BENEFIT-SHARING: FROM PRINCIPLE TO PRAGMATISM ADDRESSING PUBLIC CONCERNS ABOUT COMMERCIALISATION IN POPULATION GENETIC RESEARCH

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Introduction

With the recent international trend in the creation of population genetic databases, there has also been increasing public interest in and concern about the potential exploitation and commercialisation of these endeavours. Indeed, the question of "who profits?" is a major issue for a number of stakeholders (Bruce & Tait, 2004:212), and is connected with broader issues of public trust and confidence. At the same time, the traditional "gift" model, in which research subjects freely donate biological materials for purely altruistic reasons, is being challenged (Merz et al, 2002:965), and there is a growing belief that commercial gains from human genetic research ought to be shared with communities that make the research possible in the first place. (HUGO, April 9, 2000; Laurie & Hunter, 2004:323).

There is also emergent social science research which indicates that publics have some expectation of practical reciprocity in the donation context (Busby, 2004:52). In studies that have been done to gauge public attitudes towards population genetic databases, not only is there evidence of mistrust of commercial and business involvement in the enterprise, but also that publics expect some benefit (beyond any future potential health benefits) and control when samples are used for commercial success and profit (Levitt & Weldon, 2004).

In addition, the value of public opinion is increasingly being recognised as a way to inform good practice. A recent report of the Academy of Medical Sciences emphasises the urgent need for public debate on issues surrounding the use of personal data for medical research. The absence of knowledge about public attitudes and opinions "forces regulatory and advisory bodies to make defensive assumptions about what the public might find acceptable" (AMS, 2006:72). The report concludes that the "[d]evelopment of good practice should be informed, as far as possible, by empirical evidence on public and patients' awareness and attitudes" (AMS, 2006:72).

Tackling Community Concerns

This paper draws on an earlier article, "Tackling Community Concerns about Commercialisation and Genetic Research: A Modest Interdisciplinary Proposal" (*forthcoming*) by Haddow, Laurie, Cunningham-Burley and Hunter, in which, as a group of social scientists and lawyers, we explored the health-wealth benefits that DNA databases promise. After considering previous research and thinking on the social and ethical issues relating to DNA databases, particularly issues of profit and commercialisation, we turned our attention to a recent study conducted by Cunningham-Burley and Haddow into public opinion about the development of Scotland's first national population-based genetic

resource, Generation Scotland, and then proposed a sociologically informed, yet pragmatic, legal framework that would go some way to responding seriously to public concerns about commercialisation. We found an apposite example in the Canadian Provincial Approval Model, which is discussed below.

Taking our findings and conclusions as a starting point, this paper explores various benefit-sharing models in light of public concerns and policy considerations. While it is recognised that policy solutions may only ever partially reflect public opinion, and that any benefit-sharing model must balance public and commercial interests, it is essential to the success of population genetic database projects that there are sufficient safeguards and incentives to attract and retain participants and foster public trust. As Winickoff and Neumann have pointed out, "[t]he sustainability of large-cohort genomics will require institutional, procedural and substantive legitimacy in order to secure… the willing participation [and enduring trust] of volunteer subjects over time" (Winickoff & Neumann; 2005:10 & 8).

The Generation Scotland Study

The recent study conducted by Cunningham-Burley and Haddow provides further insight into why commercial involvement in genetic database research provokes strong, albeit ambivalent, reactions in different groups. The study found that, while public sentiment towards the project was generally favourable and there was evidence of public willingness to participate, there was resistance to allowing commercial entities access to genetic database resources. As reflected in other studies (for example, Busby, 2004,), patient groups were more willing to accept pharmaceutical involvement as a "necessary evil" for drug and treatment development. When asked whether, and in what circumstances, others would tolerate wealth benefits based on profit, respondents suggested that it was not only the making of a profit that was the issue, but also what was done with the profit. The solutions proffered by the groups themselves centred on themes of *public ownership* and *returning profits*. Generally, respondents thought it important that the database be 'publicly owned', or that there should be public or charitable representation and ethical oversight. Interestingly, in only two of the focus groups was it suggested that individuals owned their genes and, therefore, had a right to say what happened to them; the majority of respondents regarded genetic data from samples as "publicly owned", to be put to a use that contributed to the common good and in accord with the principles of the National Health Service. There was strong support for the administration of the samples by a trusted (public) third party. Participants in the study identified a number of possible benefits (or "profit pay-off"), all of which were linked to the general well-being and health of the community at large. These included cheaper drugs, monies going into public health or into Scotland, back to research, the NHS or charities linked to health. As one respondent commented: "Health is universal, and should be re-invested back into the community and the people".

