ADVANCED BIOMATRIX
A BICO COMPANY

Justification for Omission of Testing Under 21 CFR 610.40(a)(3)

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Advanced BioMatrix produces fibronectin derived from source plasma collected at FDA-licensed plasma collection facilities in compliance with 21 CFR Part 640. This source plasma is designated as an in vitro diagnostic (IVD) product for research use only (RUO), intended solely for laboratory applications and not for injection into humans. This product is not intended for any diagnostic or therapeutic purposes. As part of our quality assurance process, we have evaluated the applicability of testing requirements under 21 CFR 610.40, specifically subsection (a)(3), which mandates tests for communicable disease agents beyond those listed in 610.40(a)(1) and (a)(2) when directed by the FDA. This includes agents such as Creutzfeldt-Jakob Disease (CJD), variant Creutzfeldt-Jakob Disease (vCJD), and malaria. We hereby justify the omission of such testing for the following reasons:

1. **Regulatory Scope and Intended Use:** Under 21 CFR 610.40(a)(3), additional testing for communicable diseases like CJD, vCJD, and malaria is required only when the FDA explicitly directs it based on a determined material risk to the product's safety or use. The source plasma utilized in our fibronectin production is not transfusable plasma but is collected and processed for further manufacturing into IVD products for RUO, as defined in 21 CFR 640.60. The FDA has not mandated testing for CJD, vCJD, or malaria for source plasma intended for such purposes, as these agents are not typically transmitted via plasma-derived RUO products used in non-human applications.

2. **Risk Assessment and Purification:** CJD and vCJD are prion diseases with no validated blood screening tests available, and their transmission risk through plasma derivatives is considered negligible due to rigorous purification processes. Similarly, malaria, caused by Plasmodium parasites, poses minimal risk in U.S.-sourced plasma, where donor screening and deferral protocols (21 CFR 640.63) are in place. Our fibronectin production employs filtration techniques, such as column chromatography, which contribute to the purity of the final product. These purification steps are designed to isolate fibronectin effectively, potentially enhancing the integrity of the material by reducing impurities, including theoretical pathogens, consistent with its RUO designation.

3. **FDA Guidance and Industry Standards:** Current FDA guidance does not require routine testing of source plasma for CJD, vCJD, or malaria under 21 CFR 610.40(a)(3) for products not intended for human transfusion or injection. This aligns with industry practices for plasma-derived RUO materials, where mandatory testing focuses on viruses such as HIV, HBV, and HCV (21 CFR 610.40(a)(1)-(2)), which are addressed in compliance with FDA regulations. The additional purification processes we utilize further support the quality of the fibronectin for its intended research applications.

Based on the above, testing for CJD, vCJD, and malaria under 21 CFR 610.40(a)(3) is not applicable to the source plasma used in our fibronectin production. This omission aligns with regulatory requirements, the product's RUO classification, and the absence of FDA directives mandating such tests for this specific use case. The incorporation of filtration techniques in our process underscores our commitment to delivering a pure product, while we continue to ensure safety and compliance through adherence to all relevant CFR guidelines.

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