products, have not been determined by the FDA to be safe and effective for use in breast surgery.[4] This communication also clarified the cleared indications for use of these surgical mesh products, specifically, they are cleared for the repair and reinforcement of soft tissue where weakness exists. The FDA will continue to keep health care providers and the public informed if new or additional information becomes available.

You also include allegations in the petition related to "encouraging and promoting off-label use of Galaflex scaffolds." We note that the allegations set forth in the Petition are substantially similar to allegations that were presented to FDA in or around August 2022. Since becoming aware of these allegations, the agency has taken several steps to investigate the issues raised and assess potential regulatory violations and safety concerns. However, as a general policy, FDA does not comment on its compliance or enforcement approach regarding individual matters and therefore will not comment further.

IV. Conclusion

After review, we have determined that your petition does not contain a sufficient basis for the FDA to grant your requested action. Specifically, your petition does not provide sufficient scientific evidence to support your claim that the cited P4HB products fail to meet the device definition. Therefore, your petition is subsequently denied.

If you have any questions about this response, please contact Andrew Yeatts, Ph.D. of our Office of Policy at Andrew.yeatts@fda.hhs.gov or (301) 796-4539.

Sincerely,

Ellen J. Flannery -S

Digitally signed by Ellen J. Flannery -S
Date: 2024.05.27 14:49:19 -04'00'

Ellen J. Flannery, J.D.
Deputy Center Director for Policy
Director, Office of Policy
Center for Devices and Radiological Health

[4] https://www.fda.gov/medical-devices/letters-health-care-providers/labeling-updates-bd-mesh-products-letter-health-care-providers.