OPINIONS

Harmonizing Global Biospecimen Consent Practices to Advance Translational Research: A Call to Action

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One of the many challenges of translational medicine is working with research participants to donate biospecimens through an ethical informed consent framework. The increasingly complex ethical and regulatory differences across jurisdictions translates into limitations on use and potential value of biological specimens and their associated data in clinical research. We introduce a call to action for more uniform global standards for collection of biological specimen informed consent data to enable greater advancements in medical research.

CONSENT IN A CHANGING WORLD

Proper collection and utilization of donated biospecimens is essential to enable rapid innovations in molecular diagnostics and treatments. Understanding all intended uses for specimens at the time of collection is often impossible, and presents a challenge for development of informed consent for collection and use. Rigorous ethical standards must be in place to ensure the appropriate utilization of human biospecimens in research to ensure they are used in an ethical framework. Navigating the complex area of patient informed consent represents a major challenge to conducting research due to changing views on central issues of patient privacy, autonomy, and withdrawal of biospecimens. Guidelines governing how biospecimens and associated data are collected, shared, and stored, and for what purposes, vary tremendously in medical research across industry, academia, government agencies, and research organizations. Together, these requirements contribute to operational and logistical challenges that can pose a barrier to the translational research goals.

Informed decisions by research participants regarding biospecimen donation are based on the perceived benefits and risks of the research. Such considerations can be interpreted very differently, as evidenced by the variation in global informed consent policies and their rapid evolution over the past 10 years. A common obligation to protect participants guides current global policies. The lack of harmonization and standardization in how informed consent is collected and maintained can prevent access to biospecimens and can substantially interfere with the participant's original intent to contribute to research. Special considerations specific to future use research can further complicate matters. Requesting broad consent from participants can be important to enable future research avenues of previously collected samples, whether collected for basic research or in the context of clinical trials. Harmonizing practices and policies could substantially reduce Research and Development (R&D) costs and improve progress of future medical research.

To this end, the Global Initiative for the Ethical Use of Human Specimens (GIFT Initiative) was begun to initiate an international dialog among stakeholders so that best practices for future use biospecimens can be identified and recommendations for biospecimen consent and data management can be harmonized within an ethical framework. Initially, GIFT brought together diverse stakeholders from industry, academia, and government agencies to find common points of agreement and to build momentum for this call to action.

A reexamination of common practices guided the recommendations for standardizing informed consent (**Supplemental Material**).

CONSENT MODELS FOR COLLECTIONS

Numerous consent models exist for research utilizing biospecimens and each incorporates the same key elements of informed consent within its template. The Industry Pharmacogenetics Working Group (I-PWG) published an article outlining elements required for pharmacogenetic informed consent (**Box 1**), which have been adapted and transformed for all types of future biomedical research specimens and contexts.[1] The consent model used for biospecimen collection determines both the anticipated usage of the specimen

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Box 1. Elements of Informed Consent for Future Biomedical Research

1. Purpose of study
2. Procedures involved in collecting and handling of samples
3. Voluntary participation
4. Sample storage and distribution
5. Destruction of materials/removal of data
6. Contact information
7. Plans for sharing of genetic/biomarker results from research aim
8. Plans for sharing of unintended genetic/biomarker results
9. Risks and benefits
10. Confidentiality of subject information

Adapted from Anderson et al. 2002 (I-PWG) (1)

and data as well as the level of privacy protection. The three models described briefly below are used frequently in research studies; however, there is a need for consensus on which approach is best suited across different populations and types of study. In most cases, the model of consent chosen is dependent on study type, objectives, and population. Broad consent is most often used for future research. Tiered and dynamic consent approaches can provide flexibility in obtaining biospecimens for future use initiatives but require additional cost and operational resources to track consent, maintain contact with participants, and recontact participants with each new research study.

Broad consent allows the use of biological specimens and related data for both immediate research studies and future investigations unspecified at the time of collection. Opponents to broad consent contend that participants cannot be truly informed at the time of donation about unspecified future projects. Many groups who use the broad consent model argue that this model is both practical and ethical when participants are provided adequate information and future research is conducted under appropriate governance mechanisms. Some participants are receptive to this model of consent with its oversight mechanisms. Others are not, as there is a perception of weaker control over future use and perceived risk of misuse. Such concerns can be mitigated when researchers disclose their oversight plan and are prepared for audit and validation of compliance throughout the storage and use of the specimens. Management and communications strategies may be developed for monitoring of the specimen/data use over the lifetime in the biobank and improving the transparency of biospecimen research. Biospecimen access committees can also be utilized to enable and monitor sharing of biospecimens and controlled data sharing among biobanks and researchers. The UK Biobank has successfully used the broad consent approach to consent 500,000 participants and has established several oversight committees to ensure that policies are followed.

