



Clinical Trials and Human Subjects Research Policy (“Policy”)

Introduction

Clinical trials and human subjects research (“HSR”) are a critical and necessary phase of research and development of Barth syndrome treatments and therapies. Barth Syndrome Foundation (“BSF” or “Foundation”) is committed to ensuring that clinical trials and studies in which the Foundation participates, in any country/territory, are conducted with the utmost integrity, transparency, and respect for participants’ interests and rights. This Policy intends to clarify the ways we achieve these goals corresponding to the scope of the proposed study and covers, but is not limited to, the following types of engagements:

- 1) Funding requests of clinical trials or studies
- 2) Use of BSF resources and/or platforms to help realize clinical trials or studies
- 3) Education and outreach to inform the BSF community of enrolling trials and studies
- 4) Requests to conduct on-site research at BSF events or meetings

Research Requirements

BSF believes strongly that data collected during clinical trials and HSR should, when applicable, be employed in healthcare providers’ decisions in the care of their Barth syndrome patients, shared so participants understand their results, maximized to inform current and future research, and appropriately leveraged to expand the public’s knowledge of Barth syndrome. The requirements listed below uphold these principles, with the intent that data derived from research can be used to the full extent possible to advance our understanding of Barth syndrome and possible treatments. Importantly, BSF does not formally endorse any HSRs or clinical trials, and the decision to participate is entirely up to the participants and their families.

Approved Institutional Review Board (“IRB”) Application: Engaging BSF early in the development of an IRB application ensures it will meet the requirements stipulated in this Policy and expedite the ethical review process. Early engagement helps guarantee that the research plan actively considers a patient-centric approach and capitalizes on the wealth of institutional knowledge to incorporate technical, regulatory, and/or clinical perspectives. All clinical trials and HSRs are required to submit their IRB approval letter to BSF along with the protocol, informed consent form, and accompanying study materials (if applicable). BSF neither funds nor provides in-kind resources required for the research until the IRB approval is received and confirmed by BSF to include 1a-d as defined by the type of study in the table below.

1.a Serious Adverse Events (“SAE”s): Clinical trials and invasive research studies are required to report SAEs to BSF within the same timeframe required by the governing IRB.

1.b Inclusion of Global Unique Identifier (“GUID”): Clinical trials and HSRs are expected to implement BSF’s GUID system to assign a unique identifier to each participant, unless disallowed by local or

federal laws or if a participant chooses to opt out during the consent process. This de-identified linking code will be used to ensure the privacy and confidentiality of participants while facilitating data sharing and tracking of outcomes. See the supplementary [GUID document](#) for more details.

1.c Return of Results (“ROR”): To promote transparency and empower Barth syndrome affected participants, researchers are expected to offer participants the option to receive their results when feasible and appropriate. BSF understands that some data elements cannot be easily returned and will work with the research team to develop a mutually agreeable solution outlined in the research plan and/or consent form. See the supplementary [Return of Results](#) document for more details.

1.d Data Sharing Plan: BSF recognizes the importance of open access to research data and creating a multiplier effect for data to be leveraged beyond the finite scope of any one study. Therefore, BSF will request that a data sharing plan be developed to promote the responsible and equitable sharing of research data with the scientific community, subject to appropriate privacy protections and regulatory requirements. The data sharing plan must include the sharing of GUIDs back to BSF and demonstrate a commitment to enable data access to other researchers. See the supplementary [Data Sharing](#) document for more details.

APPROVED INSTITUTIONAL REVIEW BOARD (IRB) APPLICATION Must include:						
Type	1.a SAEs	1.b GUID	1.c RoR	1.d Data Sharing	Regulatory Engagement	BSF Approval Level
BTBS Specific Clinical Trial	Yes	Yes	Yes	Yes	Highly recommended	Board of Directors
Non-BTBS Specific Clinical Trial	Yes	Highly recommended	Highly recommended	Highly recommended	Optional	Board of Directors
BTBS Specific Invasive HSR	Yes	Yes	Yes	Yes	Not applicable	Board of Directors
Non-BTBS Specific Invasive HSR	Yes	Highly recommended	Highly recommended	Highly recommended	Not applicable	Board of Directors
BTBS Specific Non-Invasive HSR	Not applicable	Yes	Yes	Yes	Not applicable	BSF Staff*
Non-BTBS Specific Non-Invasive HSR	Not applicable	Highly recommended	Highly recommended	Highly recommended	Not applicable	BSF Staff

*If all requirements are not met, and irrespective of approval level, the BSF Board of Directors must approve BSF’s involvement in the study prior to initiation
BTBS = Barth syndrome; HSR = human subjects research; SAE = serious adverse event; GUID = global unique identifier; RoR = return of results.

DEFINITIONS

Serious Adverse Event: Any unexpected or unfavorable medical occurrence in a human subject, including any abnormal sign (e.g., abnormal physical exam or laboratory finding), symptom, or disease, temporarily associated with the subject's participation in the research is considered an adverse event. Serious adverse events are ones that result in death, life threatening, hospitalization, disability or permanent damage, congenital anomalies/birth defects, or are other conditions that are significant hazards.³

Clinical Trials - A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.¹

Data Sharing: The practice of making research data available within the scientific community, for the purpose of accelerating research discovery, validating results, and promoting data reuse for further research.⁵

GUID: GUID stands for Global Unique Identifier and it is a subject ID that allows researchers to share data on a study participant without revealing any personal identifiable information (PII) or protected health information (PHI). This allows researchers to match participants over time and across research sites, labs, and data repositories. GUIDs are generated through the secure infrastructure of the National Institutes of Health (NIH) Biomedical Research Informatics Computing System (BRICS).

Human Subjects Research - Research involving a living individual about whom data or biospecimens are obtained/used/studied/analyzed through interaction/intervention, or identifiable, private information is used/studied/analyzed/generated.²

Invasive - Any procedure that enters or exposes the body (e.g., via incision, percutaneous puncture, or instrumentation) is considered invasive. Examples include biopsy, surgery, blood draw, imaging that requires insertion of instruments, injections or infusions, and device implantation.

Regulatory engagement: Where applicable, the study sponsor invites a member of BSF and/or the Barth syndrome community to participate in meetings with regulators pertaining to the research and development efforts of a potential product with an indication or application in Barth syndrome.

Return of Results: The process of providing research participants with individual or aggregate findings from the research study. Individual results refer to the outcomes of the research assessments and/or interventions for an individual participant (e.g., lab results on bloodwork, their BMI, score on a research instrument, or imaging such as an echocardiogram). Aggregate results refer to the outcomes of the study and do not contain reference to individually identifiable data. Examples include whether the study met its endpoint or confirmed the research hypothesis.⁴

¹ <https://grants.nih.gov/policy/clinical-trials/definition.htm>

² <https://grants.nih.gov/policy/humansubjects/research.htm>

³ <https://www.hhs.gov/ohrp/regulations-and-policy/guidance/reviewing-unanticipated-problems/index.html>

⁴ <https://www.advarra.com/blog/return-of-research-results-to-study-participants/>

⁵ <https://sharing.nih.gov/data-management-and-sharing-policy/about-data-management-and-sharing-policies/data-management-and-sharing-policy-overview>