

RESEARCH HIGHLIGHT

Informed consent in the era of biobanks

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Abstract

Biorepositories collecting human specimens and health information have proliferated in recent years. Efforts to set a range of policies related to biorepositories, including those related to procedures for obtaining informed consent and recontacting participants, have been hindered by a paucity of data on the diverse forms biorepositories take and the variety of institutional settings where they are established. A recent survey demonstrates in detail, for the first time, the diversity of biorepositories in the USA.

The 'scaling-up' of research

Approaches to the way investigators obtain consent and later recontact research participants are regulated in the USA under a set of policies focused on protecting research subjects, often referred to as the Common Rule, that were published in 1991 [1]. In recent years, however, the development of novel research approaches has caused some to raise questions over the practicability of traditional procedures for obtaining consent and recontacting participants. For example, biorepositories can include very large numbers of biosamples collected from large populations of individuals. Traditional procedures used to obtain informed consent to participation in research, such as enrollment visits that can last over an hour, seem better suited to studies with participants who number in the hundreds, rather than to biorepositories whose participants can number in the hundreds of thousands.

The 'scaling-up' of research approaches has led to increased interest in identifying the best ways for investigators to engage with research participants when the number of participants becomes very large [2]. In fact, a recent proposal for revisions to the Common Rule included a suggestion that permission to collect biosamples might be obtained using a brief permission form

rather than a detailed informed consent process [3]. This and other proposed reforms to the Common Rule may be intended, in part, to address the concerns that have arisen in building biorepositories. Until now, however, our understanding of the scale of the problem of balancing adequate engagement with practicability in the development of biorepositories has been based on an incomplete picture of the biorepository landscape. Are biorepositories with hundreds of thousands of biosamples really that common? Where do they obtain their samples and with what consent approach? Which stakeholders are involved in developing and carrying out governance and oversight for these collections? In this issue of *Genome Medicine*, Henderson *et al.* for the first time provide data and analysis on the diversity of biorepositories in the USA [4]. The findings in this report are wide-ranging and will help move a number of ongoing policy debates forward.

Consent models

The two core ethical aims for informed consent encounters are: (1) to ensure that potential participants are adequately informed about the risks and benefits associated with research participation, and (2) to obtain participants' voluntary agreement to participate in research. In practice, the approaches that can be taken to achieve these aims in the setting of biorepositories are numerous. In the procedures adopted by many biorepositories, participants are informed of the general scope of planned research and asked to consent *en bloc* (that is, provide 'blanket' consent) to all future research. The alternative is to recontact participants periodically to request consent for use of stored biosamples in newly developed research projects.

Even though the findings reported in Henderson *et al.* [4] do not address the consent approach adopted by biorepositories, they do help place this choice into context across the range of biorepositories currently in operation in the USA. Fifteen percent of biorepositories report having fewer than 500 samples. For these biorepositories that are similar in size to more traditional types of medical research studies, a 'blanket' consent approach may not be necessary.

However, a number of biorepositories are extremely large. Over 20% of biorepositories contain more than

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100,000 specimens, and at least one biorepository reported collecting biosamples from more than 10 million individuals! Since the majority of biobanks (75%) obtain samples directly from the individuals donating them, we can begin to see the scale of the effort needed to obtain consent from participants on just one occasion. Despite the many salutary features of the periodic recontact model, the data from this study indicate that this model may not be feasible for a significant percentage of biorepositories.

The passage of time poses another challenge to the recontact approach. Henderson *et al.* [4] found that 17% of biorepositories were established prior to 1990. Although we do not know whether samples collected prior to that time are still in use, it is daunting to consider the operational challenge of recontacting participants over a 20 year period!

While these findings put a number of claims into their empirical context, they can provide no direct resolution of the debate. For example, although a significant number of biorepositories are either very large or have been in operation for a long time, Henderson *et al.* have not reported whether any face both challenges. And going beyond these findings, it is clear that under exceptional circumstances, large, long-term research projects can maintain meaningful engagement with participants [5]. Finally, even biorepositories that have adopted a one-time, 'blanket' consent model may later find that they need to recontact participants, such as when the scope of planned research changes or when plans to share data are developed [6].

Return of results

Just as the size and duration of biorepositories can pose challenges to recontacting participants for the purpose of expanding consent, they can also create barriers to returning research results to participants. If we imaginatively combine the findings provided by Henderson *et al.* with recent studies that demonstrate that incidental findings generated through DNA-based tests are relatively common [7], we may conclude that returning incidental findings to 100,000 or 500,000 participants included in a genomic biorepository could represent a remarkably expensive and time-consuming effort. This is of particular interest, since 41% of biorepositories already consider long-term sustainability to be a major concern.

The scope of this challenge is mitigated significantly, however, if we assume that only those results expected to provide significant and timely clinical utility should be returned. Taken in this light, DNA-based biorepositories may not pose the most significant challenge in terms of return of results, since we may expect them only infrequently to generate findings that are both urgent and diagnostic. But as scientific knowledge increases in

coming years, a great number of RNA and protein-based biomarkers are likely to emerge as both highly predictive and timely markers for disease. Although nearly 50% of biorepositories currently focus on DNA research, the findings of Henderson *et al.* [4] raise our awareness that 24% of biorepositories are focused primarily on RNA and 7% are focused primarily on protein. In this way, these findings direct our attention beyond return of genomic results toward results that we may soon find are far more convincing - and urgent - candidates for return to participants.

Looking ahead

In this brief article, I have addressed only one narrow area of interest in ethics and policy issues related to biorepositories. My aim has been to demonstrate how the new empirical findings reported by Gail Henderson and her colleagues can serve as a starting point for grounding discourse on a range of issues related to biorepository design, oversight and governance.

At the same time, these findings direct our attention toward emerging challenges. As the trends revealed in this report indicate, widespread innovation in approaches to research is likely to continue. With this innovation will come a continuing need to evaluate the advances that are taking place in all quarters, especially since they are likely to bring new challenges to efforts to enact ethical, legal and societal commitments into practicable policies.

Competing interests

The author declares that he has no competing interests.

Published: 25 January 2013

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doi:10.1186/gm408

Cite this article as: Brothers KB: Informed consent in the era of biobanks. *Genome Medicine* 2013, 5:4.