

Reclassification of Becton Dickinson's Poly(4-Hydroxybutyrate) Based "Medical Devices" to "Biologics".

Date: 9/29/2022

The undersigned submits this petition under Statute 10.30 of the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act to request the Commissioner of Food and Drugs to reclassify Becton Dickinson's Poly(4-Hydroxybutyrate) (i.e., P4HB) based "medical devices" to "biologics".

A. Action Requested

Revoke the "medical device" classification of P4HB based, Phasix™ and GalaFlex™, products commercialized by Becton Dickinson (BD) of Franklin Lakes, NJ – and reclassify these products to "Biologics" for clinical testing and commercialization purposes.

The present citizen petition is respectfully requesting that the commissioner immediately revoke the medical device classification of P4HB based products from Becton Dickinson and reclassify these to a "Biologics" – in order to ensure stringent clinical safety and efficacy testing of this material – most notably in cancer patients.

B. Statement of Grounds

This Citizen Petition claims that FDA's CDRH has unsafely misclassified P4HB based products as "Medical Devices". These products include Becton Dickinson's Phasix™ mesh and GalaFlex™ scaffold. This FDA misclassification of P4HB-based materials has led to their potentially unsafe introduction into the oncology space without adequate preclinical and clinical testing to ensure safety.

As Background, Poly(4-Hydroxybutyrate) is a transgenic hydrocarbon which is exclusively produced in bacteria using a fermentation process. BD has commercialized the scale of P4HB production through its recently acquired subsidiary company *Tepha Medical Devices*.

Several characteristics of P4HB make it critically important that this any geometrically configured products made monolithically of this organic biochemical material be classified as a "Biologic" - NOT a "medical device". These facts include:

- 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*.

The following scientific papers are demonstrative of the above the listed biological characteristics of P4HB:

<https://www.frontiersin.org/articles/10.3389/fbioe.2020.00257/full>

<https://www.sciencedirect.com/science/article/abs/pii/S2468498818300192>

<https://derekswang.com/publication/molina-2019/molina-2019.pdf>

The misclassification of P4HB based bioactive mesh and scaffold material as "medical devices" is posing a potential threat to public health in the oncology space. Specifically, because these misclassified biologically active materials, with potential oncogenic properties, are being commercialized for use in cancer patients by Becton Dickinson and its associates - WITHOUT adequate *in vivo* preclinical studies and WITHOUT proper phase 1 clinical safety testing to ensure oncological safety in these patients.

Specifically, Becton Dickinson is actively encouraging and promoting off-label use of GalaFlex scaffolds in women undergoing cosmetic breast reconstruction and re-modelling. In the breast cancer space, BD and its collaborators have been experimenting with the use of P4HB material for breast reconstruction in women with breast cancer. This experimental clinical work, named LOTUS, was performed by a BD collaborator in the state of Florida, along with colleagues at the University of Pittsburgh led by Professors S. Badylak and J. Peter Rubin, without an Investigational Device Exemption from FDA:

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6750512/>

Additionally, as of July 2022, BD was scheduled to begin a multinational clinical trial of P4HB based reconstruction in women with breast cancer, akin to LOTUS, named Project ROSE. This clinical trial was not based on any in vivo preclinical studies to demonstrate the oncological safety of P4HB and, being a PMA-directed clinical trial, did not include a Phase 1 trial to assess the oncological safety of P4HB material in the breast cancer resection space. Specifically, it is unclear whether P4HB induced inflammation of the mastectomy reconstruction space in women would: 1) interfere with radiological surveillance for recurrent cancer and 2) potentiate cancer recurrence rates. These metrics are critically important to public health and safety in the breast cancer space anytime a biologically active substance is placed in direct contact with an oncological resection space.

Unfortunately, FDA's "medical device" misclassification of BD's P4HB based mesh and scaffold products, blocks the need for proper phased clinical trials to demonstrate the safety and efficacy of this bioactive material when used in cancer patients.

In summary, by classifying Becton Dickinson's metabolically active P4HB based biomaterial products as "medical devices", the FDA is permitting the non-stringent and unproven use of a potentially hazardous biochemical material in cancer patients. The present citizen petition to the FDA commissioner is a request for an immediate suspension of P4HB based products' marketing as medical devices in the United States – and a reclassification to the "Biological" category for commercialization purposes.

C. Environmental Impact

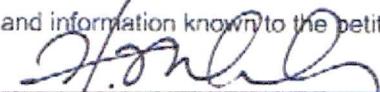
Subject to Statutory Exemption

D. Economic Impact

This information can be furnished to the FDA commissioner upon request.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.



(Signature)

Hooman Noorchashm MD, PhD

(Name of petitioner)

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(Mailing address)



(Telephone number)