Commentary

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How mutually recognizable is mutual recognition? An international terminology index of research ethics review policies in the USA, Canada, UK and Australia

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"What's in a name? That which thy call a rose by any other name would smell as sweet."
– William Shakespeare

Could this Shakespearean adage be true of the policy terms used to describe research ethics review processes based on the principle of mutual recognition? Today, biomedical research is contingent on sharing research data [1–3] often across international borders [4]. This is because of the size of datasets necessary to make scientifically sound links between the human genome and underlying determinants of disease [5]. The degree of collaboration between researchers/research institutions typified in genomics and related 'omics disciplines' can therefore pose significant challenges for research ethics review where approval is sought on an institution-by-institution basis [6]. Policy initiatives and legislation adopted to streamline research ethics review in North America, Europe and Australia are unified in their motivation and philosophy [7–9]. The motivation is that research ethics review processes must complement the collaborative and data-centric nature of biomedical research if they are to enable clinical innovation [10]. The philosophy is the principle of mutual recognition, generally understood to describe an arrangement whereby one research ethics review committee (REC) accepts the processes used to come to decisions of other institutional RECs.

The plurality of terms used for policies and models of research ethics review that activate the principle of mutual recognition is the focus of this paper. An index of the terms equivalence, reciprocity, centralization and mutual acceptance from the USA, Canada, UK and Australia, respectively, will be compared. In addition to differences in nomenclature, policies that operationalize mutual recognition between RECs also vary in their degree of legislative formality. Although some policies pursuant to mutual recognition are legislated, not all can be centrally enforced. This is particularly true of countries with federated health systems such as Canada and Australia. The tediousness of the ethics approval process for principal investigators involved in multisite/jurisdictional projects was the primary motivation for reform in these countries, where memoranda of understanding and interinwstitutional agreements are still used to operationalize mutual recognition (see Figure 1).

Equivalent protections – USA

Equivalent protections was embedded in the 2001 Revisions of the Common Rule in the US, but laid dormant until its revival in more recent years. The concept of equivalent

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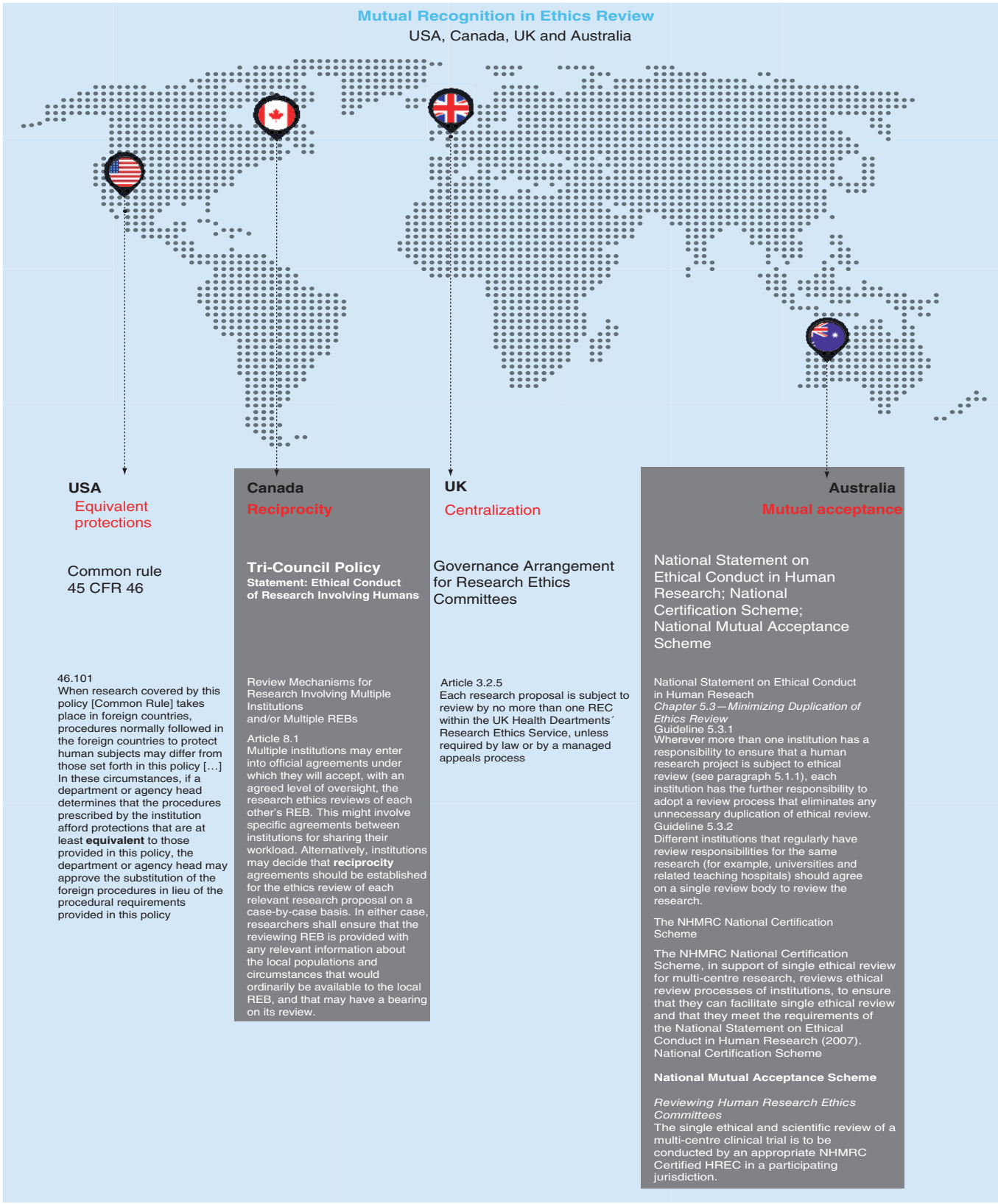