What emerges from the focus group research is that public concerns distil around issues of injustice and fairness (about private profit being made through public exploitation); the lack of institutional control over that profit; and a perceived disrespect to people by the commercialisation process itself. While publics generally accept the commercial realities of these research endeavours (albeit sceptically), there is an expectation of some return, either in terms of direct health benefits, or a share of the profits to be used for the wider public good, when freely donated biological materials are used for commercial gain. What is striking is the emphasis on 'public' or 'community' benefit in the broader sense, and not on personal financial compensation. Indeed, participants expressed a strong communitarian

sentiment, not only about the ownership of genetic data, but also about how profits from the use of such data should be distributed.

Benefit-sharing in principle

As we noted, the underlying unease with commercial involvement appears to be a sense of injustice – that commercial gains are pursued at the expense of publics' interests. This raises related deontological considerations of fairness. We suggested that the challenge would be to devise an approach for sharing benefits which would temper, but not unduly diminish private financial interests in the name of the public good; which might act as an incentive to participate in research; and which would redress the perceived imbalance and further a wider set of community interests. We contended that a benefit-sharing model would fulfil these ends as it embodies a direct commitment to share profit and so directly addresses perceived injustices surrounding commercialisation; it entails a commitment to justice which would go far in restoring some degree of public confidence in the research enterprise; new obligations to share could easily be incorporated into the existing ethical framework with minimal disruption; research participants might have a role in influencing or directing sharing thereby reducing their passivity in the research exercise; and it respects and recognises the status of DNA both as an object/subject that comes from individual research participants, but also for its communal or collective value as a research tool and as a representation of a community interest in the outcomes of the research.

Indeed, the aim of benefit-sharing is to build greater trust and reciprocity with participants, and to counter perceived exploitation and commodification, through transparency and consultation (Knoppers, 2000:214; Hug, 2006). Although the HUGO Ethics Committee suggests that companies involved in human genetic research may have special *moral obligations*, including the obligation to share benefits with groups or communities that participate in human genetic research (HUGO, 2000), the concept of benefit-sharing does not attempt to denounce commercialisation (Hug, 2006), nor does it endeavour to curtail it. In fact, benefit-sharing acknowledges the commercial realities of current human genetic research, while seeking to mediate any potential power imbalance between organisations carrying out research and the communities providing biological material for that research (HUGO, April 11, 2000). Moreover, by encouraging industry to institutionalise benefit-sharing, it also seeks to avoid unnecessary legal wrangling and potential over-regulation.

Benefit-sharing in practice

If we accept benefit-sharing in principle, how might it be put into practice? Knoppers has pointed out that the adoption of benefit-sharing by corporations can come in different forms: corporate, state or contractual (2000:213). An example of the contractual approach has already been adopted in practice. PXE International has negotiated a contract with researchers in which the foundation retains ownership rights in any patent application arising from the research, thereby enabling the Foundation to share in any revenues, to influence future licensing agreements and to ensure widespread and affordable genetic tests (Gitter, 2004:262&315). While the contract model may embody "the ideal of autonomy by allowing donors direct input and negotiating power in the context of commercial genetic research" (Porter, 2004:90), it may hold more promise as an effective solution in cases such as *Moore*, "where an individual's biological material or characteristics are known to be commercially valuable", or where there is a homogeneous disease community (such as PXE International) with significant bargaining power, rather than for large-scale genetic database projects, where the donor group is more heterogeneous (Porter, 2004:90). In addition, it

