

BRISTOL-MYERS SQUIBB DATA SHARING INDEPENDENT REVIEW COMMITTEE (IRC) CHARTER

Charter Effective Date:

v1.0

10 July 2014

Introduction

This Charter describes the roles and responsibilities of the Independent Review Committee (IRC) for the Bristol-Myers Squibb (BMS) Data Sharing Initiative. This program has been initiated by BMS to enhance the transparency of its clinical trial programs and to make available data from clinical trials to qualified researchers for analysis.

1. Purpose of Data Sharing Initiative

There is an escalating call for improved transparency in clinical research, particularly by the pharmaceutical industry. This includes the improved communication of clinical trial results and availability of study data to researchers for additional analysis. In response to this movement, the Pharmaceutical Research and Manufacturers of America (PhRMA) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) released the [Principles for Responsible Clinical Trial Data Sharing](#) in July 2013. This includes the following commitments:

- a. Enhancing data sharing with researchers
- b. Enhancing public access to clinical study information
- c. Sharing results with patients who participate in clinical trials
- d. Certifying procedures for sharing clinical trial information
- e. Reaffirming commitments to publish clinical trial results

BMS has initiated a series of efforts to enhance transparency of its clinical trial programs. Specifically, this includes launching a program to make data from in-scope clinical trials available to qualified researchers for analysis. Acknowledging the challenges balancing the risks of disclosure with scientific quality and public perception, BMS seeks to leverage the collaborative relationship with Duke to assist in this endeavor.

2. Scope of Data Sharing Initiative

The data sharing initiative pertains to BMS-sponsored Phase I-IV interventional trials in patients which completed after January 2008 in which patients participated. This includes patient-level and study-level clinical trial data, full clinical study reports and protocols from clinical trials conducted in patients for medicines and indications approved in the U.S. and/or EU. Requests are subject to terms necessary to protect patient privacy and respect patient's informed consent.

3. Proposal Submission/Research Protocol

Proposals will be submitted electronically via a website maintained by BMS. The research proposal will include key information on the data request, such as:

- a. Title of proposed research
- b. Proposal summary
- c. Study design
- d. Description of studies selected and patient populations
- e. Primary and Secondary endpoints for the proposed study
- f. Statistical analysis plan
- g. Publication plan
- h. Qualifications and experience of the research team (include Curricula Vitae)
- i. Source of research funding
- j. Any potential conflicts of interest
- k. Other supporting documents

4. Independent Review Committee (IRC)

To facilitate an independent review process for all submitted proposals, BMS has engaged with Duke University, through its Duke Clinical Research Institute (DCRI) to delegate the review and recommendations authority as an outside, reputable academic entity with experience in design, conduct and analysis of clinical trial data.

Composition of the IRC

The IRC will be comprised of two co-chairs plus three to four core members representing three broadly defined areas of expertise; clinical, statistical/data-related and bioethical/protection of human subjects (more detailed information on the members is available by request). To ensure adequate expertise is applied to each review, additional core members or other experts from within Duke or external to Duke may be asked to participate in an IRC meeting at the discretion of the co-chairs.

Qualifications of the IRC Reviewers

- i. Clinical, statistical, data-related, bioethical or protection of human subjects expertise related to the area of the proposed study
- ii. General knowledge of clinical trials
- iii. Availability and commitment to the goals and timelines of the program
- iv. Remain in good professional standing
- v. Independence from requestor of data or any affiliate(s)
- vi. Provide disclosure of potential conflicts of interest that will be reviewed by the IRC co-chairs, if necessary.

Information about the IRC reviewers can be found here:

<https://dcri.org/education-training/irc/independent-review-committee>

5. Review Process

BMS will review each proposal for completeness and availability of the data requested and meeting pre-qualification criteria (as stated here: http://www.bms.com/clinical_trials/pages/disclosure.aspx), and may provide a recommendation to the IRC on the feasibility of the request. If the submitted request for data is out of scope and does not meet pre-specified criteria, such as data availability, BMS will inform the requestor and ask them to update or modify the proposal. Comments generated by BMS staff during this initial review that relate to the evaluation of the proposal will be provided to DCRI for consideration by the IRC. BMS may also suggest to the IRC that the proposal be evaluated following the expedited review process. The following outlines the review process, also summarized in Appendix A.