Figure 1. International comparison of policy terminology and relevant legislation of research ethics review based on the principle of mutual recognition in the USA, Canada, UK and Australia.
NHMRC: National Health and Medical Research Council; REB: Research ethics board; REC: Research ethics committee.

protections was inspired by policy recommendations from the then National Bioethics Advisory Commission (now the Presidential Commission for the Study of Bioethical Issues). The National Bioethics Advisory Commission debated the functionality of local research ethics review, concluding "as long as an accredited IRB reviews and approves the research protocol, multiple IRB reviews of the same research protocol are not always necessary to ensure the protection of research participants. For research studies conducted solely by one institution, it often makes sense for that institution's IRB to conduct the review. But for cooperative research, IRB review by all institutions participating in the research should be the exception" [11].

Equivalent protections effectively recognize the decisions of RECs in jurisdictions where ethical safeguards for research participants are comparable to those established in the Common Rule. The Office of Human Research Protections determines eligibility for jurisdictions in which equivalent protections holds. The recent notice of proposed rulemaking makes explicit its recommendation that "US institutions engaged in cooperative research rely on a single IRB for that portion of the research that takes place within the USA, with certain exceptions" [12]. The Common Rule regulations may well transition to the centralized approach if the recommendation currently found in the notice of proposed rulemaking is adopted [12].

Centralization – UK

Centralization of ethics review in England is likewise prescriptive in its federal health legislation. The National Research Ethics Service was established in December 2011, and is a core part of the Health Research Authority. The Health Research Authority appoints RECs in England, and works collaboratively with equivalent appointing authorities in Scotland, Wales and Northern Ireland [13]. The appointed RECs review applications for research conducted at all National Health Service (NHS) institutions, and use the integrated research application system to coordinate all applications to regulators and research sites. As of August 2013, 69 RECs have been appointed by the NHS in England, which review approximately 6000 protocols per year [13]. This centralized model also ensures that RECs comply with relevant laws and regulations related to information governance, including data protection [14].

