did not achieve harmonization for the use of data for medical research. In fact, there are even substantial differences in what constitute personal data depending on national jurisdiction. In the United Kingdom and the Netherlands, for example, research using coded data or samples, for which investigators do not have access to the code, is not considered to be research involving personal data[11,12]; in contrast, the majority of other European countries do consider such research as involving personal data. Although a European Commission report on the implementation of data protection in member states did not decide whether such data are personal or not, it did state that the definition in Directive 95/46/EC should be applied with (in my words) common sense[13]. There are also differences in the kind of authorization required to use data, and therefore tissue, for research. In the Danish case, if data or tissue are not fully anonymized, an investigator must have permission from the Danish Data Protection Authority to use the associated data[14]. No such authorization is needed for the use of coded data and tissue in, for example, the United Kingdom, Austria or the Netherlands[7]. Nuances such as these are lost in Maschke's description.

In the United States, Maschke also oversimplifies the situation by referring to the US Health Insurance Portability and Accountability Act (HIPAA), but neglecting to mention the applicable part of the Code of Federal Regulations(the so-called common rule)[14] and to comment on the role of the US Office on Human Research Protections. The latter stated in a guidance that research with data and tissue that, though coded, are unidentifiable at the level of the researcher is not considered human subject research[15]. Therefore, although research on anonymized tissue, even if it is coded, lies outside the common rule, it may contain protected health information according to HIPAA, which is subject to restrictions on use and disclosure. The US situation is further complicated at the state level by the impact of 'genetic privacy' legislation in several states that may apply to research on residual tissue[16].

To sum up, then, by failing to differentiate between the two fundamental types of tissue collected by tissue banks—residual tissue and tissue specifically acquired for research purposes—Maschke creates confusion about relevant regulations. For tissue-banking projects using residual tissues, a distinction could also have been made between those that involve retrospective studies and those that involve prospective studies. All of these differences are relevant to the regulatory regime and ethical considerations.

By heaping together and conflating issues, perhaps owing to lack of space, Maschke oversimplifies and muddies the legal situation with regard to research on human tissues in several national jurisdictions. As suggested by the article's title, human gene banks do present an "ethical patchwork" and legal comparisons between regulations in different countries are laborious and defy generalizations. Any article that suggests the contrary should be read with caution.

Ben-Evert van Veen

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1. Art. 18 b of the Danish Act on Patient Rights, as amended in 2004.
2. Commons Hansard Debates for 28 June 2004 (pt. 31).
3. UK Human Tissue Act Chapter 30, part 1, subsections 8 and 9.
4. Draft Code of Practice Consent, Code 1. The Human Tissue Authority, Crown, 2006; Section 29 <http://www.hta.gov.uk/download/Code%20of%20Practice%201%20Consent.pdf> (last accessed February 2006).
5. Art. 1243-3 Code de la Santé Publique.
6. Chapter IX of French Data Protection Act as amended in 2004.
7. As explained at section 3 in van Veen E.B. Comments on the Draft CIOMS Guidelines for Ethical Review of Epidemiological Research, The Hague, 2005 <http://www.medlaw.nl/documenten/comments.pdf> (last accessed March 2006).
8. Dutch Act on Medical Research with Human Subjects <http://www.ccmo-online.nl/main.asp?pid=21&thid=7> (last accessed March 2006). For an English version of the Act, before the implementation of Directive 2001/20 EC, and a commentary see <http://www.healthlaw.nl/humsub.pdf> (last accessed March 2006).
9. Dutch Act on the Medical Treatment Contract <http://www.dutchdpa.nl/indexen/en_ind_wetten_wbp.shtml> (last accessed March 2006).
10. Art. 37.2 of the Dutch Data Protection Act, see http://www.dutchdpa.nl/indexen/en_ind_wetten_wbp.shtml (last accessed March 2006)
11. van Veen, E.B. *Privacy Informatie* **6**, 259–262 (2003).
12. van Quanthem, K. *Privacy Informatie* **8**, 155–161 (2005).
13. First Report on the Implementation of the Data Protection Directive (95/46/EC) (Commission of the European Communities, Brussels, 2003) <http://europa.eu.int/eur-lex/en/com/rpt/2003/com2003_0265en01.pdf> (last accessed February 2006).
14. Art. 45 and art. 50 of the Danish Data Protection Act.
15. Chapter 45 of the Code of Federal Regulations (CFR), part 46.
16. Guidance on Research Involving Coded Private Information or Biological Specimens (Office for Human Research Protection and Department of Health and Human Services, Bethesda, MD, USA, 2006) <http://www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf> (last accessed February 2006).
17. Hakimian, R., Taube, S., Bledsoe, M. & Aamondt, R. *50-State Survey of Laws Regulating the Collection, Storage and Use of Human Tissue Specimens and Associated Data for Research* (U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute, publication no.05.5628, November 2004).

