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PROTOCOL APPROVAL WITH MODIFICATIONS

DATE:	20 Sep 2022
TO:	WIlliam Denman, MD, FRCA
PROTOCOL:	Entrinsic Bioscience, LLC - EBSIBSD1, An evaluation of tolerability with daily consumption of EBS Advanced IBS-D among patients with diarrhea predominant irritable bowel syndrome (IBS-D): A pragmatic open-labelled home use study. (Pro00065894)
APPROVAL DATE:	15 Sep 2022
EXPIRATION DATE:	15 Sep 2023

IRB APPROVED DOCUMENTATION:

Protocol Version(s):
- Protocol Version 1.0 (Dated 12 September 2022)

Consent Form(s):
- Informed Consent Form (Advarra IRB Approved Version 19 Sep 2022)

Other Material:
- 1ST EMAIL (Not Dated)
- 2ND EMAIL (Not Dated)
- 2ND EMAIL (If person did not open first email) (Not Dated)
- IBS-D SMS Messaging (Not Dated)
- Questionnaire, Landing Page (Not Dated)

The IRB approved the above referenced protocol and your site with the modifications listed below on 15 Sep 2022:

- **Modifications to the Informed Consent Form**
- **Modifications to the 1ST EMAIL, 2ND EMAILs, IBS-D SMS Messaging, and Landing Page**

On 19 Sep 2022, the IRB reviewed and approved additional revisions to the Informed Consent Form.

The above referenced recruitment/subject material is available on your Advarra CIRBI Platform under the "IRB Issued Documents" tab.

Use of eConsent is Approved.

Based on the confirmations provided to the IRB, it is expected that:

1. The eConsent(s) will include the complete and exact contents of the most current, IRB approved study consent(s).

2. The eConsent process includes obtaining signature(s) in compliance with applicable law and a method to confirm the identity of the signer(s).
3. The stored eConsent(s) identify the signers and date (time, if applicable) of signing; signed eConsent(s) are stored with appropriate access, and all versions are retrievable.
4. The signers must review all consent contents prior to signing the eConsent (i.e., there is no function available to skip directly to the signature field(s)).
5. All subject-facing materials used during the eConsent process (e.g., web-linked materials, graphics, videos, glossary, etc.) will be submitted for IRB approval.
6. If CIRBI eConsent Attestation responses change, an eConsent Modification will be submitted to the IRB for review. Note: An eConsent Modification is not required when revisions are only to the IRB approved study consent document(s).

If the study is expected to last beyond the approval period, you must request and receive re-approval prior to the expiration date noted above. A report to the Board on the status of this study is due prior to the expiration date or at the time the study closes, whichever is earlier. It is recommended that you submit status reports at least 4 weeks prior to your expiration date to avoid any additional fees or lapses in approval.

If this study is in an FDA 30-day wait period, subjects **may not** be consented or screened, as consent would be required before study-specific screening activities may begin. However, some initial activities related to determining a potential subject's interest in the upcoming study may occur. Such activities should be limited to recruitment efforts to inform potential subjects, or a community that a study may soon begin on a given condition. However, screening subjects to determine eligibility would not be acceptable until the IND is in effect.

If you wish to appeal the IRB's determinations and/or imposed modifications, please submit supporting documentation to address the IRB's concerns by creating an Appeal Modification in CIRBI.

Approved investigators and sites are required to submit to Advarra for review, and await a response, prior to implementing any amendments or changes in the protocol; informed consents; advertisements or recruitment materials ("study-related materials"); investigators; or sites (primary and additional).

Approved investigators and sites are required to notify Advarra of the following reportable events, including, but not limited to unanticipated problems involving risks to subjects or others; unanticipated adverse device effects; protocol violations that may affect the subjects' rights, safety, or well-being and/or the completeness, accuracy and reliability of the study data; subject death; suspension of enrollment; or termination of the study.

Please review the IRB Handbook located in the "Reference Materials" section of the Advarra CIRBI™ Platform (www.cirbi.net). A copy of the most recent IRB roster is also available.

Thank you for selecting Advarra IRB to provide oversight for your research project.