- a. BMS will compile the proposal materials and send to DCRI project leader via email for review by the IRC.
- b. Upon routine checks for completeness, the project leader will forward the request to the IRC chair.
- c. An IRC Chair will perform an initial evaluation of the proposal to 1) determine if an expedited review, rather than full committee review is acceptable; and 2) determine if subject matter expertise beyond the core IRC membership is required to appropriately review the proposal. The presiding IRC Chair has the sole discretion to invite additional reviewers to participate in the IRC review of a proposal.

- i. Full committee review meetings will include a chair plus members representing each of the three designated domains to achieve quorum.
 - ii. Decisions reached by the IRC when a quorum is achieved will be considered final; subsequent reviews from additional committee members will not be supported.
 - iii. Expedited committee review meetings will include the chair plus one other member. If the two members are not unanimous in their recommendation the proposal will go for a full committee review.
- d. Invited members of the IRC may include any individual with the expertise deemed necessary to review a proposal. This may be an employee of Duke University or a subcontractor. Academic faculty status will be typical, but is not required.
- e. After the IRC members have been identified, the project leader will send them all review materials and schedule a meeting, held in person or by a teleconference.
- f. Specific portions of IRC meetings may be 'open' to discussion among IRC reviewers, BMS employees (e.g. statisticians and medical leads familiar with the trial datasets or researcher making the request) and potentially the submitting investigator. A portion of the meeting may be closed to ensure proposals can be freely discussed among IRC reviewers. The IRC will have the final decision-making authority for the disposition of a proposal. Meeting minutes will be recorded by the project leader using a standard form.
- g. The IRC recommendation will be sent to BMS. The IRC and/or BMS will communicate feedback on the proposal to the requestor. In the event that a request is not approved or requires revisions, a detailed explanation of the problems with the proposal in its current form will be provided to the requestor by the IRC.
- h. All decisions and rationale supporting decisions regarding data requests will be posted to bms.com
- i. The submitting investigator shall be expected to obtain IRB and/or ethics committee approval or documentation of exemption before receiving the data and performing the research.
- j. The research team will be responsible for entering into a data sharing agreement with BMS prior to data being provisioned if the proposal is approved.
- k. BMS will be responsible for provisioning the data to the investigator, DCRI/IRC will be informed of the methods and status of this activity, but will not be directly involved with the implementation of this process.

In cases where a perceived conflict of interest arises, (e.g. review of a proposal from a Duke researcher or a request for data from Duke-led studies) experts from outside of Duke may be more appropriate to provide clinical, statistical or ethical insight and will be included in the IRC. In these situations, one of the Duke IRC co-chairs will work with an external co-chair to determine the potential perception of conflict and the extent to which non-Duke faculty should be included in the review.

6. Review Criteria

The IRC shall ensure that only scientifically appropriate research on clinical trial datasets is approved. The goal is to safeguard scientific validity without creating undue burden by requiring particular statistical methodology. The IRC may make requests to BMS or the requester for additional information or clarification that may be needed to adequately review a proposal.

Research protocols will be reviewed using pre-defined criteria, such as:

- a. Is the research question clearly defined with a scientifically valid rationale?
- b. Is there a well-documented and rigorous Statistical Analysis Plan?
- c. If the protocol includes combining data across trials, is there a clear plan to standardize data sets to ensure comparability?
- d. Is there an adequate publication plan to disseminate findings in a peer-reviewed journal or at a scientific meeting?
- e. Is the applicant willing to declare all professional interests, affiliations, possible conflicts of interest and all sources of support for the research as part of the dissemination of their results? The IRC will provide feedback as to if the plans for mitigation of the perceived conflict are acceptable.
- g. Does the research team have sufficient expertise and qualifications to perform the proposed investigation?
- h. Is the privacy of the human subjects whose data will be used as part of this research adequately protected?

After review the IRC will make one of the following recommendations:

- a. Not approved: The proposal is deemed as scientifically invalid or violates human subjects' protection and substantial change would be required to rectify the issues.
- b. Approved: The proposal is approved as submitted.
- c. Revise and resubmit: The proposal holds scientific merit; however, there are issues the IRC will require to be resolved before the proposal can be approved. The IRC will provide detailed feedback to the investigator. Revised proposals will be re-evaluated by the IRC to determine final disposition.

7. Final Review of Research Results

Requesters who received access to BMS data are expected to submit the results and draft publication of the analysis to BMS and the IRC. The IRC will review the materials to ensure that the methods utilized are concordant with those in the approved proposal and that the interpretation/conclusions drawn are not beyond those of the results presented.

BMS Data Initiative Review Process

