participating in discussion on return of results, including from the Mayo Clinic and Boston Scientific.

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Return of research results from genomic biobanks: a call for data

To the Editor: We welcome the letters from Susan Wolf[1] ("Return of Results in Genomic Biobank Research: Ethics Matters") and Les Biesecker,[2] ("Secondary Variants and Human Subjects Research") that comment on our recent paper, "Return of Research Results From Genomic Biobanks: Cost Matters,"[3] and provide the opportunity to continue the dialogue on this important and complex topic. We agree that ethical responsibilities to research participants cannot be ignored. However, consideration of these ethical responsibilities must include not only arguments favoring return of research results, but also the potential risks to individuals, and the burdens and costs to individuals, the research enterprise, and society as a whole.

In Susan Wolf's letter to the editor,[1] she points out that the discussion section of their article[4] addresses cost as a critical issue and maintains that sufficient flexibility for biobanks is provided. Indeed, the article notes the crucial role that research and biobank funders and regulators would have to assume in order to sustain adequate support for the responsible management of incidental findings and research results. The suggestion is made that by using strict criteria for deciding which results to return, biobanks would be able to limit costs. In addition, financial responsibility would not have to rest completely on the bank; investigators could bear some of this responsibility. Although we agree that the discussion section of the article does address costs and provides some flexibility for biobanks, these considerations are not adequately reflected in the recommendations. We are concerned that policy and law makers may reasonably conclude from the way the recommendations of the paper by Wolf et al.[4] are written that biobanks should be principally responsible for the evaluation of findings and ensuring return of research results from any biobank in which it is possible to reidentify participants. We contend that regardless of who assumes the responsibility, these costs are likely to be substantial in many cases. Although developing strict criteria for the return of research results from some biobanks would directly affect the cost, it is unclear how much savings it would provide given the expense of setting up an extensive infrastructure for evaluating and ensuring appropriate return of findings. Given the current funding constraints on the whole research enterprise, there is a real ethical tension between being able to afford to do the kind of research that leads to tangible benefits for a large number of people versus the need to manage and deliver validated individual research results in a meaningful and ethically appropriate way. We believe that the debate around personal versus community benefit based on real economic evaluation and practicability must also be included in any analysis of the ethical issues of return of research results.

Dr Biesecker's letter to the editor[2] raises several issues that merit further discussion. He states that in our recent commentary, we appear to discourage any return of results in research involving biobanks except when the biobank maintains the kind of direct involvement with participants as seen in ClinSeq. We, however, do not make this assertion; rather, our reason for mentioning ClinSeq was to use it as an example of a bank that generates primary research results and in which there is direct interaction with participants. These characteristics provide a stark comparison to the dbGaP model, in which the biobank has no relationship with the participant and in which data are shared with many investigators for secondary research projects. Our goal was to simply emphasize how different models present very different challenges in the discussion of return of results.

Dr Biesecker's letter addresses the importance of participant engagement in any discussion of return of research results. He raises the question of whether the field would benefit more from a larger number of less expensive, narrowly defined biobank studies with no participant engagement or a smaller number of more expensive studies with high degrees of ongoing participant engagement, iterative phenotyping, and return of results. We agree that it is important to engage research participants in biobanking research through direct interaction whenever it is possible to do so. However, we do not agree that it is ethically required, nor do we think that all biobanking research must be performed using participant engagement models similar to ClinSeq. Biobanks that are established from existing specimens (e.g., pathology archives or specimens from previously collected projects) are also needed, even if it is not possible to reidentify participants/contributors or to provide them with individual research results. Many of these existing collections may be uniquely valuable because of extensive amounts of clinical follow-up data or due to changes in standards of care (e.g., untreated, node-negative breast cancer cases), and they could not be established prospectively today. Furthermore, it is arguable whether participants/contributors must derive personal

benefit from return of research results to be engaged in the research; there are many other ways of engaging participant/contributors in biobanking research.

In summary, biobanking must be conducted in an ethically responsible way. However, continued discussion is needed regarding the ethical obligations and practical implementation issues for returning research results from biobanks. Good data are needed on the actual benefits, risks, and burdens of the return of individual findings from research. This is an evolving issue that must be informed not only by advances in the science but also by experience addressing the challenges of incorporating genomic information into the clinic. Recent discussions on this topic raise questions about our ability to manage the return of genomic findings even in the clinic.[5] Care must be taken so that the return of individual findings generated in research does not get ahead of what is acceptable for return in clinical care. Additional data in these areas will help inform the development of guidance and approaches to this topic that will respect participants/contributors, while advancing important and ethically responsible research. In the meantime, we refer those interested to the forthcoming Australian guidelines,[6] which take a different approach to this problem and which we believe may provide a clear way forward for the foreseeable future.

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DISCLOSURE

M.J.B. is a program manager for the Department of Veterans Affairs biorepositories and biobanks and is a member of the International Society for Biological and Environmental Repositories (ISBER). N.Z. operates a cancer biobank at St. John of God HealthCare within its Pathology Practice in the Bendat Family Comprehensive Cancer Centre. He is a member of ISBER and the Australasian Biospecimen Network Association. W.E.G. operates tumor banks as part of the Breast, Pancreatic, and Cervical Specialized Programs of Research Excellence at the University of Alabama at Birmingham and the Pulmonary Hypertension Breakthrough Initiative and prospective tissue repositories as part of the Cooperative Human Tissue Network and the Comprehensive Cancer Center and is a member of ISBER. He is a member of the ethics committee of the U54 grant, U54 MSM/TU/UAB Comprehensive Cancer Center Partnership. E.W.C. has long been involved in the creation, maintenance, and assessment of BioVu and has been studying ethical issues in genetics/genomics research for many years. She was part of the working group on biobanks convened by Professor Wolf but is not an author of its final document because she did not endorse its analysis and conclusions. A.L.M. and P.P.O. declared no conflict of interest. The authors are funded by their affiliated institutions.

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