

**Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard
Bioethics Collaborative | April 24, 2018**

**Return of Individual Results to Research Participants and Axes of Communication
Meeting Summary**

The sixth meeting of the MRCT Center Bioethics Collaborative brought together 26 stakeholders from academia, government, industry, patient advocacy organizations, foundations and independent IRBs to examine **Return of Individual Results to Research Participants and Axes of Communication**.

Introduction

The return of individual results of clinical trials to research participants has been a central topic of discussion over the past two decades. At issue is (1) whether and when individual results should be shared with research participants, and (2) whether, when, and by whom incidental findings should be communicated. With the growing presence of precision medicine and the reciprocal rise of research studies that include whole genome sequencing, the resolution of these issues promises to profoundly impact the design and conduct of human subjects' research. The sixth meeting of the MRCT Center Bioethics Collaborative confronted these timely topics by exploring the ethical principles underlying the return of individual results, as well as by considering the roles and responsibilities of various stakeholders in the clinical research ecosystem.

Meeting Summary

The MRCT Center Bioethics Collaborative meeting began with a high-level overview of the three resources generated by the MRCT Center's Return of Individual Results (IRR) working group: (1) a [recommendations document](#),¹ (2) [a toolkit](#),² and (3) an [ethical principles document](#).³ These resources, released in late 2017, prioritize the integrity of the research while protecting the safety and welfare of the participant; categorize research results by degree of urgency, medical significance, analytical validity, and personal utility; appreciate the right of an individual to choose whether to receive results; and recognize that genetics and genomics results are worthy of special consideration, among other principles.

Discussion of these resources centered on the interplay between the IRR working group's efforts and

¹ version 1.2, see <http://mrctcenter.org/wp-content/uploads/2017/12/2017-12-07-Return-of-Individual-Results-Recommendations-Document-V-1.2.pdf>

² version 1.2, see: <http://mrctcenter.org/resources/2017-11-22-template-mrct-return-individual-results-participants-toolkit-version-1-2/>

³ version 2.1, see <http://mrctcenter.org/wp-content/uploads/2017/12/2017-11-20-Return-of-Individual-Results-Principles-Nov-2017.pdf>

the European Union’s General Data Protection Regulation (“GDPR”) that took effect on May 25, 2018. Given that the GDPR applies to “any information relating to an identified or identifiable natural person (‘data subject’),” attendees contemplated whether and how the return of individual results to research participants may be affected by the new regulations. The data that falls under the purview of the GDPR, it was noted, is far broader than that which falls under the US Department of Health and Human Services Health Insurance Portability and Accountability Act of 1996 (HIPAA) and many other privacy laws in other jurisdictions. Moreover, the GDPR applies extraterritorially and is agnostic to the citizenship of the data subject. Since the GDPR differs from other privacy regulations in several key ways, the GDPR will likely create numerous challenges for global investigators and sponsors who may wish to return individual research results to participants. For example, and relevant to the US, the GDPR endows data subjects with broad rights of access, granting them the ability to request research results that were generated in non-CLIA⁴-certified labs. Because the provision of research results from non-CLIA-certified labs is prohibited under US law, the attendees at the MRCT Center Bioethics Collaborative recognized the need for U.S.-based entities to identify the circumstances under which organizations may receive and process personal data from European Economic Area (EEA) member states (the 28 EU member states, Iceland, Lichtenstein, and Norway.) The rights of access and portability mandated by the GDPR pose nuanced challenges for sponsors and clinical research personnel globally.

Following discussion of the GDPR, attendees explored research participants’ perspectives on requesting and obtaining data from clinical trials. It was acknowledged that research participants’ preferences may vary, but that the majority of participants express an interest in receiving plain language summaries of both aggregate and individual research results.⁵ A recent [TransCelerate Biopharma, Inc. study](#)⁶ reveals that 66% of clinical trial participants perceive the return of individual research results to be an important factor in deciding whether or not to enroll in a study. Eighty-one percent of respondents expressed a desire to receive their own information (test or lab results) during the course of the clinical trial, and 80% of respondents expressed a desire to receive general results after trial completion.

Despite research participants’ overwhelming interest in obtaining both individual and aggregate research results, few participants report actually receiving this information. Attendees acknowledged several reasons why this may be the case: (1) many participants assume that their healthcare provider(s) will communicate any information that may affect their health—including, but not limited to, “actionable” findings; (2) research participants are not systematically informed of study staff’s plans to return individual and/or aggregate results; and (3) research participants are uncertain about who and how to ask for additional information. Additionally, although some sponsors post plain-language

⁴ The Clinical Laboratory Improvement Amendments (CLIA), regulating all laboratory testing (except research) performed on humans in the U.S., ensures quality laboratory testing. <https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/index.html?redirect=/CLIA>. Accessed 4 June 2018.

⁵ See <https://www.ciscrp.org/download/2017-perceptions-insights-study-the-participation-decision-making-process/?wpdmdl=8768>. Accessed 2 June 2018.

⁶ See <http://www.transceleratebiopharmainc.com/wp-content/uploads/2017/11/What-do-Patients-Want-Visualization.pdf>. Accessed 2 June 2018.

aggregate summaries publicly after results are published, unless study participants are informed at the time of posting, few will actually be aware of their availability. Even participants who *did* know who and how to ask may be reluctant to do so because of the uncertainty and lack of clarity as to what they are permitted to receive.