does not readily lend itself to addressing broader community concerns. In fact, it has been observed that the contract model could pose a 'devil's dilemma', in that IP rights retained by one group might lead to a conflict of interest – the group holding the monopoly might further its own interests at the expense of those suffering from other diseases (Bovenberg, 2006:198). Although it has been suggested that "contractual [benefit-sharing] arrangements if successful and respected may well forestall State intervention through mandated 'sharing' or State prohibition on DNA collection and use except under heavy bureaucratic and administrative requirements" (Knoppers, 2000:214), private contractual agreements may, in fact, require state intervention "where a dogmatic interpretation of 'freedom of contract' [perpetuates] inequality, exploitation and imbalances of power" (Porter, 2004:91), the very things publics are concerned about and benefit-sharing aims to counter.

Whereas the contract model rests on the notion of individual autonomy, the Biotrust model, developed by Winickoff and Neumann, aims to bolster community involvement and participation in genomic governance. Building on the Charitable Trust Model, first proposed by Winickoff and Winickoff in 2003, the core idea of the Biotrust it to use the charitable trust as the legal framework for genomic biobanks (Winickoff & Neumann, 2005:10). In the model, donors would transfer their property interests (assuming that these exist in the first place) through a series of trust instruments to the same trustee – the Biotrust Foundation – which would hold title to the trust property for the benefit of the beneficiary. In a charitable trust, the beneficiary is the general public (Winickoff & Winickoff, 2003:1182). The Foundation would be managed by its own by-laws, which the donors would agree to, and which would define the charitable purpose and the terms of public benefit. Added to this basic charitable trust framework, the by-laws would specify that use of the trust property would be contingent on review approval of two bodies – the Ethical Review Committee (ERC) and the Donor Advisory Committee (DAC). The organising principle of the trust would be public benefit, not profit, and funding models that establish research partnerships, and not "tissue buyers", would be encouraged (Winckoff & Winickoff, 2003:1183). Under a trust model, "[t]he trustees would negotiate shared intellectual property arrangements with the researchers so that a portion of profits derived from the material would finance the operation of the trust and provide a charitable health fund. The trustees would decide how to disburse this fund" (D.E. Winickoff, 2003:222). Research applications could, in the first instance, be evaluated by the trustees according to a set of criteria that would ensure public benefit (eg. by addressing public health failures) (Winckoff & Winickoff, 2003:1183), and benefits could be allocated either to the general public or to specific groups, depending on the biobanking situation, such as the composition of the donor group or some heightened need of a particular segment of the public (Winickoff & Neumann, 2005:10).

While there are a number of advantages to the Biotrust Model, particularly its flexibility to give donor groups a potential advisory role in the governance of the trust, it does raise a number of practical issues. Much like the contract model, and as D.E. Winickoff himself has noted, while a trust model may be appropriate where there is a pre-existing volunteer group with a strong community identity and common goals, it may be of less value where the volunteer/donor group is more heterogeneous and disparate (D.E. Winickoff, 2003:226). Whereas PXE International, for example, has one goal - to encourage researchers to study the genetic basis of PXE to develop therapies (D.E. Winickoff, 2003:223) - individuals and groups involved in large-scale population studies would likely have different, and potentially conflicting, goals. This begs the question of how trustees

could "safeguard the interests of donors and other beneficiaries", when the "beneficiaries" are, variably, the donors, the general public and investors (Winickoff & Neumann, 2006:10 and note 16). In addition, the Biotrust Model does not address how the trustees would manage profits, what percentage of profits would go to the charitable health fund, what might qualify as "public benefit" (beyond public health failures), what types of benefits might be allocated to the general public or to specific groups and on what basis, whether the Donor Advisory Committee would have input into how benefits would be distributed, or how research participants would be made aware of the benefit-sharing arrangements. Indeed, many of the issues around benefit-sharing will be left to be determined in the by-laws, rather than in the governance framework itself, a problem Boggio (2005:47) identified in relation to access under the Charitable Trust Model. Winickoff and Neumann have suggested, however, that the by-laws could be negotiated "before the architecture is set up, perhaps through a process of public consultation", and could be later refined "in the interest of pragmatism" (2006:15). This would provide a means for public input into benefit-sharing arrangements in the first place, and a mechanism by which the by-laws could be re-negotiated and interests re-balanced later.