Karen Maschke responds:

Although Evert-Ben van Veen provides some important clarifications in his letter, he raises several points with which I respectfully disagree.

He correctly points out that Iceland is not the only country permitting presumed consent in the tissue research context; however, my statement that the Act on Biobanks in Iceland is "unique in that it permits presumed consent. . .to govern the storage of samples in a biobank if they were obtained for the purpose of clinical tests or treatment" was made in the context of comparing the Icelandic Biobank project to the other population-based biobank projects listed in Table 1 of my article. Readers should be aware, though, that several countries have legislation governing a broader array of tissue research that includes presumed consent provisions. van Veen also points out that countries differ in how they regulate the use of personal data associated with human tissue and that in addition to the federal HIPAA privacy rule, many states in the United States have privacy legislation that may apply to data obtained from research with human tissue. The National Conference of State Legislatures provides a summary of state genetic privacy laws that is updated at least once a month[1].

van Veen's perspective on the ethical and regulatory issues involving tissue collected from patients in the clinical setting—what he refers to as 'residual tissue'—is not a perspective that I and others share. van Veen says that "from a regulatory (and also ethical) standpoint, there is a huge difference between residual tissue and tissue collected specifically for research." In the United States, this is not true from a regulatory perspective. Moreover, the vast literature on the ethics of research with human tissue suggests there is disagreement about constructing different ethical frameworks for residual tissue and for tissue collected specifically for research, as well as over whether tissue research constitutes human subjects research. As Weir and Olick[2] show in their book regarding research with stored tissue, the debate from the outset (in the United States at least) over the use of stored tissue centered on the fact that residual tissue had long been used for research purposes without explicit consent for such use. They and others challenge the claim that coding or anonymizing residual tissue obviates the need to obtain informed consent because doing so fails to take seriously the fact that some people have concerns and interests about how their residual tissue will be used. This concern also

applies to future use of tissue collected for a specific research project. Public opinion surveys in the United States reveal that some people do not want their tissues used for certain kinds of research[2]. Even if residual tissue is coded or anonymized, the potential exists for social, psychological and other harms to accrue to individuals, families and identifiable populations because the tissue and associated data may be linked to geographic region or ancestry (for example, tissue and data from Ashkenazi Jews, named Native American tribes or other indigenous peoples)[2]. Additional concerns have been raised about anonymizing residual tissue without obtaining consent to do so, and about anonymizing without consent tissue collected for specific research purposes that investigators later want to use in different studies[2,3]. Although it is true that the US Office for Human Research Protections (OHRP) issued a guidance indicating that research with tissue and data that is coded and for which the investigator cannot 'readily ascertain' identifiable private information about the source of tissue or information does not constitute human subjects research, this is not a legally binding regulatory requirement. Indeed, institutional review boards (IRBs) do not necessarily follow this guidance, as some may require IRB review and approval of studies using coded and/or anonymous samples.