Attendees further explored these issues by questioning the role of healthcare providers in returning individual research results to participants. A collaborative survey study by the MRCT Center and CenterWatch revealed that a majority of investigators and treating physicians believe that clinical trial results in general, and urgent findings in particular, ought to be shared with research participants.⁷ Investigators' responses support the belief that investigators should share results directly with patients – including aggregate results, study group assignment, and participant level data for primary endpoints—but that several barriers that inhibit investigators and treating physicians from fulfilling these responsibilities. The most commonly cited barrier to communication of individual findings was insufficient access to research results from study sponsors.

To streamline disclosure and communication of aggregate and individual research results, attendees explored several innovative tools. The [Nucala Real World Evidence \(RWE\) study](#)⁸ was highlighted as an innovative digital solution to communicate study results via a phone app. The app, which research participants were invited to download at the beginning of the study on a voluntary basis, monitors participants' levels of asthma control and stores that data in the Internet. Participants are then able to securely download that data in order to view, understand, and better manage their conditions. The app combines the data that patients entered with other publicly available data and presents the information back to patients using clear data visualization and graphics. This app is a direct way to share certain types of data/results with patients, which they can then share with study or treating physician if they choose to do so. [Trial Scope's Trial Results Summaries Portal](#)⁹ was also recognized as an efficient mechanism by which clinical trial sponsors may post plain language summaries of aggregate results. The third solution discussed by attendees was the Patient Data Access Initiative— a consortium of a small number of pharmaceutical companies working together to facilitate sponsors to share clinical trial data directly with patients. A similar undertaking was recently unveiled by the Centers for Medicare and Medicaid services (CMS) through [MyHealthEData](#)¹⁰ which provides patients with access to their complete electronic health record and is intended to increase competition amongst providers and reduce overall cost. [Blue Button 2.0](#)¹¹ was also relaunched and allows traditional Medicare beneficiaries to access and share personal health data in a universal digital format, thereby enabling claims data to be connected to providers via secure web applications.

⁷ MRCT Center and CenterWatch, manuscript in preparation.

⁸ https://www.pei.de/SharedDocs/Downloads/awb/nis-0301-0400/0385-beoplan.pdf?__blob=publicationFile&v=1. Accessed 2 June 2018.

⁹ <http://www.trialscope.com>. Accessed 2 June 2018.

¹⁰ <https://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2018-Fact-sheets-items/2018-03-06.html>. Accessed 2 June 2018.

¹¹ <https://www.healthit.gov/topic/health-it-initiatives/blue-button>. Accessed 2 June 2018.

The CMS initiatives aim to empower patients and improve their experiences by providing them with access to healthcare data and can be used as models for how to return results from clinical trials. Sharing data through the return of individual results to research participants seeks to do the same. Interactive portals, real-time data capture, and dynamic Internet-based data storage could be leveraged by sponsors, academic institutions, investigators, and healthcare providers to enable the process of return of results to be both simpler and more efficient. It is critical, however, that these technologies be utilized in a manner that is compliant with the foundational ethical principles of clinical research.

To highlight the complexities surrounding the return of individual results to research participants—as well as the potential utility of integrating technological communication platforms into the disclosure process—a series of case studies was examined. The first case study explored the challenges that sponsors face in sharing genomic data with participants. Because sponsors do not communicate directly with study participants during the course of a trial, this case study queried the role of investigators and genetic counselors in sharing genetic information with research participants. The second case study probed the types of genetic data that could be shared with participants who reside in a country that requires unobstructed access to personal information (such as EEA member states) as well as how to balance the timing of requests with the availability of data. Third, attendees considered the obscurities around providing research participants with results from non-FDA approved tests at an otherwise accredited lab. The fourth case study questioned the scenario in which the sponsor informs a physician-investigator of an actionable mutation for a participant who is no longer under his/her care. Finally, the fifth and sixth case studies examined how to return incidental genomic results that are unrelated to the primary aims of the research study. Special attention was paid to situations wherein the informed consent form had included the possible return of incidental findings and those wherein it had not.

Each of these cases illustrates the complexity surrounding the return of individual results to research participants—including different geographical regulations and customs, uncertainty regarding the seriousness of incidental findings, and the ephemerality of relationships between investigators, physicians, sponsors, and participants. The burden of returning individual results is not the sole responsibility of any single stakeholder, but a shared responsibility that should be more evenly distributed. Further, GDPR requirements would also support the notion that rights of access and portability may be an additional responsibility shared by sponsors and investigators. Technology was heralded as a mechanism by which this vision may advance, as there is evidence of its success in clinical care. By introducing a participant-facing digital platform into clinical research, individual and aggregate results may be shared more conveniently and intelligibly among sponsors, investigators, physicians, and participants.

Potential Future Work:

Participants of the MRCT Center Bioethics Collaborative discussed next steps to further advance and operationalize the communication around sharing of results. These included the following:

- Update the current version of the Return of Individual Results document to reflect the evolving clinical trial landscape and the needs of sponsors and other stakeholders to move towards application. This can include documenting and sharing case studies around the complexities of returning research results, with particular attention to differences between interventional trials, and trials that provide genetic information. A framework that includes ethical principles, empirical analysis, and case studies was suggested.
- A toolkit that incorporates educational materials that consider a participant’s journey along the clinical trial landscape, from informed consent to final visit study, with information about what to ask the investigator and study team.
- To advance the utility and implementation of the Patient Data Access Initiative, the currently engaged pharma companies may invite colleagues from academia to review the current instance, make suggestions, and participate in agile development of the solution cooperatively.