Tiered consent requires that several options be explained to the research participant in a detailed form. This approach allows participants a higher degree of autonomy, as they are able to choose from a list of options for biospecimen/data usage that may include general permission for future use and data sharing. Each level of consent must be tracked to ensure that the data used for future studies match the consent choices. Using a tiered approach so that participants can tailor research participation can be a compliance risk for researchers and risk confusion and contradiction in choices over time. It requires that monitoring plans review and attest to each individual's nuanced consent request across sites for a clinical trial, thus introducing cost and compliance risk for large global trials while also limiting interoperability and sharing. Although tiered consent in theory provides more options to research participants, the complexities of managing tiered consent can result in underutilization of donated biospecimens.

Dynamic consent also respects patient autonomy and enables multiple opt-in or opt-out choices.[2] Contact between participant and researcher is maintained in order to provide more information to the participant regarding new research projects. Dynamic consent requires reconsent and the tracking of participants. This raises several problems for the researcher: it is expensive, time-consuming, and can be difficult to locate a study participant after initial consent. Web-based tools can provide fast and efficient communication strategies for reconsent if participants have access to computers and the Internet, and the approach is not considered intrusive. A requirement for reconsent can limit study participation but may be feasible in small studies when recontact is convenient, personalized, and not construed as harassment.

CLINICAL TRIAL CONSIDERATIONS

Biospecimens collected from patients enrolled in clinical trials are vital to the current strategies of drug development and targeted therapeutics.[3,4] With the majority of early-phase studies, and a growing number of late-phase studies, incorporating biomarkers into pharmaceutical research, there are potentially millions of patients who must be asked, within an informed consent framework, to donate biospecimens for studies that will identify patient drug response populations and address questions regarding drug safety.

The impact of research utilizing these valuable biospecimens and the advancement of targeted therapies hinges upon the availability of properly consented biospecimens derived from diverse populations. Broadly consented biospecimens for future use, largely representative of clinical trial populations, are difficult to obtain due to a variety of hurdles outlined in the literature (**Box 2**).[5]

In addition to the outlined challenges (**Box 2**), each country has its own laws and regulations governing biospecimen collection and data sharing. These regulations are often in flux, increasing the difficulty of tracking informed consent across clinical trials and burdening the public and private sharing of biospecimens and data that is intended to advance research studies. No comprehensive source exists that details

Box 2. Challenges to Obtaining Biospecimens for Future Use

1. Ethics Committees rejection of genetic studies in clinical trials due to the perception that such studies present a greater risk to patient privacy.
2. Differing positions by ethics committees and investigators regarding requests to use biospecimens for future use, including additional requirements for return of research results.
3. Wording of informed consent and effective communication of the spirit and content of the consent by clinical investigators.
4. Investigators who choose not to present optional consent for sampling to patients.
5. Clinical team internal concerns that requests and sampling will delay trial start.

Adapted from Warner et al. 2011 (I-PWG) (5)

global laws and regulations governing biospecimen collection, further complicating the process of obtaining informed consent for clinical trial biospecimens. Success stories within research involve dedicating specialized resources, to maintain future use consent and protocol language, global regulation, site performance, and therapeutic area pitfalls.

GIFT proposes that interoperable biospecimen consent and data management processes is achievable through the development of globally consistent consent best practices and by maintaining compliance of these consent processes with an organized and rigorous oversight governance committee structure. Such consistency would both speed research progress and respect research participants' intent to contribute to research.

The primary goals of external research oversight committees are to ensure the ethical conduct of research and support transparency and accountability of operations for future initiatives. Oversight should also include standards for data access, usage, sharing, and security. Compliance can be cross-checked against tracking mechanisms that are used to reconcile consent and permissions for biospecimen and data usage for future research to respect patient autonomy. In addition, security measures can be implemented to minimize breaches in patient data and minimize harm. Solutions should be efficient, economical, and ethical. One key example of effective oversight for future use studies is the UK Biobank, which uses an independent committee to advise the biobank and oversee activities to ensure that policies adopted under the Ethics Governance Framework are followed. Effective oversight models and other successful governance structures should be designed with stringent measures to safeguard the rights of research participants.

New discoveries related to drug response and disease risk are founded upon the voluntary consent of research participants and the donation of biospecimens for biomedical research. The lack of specific and consistent global guidelines for biospecimen informed consent collection, coding, and processing is currently creating inefficiencies, diluting the research potential and limiting the inherent value of donated biospecimens. GIFT recommends an international consortium should address, proper tracking, and management of biospecimen data through unified guidelines and governance approaches to prevent conflict against a backdrop of global differences. In this effort, streamlined processes and collective understanding regarding consent will foster research participant trust and continue to advance biomedical research. Additionally, identification of appropriate governance bodies should be determined and instituted globally.

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AUTHOR CONTRIBUTIONS

All authors contributed to writing the article.

CONFLICT OF INTEREST

None of the authors report a conflict of interest.

Additional Supporting Information may be found in the online version of this article.

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