As an alternative to these benefit-sharing models, Bovenberg has recently suggested a tissue tax. The rationale for a tissue tax rests on the assumption that the human genome and, by extension, human tissue and cells, constitute a natural resource. The tax could be levied on profits made, for example, on a gene patent, or a biological product developed from human sources. It would provide "an effective, if indirect, mechanism for letting a community share in the benefits resulting from the efforts of the taxpayer and to make a licensee pay for the exclusive use of natural resources" (Bovenberg, 2006:200). Compared with other benefit-sharing models, taxation has, Bovenberg suggests, numerous advantages, including that it is enforceable and collectible; it applies regardless of whether people have specific genes or whether they participated in the research; it preserves existing incentives, such as patents; it does not involve endless negotiations over the sharing of uncertain future benefits; it avoids speculation over the relative contributions of specific tissue to the end-product; is only due when an actual profit is made; and its collection and redistribution are subject to democratic control. While several practical aspects of a taxation system are preferable to, for example, a contract model, in that it would avoid complicated, possibly protracted, negotiations and would allow the larger community to share in any benefits that might accrue, there are a number of drawbacks to the model. First, human DNA is not like other natural resources and there are strong policy and ethical reasons not to view it as such (see Pullman & Latus, 2003:31ff). To impose a tax on DNA would be to treat it like any other taxable 'commodity'. Second, a taxation system does not provide for direct public/community input into the way in which benefits are distributed, except (one might argue) to the extent that the government may be democratically elected and representative of publics. In addition, as Bovenberg himself admits, a taxation system would not accommodate access to "the tangible fruits of biomedical research"(Bovenberg, 2006:200), such as therapies or new drugs, something identified by publics as being an important "profit pay-off". Finally, it is questionable whether a taxation system would engender public trust and confidence – there is no *direct* commitment to share, nor a commitment to justice. It is, essentially, a form of mandated sharing at a distance between researchers and the state, which continues to keep publics out of the picture.

In contrast to all this, the Provincial Approval Model developed by Pullman and Latus provides an example of how public attitudes towards the commercialisation of genetic

research might be put into practice. The central element of the model is the requirement that anyone proposing to conduct research in Newfoundland and Labrador that includes a human genetic component must seek approval not only from the Provincial Health Research Ethics Board (PHREB), but also from a Standing Committee on Human Genetic Research (SCHGR). Researcher sponsors would be required to submit a proposal for benefit-sharing to the SCHGR, along with a rationale for the proposal, and final approval for the research project would only be granted if the Standing Committee were satisfied that an adequate benefit-sharing arrangement had been made. This requirement would be mandatory and would apply to *all* proposed research studies. (Pullman & Latus, 2003:50). Although the authors do not advocate a 'one size fits all' approach to determining whether a benefit-sharing arrangement is reasonable or not, they do, nonetheless, provide some guidance: benefits may be both 'in kind' (e.g. research facilities, equipment, jobs) and 'monetary' (royalties, percentage of gross profits etc.); the size of the benefit should be proportional to the significance of the contribution of the province to the overall success of the project; and where the population is projected to make a substantial contribution to some discovery, residents should generally receive free access to any test or treatment (Pullman & Latus, 2003:53-54). Participants would be informed of the benefit-sharing arrangements through the informed consent process.