Because millions of stored residual tissues were collected years ago without consent for research purposes (and many were obtained for research but without consent for secondary uses), an argument can be made that an acceptable alternative to the cost and effort of contacting individuals for consent for research use of these stored samples is ethics board approval for anonymizing tissues. However, it is difficult to justify continuing the practice of collecting tissue in treatment and diagnostic settings, and specifically for research purposes, without obtaining consent for future research use[2]. That such practices took place in the past does not mean that they should continue.

Because my article addressed the ethical and policies issues involving genetic research in the context of describing and comparing population biobank projects (Table 1 in my original article), many of the nuances that van Veen points out were unavoidably lost. However, van Veen's comments reinforce the theme of the piece: that there is a patchwork of ethical and regulatory policies regarding genetic research with human tissues. van Veen's comments also reveal that there remains disagreement over what constitutes ethical research with human tissues and that what is legal and customary may not be the same as what is ethical.

1. National Conference of State Legislatures. State Genetic Privacy Laws (http://www.ncsl.org/programs/health/genetics/prt.htm).
2. Weir, R.F. & Olick, R.S. *The Stored Tissue Issue* (Oxford Univ. Press, Oxford, UK, 2004).
3. Clayton, E.L. *J. Law Med. Ethics* **23**, 375–377 (1995).

Transgenic plant science priorities

To the editor:

A letter by Vain in the November issue (*Nat. Biotechnol.* **23**, 1348–1349, 2005) reports a study of two major science literature databases and tracks broad trends in plant transgenic science knowledge from 1973 to 2003. The study identified 30,624 papers, of which 14.8% related to technology development, 71.3% related to applications of technology and 13.8% related to development of genetically modified (GM) crops or feed. The author expresses the concern that the expanding gap between technology applications and development since the 1980s may limit future transgenic science and the ability to address issues related to GM crops.

One of the issues related to GM crops is food safety. Vain's study did not seek to quantify the literature on this topic, but some studies using a more limited database have done so. One study's author searched the US National Library of Medicine Medline publications and documented 101 papers containing the terms 'food safety' and 'genetically engineered foods.'[1] Only eight of these papers reported findings from original rodent studies, with most of the remaining papers offering opinions and commentaries without supporting data. A search of the US Department of Agriculture's Current Research Information database (http://cris.csrees.usda.gov/) from 1994 to 2002 identified 3,041 funded research projects related to plants and to biotech and/or transgenics, of which 145 related to toxins and 19 related to allergens[2]. Examination of these abstracts revealed that most of the toxin studies focused on enhancing pest protection through the use of plant toxins. Two of the toxin studies and five of the allergen studies were specifically using transgenic methods to study or alter known human toxins, allergens or allergenic foods. Two projects in 2001 sought to develop an animal model to test for unexpected allergens in GM foods. None of the 3,041 transgenic plant projects related to the appearance of unintended toxins or allergens in GM foods. It would be of interest to use Vain's more comprehensive databases to further characterize the empirical science on the safety of GM foods.

The paucity of studies on food safety has hampered national and international efforts to develop regulations and has been noted by two committees of the US National Academy of Sciences, both of which have recommended expanded research in this area[3,4]. Similarly, a paucity of experimental studies related to ecological risks has been documented[5] and led an Academy committee to identify a number of high-priority research topics to better inform the development of regulations[6]. More broadly, these findings both document that transgenic research has overwhelmingly emphasized technology application over basic or risk-related research and suggest a need to examine transgenic funding priorities.

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2. Pelletier, D. *Nutrition Reviews* **63**, 210–223 (2005).
3. National Research Council. *Genetically Modified Pest-Protected Plants: Science and Regulation* (National Academies Press, Washington, DC, 2000).
4. Institute of Medicine. *Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects* (National Academies Press, Washington, DC, 2004).
5. Wolfenbarger, L. & Phifer, P. *Science* **290**, 2088–2093 (2000).
6. National Research Council. *Environmental Effects of Transgenic Plants: The Scope and Adequacy of Regulation* (National Academies Press, Washington, DC, 2002).