The model, which is supported by the principles of distributive justice; the unique and communal nature of human DNA; and health as a common public good (Pullman & Latus, 2002:3), provides a principled and pragmatic approach to benefit-sharing that reflects both public sentiment and ethical considerations about the commercialisation of human genetic research. First, as we noted, the model responds to general concerns about justice and fairness in a commercial genetic research setting (thus challenging the traditional gift model) and reflects the commonly-held view that DNA carries special significance from which moral obligations flow when it is used/commercialised (Pullman & Latus, 2003:20). It adopts a community-focused approach as to *who* should share in benefits, and an expansive notion of *what* constitutes a benefit (reflecting the importance of recognising the community's interest in health and wealth benefits). Finally, by making participants aware, through the informed consent process, that the province will share in any financial benefits that may result from the research and that these benefits will be used to enhance health care and/or further health care research in the province, it also promises to engender public trust and confidence. In terms of how the model might work in practice, we found the outline of a viable approach embodied in the work of Pullman and Latus, typified by a central role for a brokering body, which might have the dual role of scrutinising benefit-sharing proposals for "fairness" (both to the community and to the researchers); and determining how benefits might be shared in the broader community. This might be accomplished through a fund, administered by this body, to which applications might be made by patient groups, advocacy groups, or even individuals, according to a set of agreed criteria for eligibility, or by a commitment from researchers to contribute benefits in-kind.

Conclusions and Further Considerations

While the Provincial Approval Model may provide a principled approach to sharing benefits with research participants and the broader community, a number of practical inter-related issues require further consideration. First, it is important to note that the model was designed to take account of the specific historical-political-economic circumstances of Newfoundland and Labrador, Canada. As such, it "may not be directly applicable to other contexts in the manner specified" (Pullman & Latus, 2002:2). Second, the model was not

designed as a framework for population genetic databases; in fact, the authors specifically reject 'mega-project' approaches, partly because of the history of failed mega-projects in the province, but also for purely pragmatic reasons (Pullman & Latus, 2003:42-43). These issues raise questions about whether and how we might construct a benefit-sharing model that is appropriate for different cultural contexts and governance frameworks. First steps must surely be to determine what publics might want and tolerate. As HUGO has observed, prior consultation is a preliminary basis for future distribution of benefit and may be considered a benefit in itself (2000).

One of the major drawbacks of the Provincial Approval Model is the lack of public involvement in the decision-making process. While the model may well reflect the attitudes of the people of Newfoundland and Labrador, it was not developed out of public consultation but, rather, with "experts" in genetics, law, health policy, business and bioethics; input was also sought from industry (Pullman & Latus, 2003:8-9). This is reflected in the governance framework as well. Pullman and Latus have proposed that the SCHGR (the body responsible for reviewing benefit-sharing proposals) would consist of people with expertise in genetics, medicine, pharmacology, business, law, health policy and medical ethics (Pullman & Latus, 2003:50); there is no indication that members of the community or donor group representatives would be included. As noted above, the greatest challenge for large-scale population databases is to engender on-going public trust and confidence. This might be achieved, in the first instance, through public consultation (see HUGO, 2000) or through public participation in the management of these collections (Boggio, 2005:44). A body such as the SCHRG could, of course, accommodate public representation and, while there would still be practicalities to consider about how 'representativeness' could be achieved, this might go some way towards redressing any real or perceived exploitation, creating greater transparency and fostering public trust.

Although there are beneficial elements to each of the models outlined in this paper, none to date provides a sufficiently robust, pragmatic solution to address the kinds of public concerns emerging from public engagement exercises. While much work has been done to articulate the principles that support benefit-sharing – justice, respect, trust and non-exploitation - more is required to distil from these principles a viable pragmatic approach. Such an approach would include, as a first step, *public consultation*, in order to determine "needs, values, priorities and cultural expectations" (HUGO, 2000). It would also include a *clear commitment to share benefits* and to involve publics in the process of sharing, both in terms of being beneficiaries and in deciding who will share and on what basis, something the models to date do not adequately address. In order to give substantive effect to public consultation and participation, however, it is necessary to go beyond merely paying 'lip-service' to public concerns. Our project, outlined at the beginning of this paper, has not only consulted with publics, but is trying to respond to their core concerns in policy terms. This is not to suggest that we advocate "a crude calculus that 'what the public wants, the public gets'" (Haddow et al., 2006); rather, it is about developing socially-informed policy responses to public concerns about commercialisation, in order to articulate and justify the objectives that are trying to be reached.

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