Reciprocity – Canada

Healthcare delivery and health policy – including the organization of research ethics review – is the jurisdiction of the provinces in Canada. The Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans establishes the national research ethics guidelines in Canada, although it is only legally binding for researchers who receive federal funds. In 2010, the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans introduced three alternative models of institutional ethics review where research involves multiple RECs: independent, delegated and reciprocal [15]. While the independent model preserves locally specific oversight of ethics review, it imposes practical and resource challenges for multisite/jurisdictional projects. The delegated and reciprocal models both manifest the principle of mutual recognition albeit through slightly different mechanisms. Whereas the delegated model "may allow research on specialized content or research methods to be reviewed by an external, specialized or multi-institutional research ethics board (REB)," the reciprocal model establishes that "institutions may enter into official agreements under which they will accept, with an agreed level of oversight, the research ethics reviews of each other's (RECs)" [16].

Until recently, the independent model of ethics review was the most widely adopted in Canada. Four provinces have since transitioned, or are currently in the process of transitioning to either delegated or reciprocal models since 2010 (Alberta, British Columbia, Newfoundland/Labrador and Quebec [9]). Mutual recognition has also been operationalized for ethics review of discipline-specific research, including cancer [17] and maternal–infant clinical research [18]. The Ontario Cancer Research Ethics Board of the province of Ontario oversees multicenter clinical trials and serves as the board of record for 26 research sites with established agreements. As such, the Ontario Cancer Research Ethics Board accelerates the ethics review process, and is wholly accountable to the institution for initial and ongoing ethics review of the trials. In 2013, the Maternal Infant Child and Youth Research Network negotiated a partnership between the Universities of British Columbia (Canada), Alberta (Canada) and Saskatchewan (Canada) to pilot test ethics review reciprocity agreements specific for research in the area of maternal/infant/child health.

Mutual acceptance – Australia

Two recent initiatives in Australia introduced a national approach to ethics review via REC certification and mutual recognition agreements [19]. This dual policy plan for a streamlined system "applies to all human research as defined in the Australian National Statement on Ethical Conduct in Human Research (2007; or any replacement of that document published by the National Health and Medical Research Council [NHMRC]), for which an application must be made to a human research ethics committee (HREC) for the

purpose of conducting research at a public health organization" [20]. First, the National Certification Scheme qualifies existing HRECs to review studies that span multiple research centers [21]. Once certified, HRECs are entered into a registry that collects administrative data such as the average time between submission and approval for multicenter projects, costs and review outcomes. Thus, not only do certified HRECs operate in the spirit of mutual recognition, but the registry also enables HREC quality improvement/assurance.

Second, the National Mutual Acceptance program, superseded a previous interstate agreement. It was introduced in November 2013 as a phased approach in four jurisdictions: New South Wales, Queensland, South Australia and Victoria. According to the standard operating procedures, "each proposal will be ethically and scientifically reviewed once only by a public health organization HREC that has been certified by the NHMRC." Multicenter clinical trials at certified institutions within these jurisdictions may be eligible for a single, ethical and scientific review under the National Mutual Acceptance (with some exceptions). A site-specific assessment of the protocol submitted for review is also required, and must comply with the standard procedures outlined in each of the four participating jurisdictions.

Discussion & conclusion

The principle of mutual recognition lays the groundwork for international harmonization of ethics review, particularly for biomedical research that is becoming increasingly collaborative and globalized. The 'rose' of mutual recognition is known by four different policy names across the jurisdictions compared in this analysis (USA, Canada and Australia and the UK). These various policy manifestations are unified, however, in their motivation to streamline the ethics review process in the name of innovation efficiency and continued clinical progress. They differ in two significant ways: legislatively and organizationally. The legislative formality of the policies that actualize the principle of mutual recognition are determined in accordance with the health systems organization in each country, for example, federated versus non-federated. Future research is needed to compare the procedural efficiency and performance of such models. Exploration of both researcher and REC member perceptions are important lines of qualitative inquiry that could attest to these aspects of review models based on the principle of mutual recognition. Indeed, such research is currently underway as part of the Ethics Review Equivalency Task Team of the Global Alliance for Genomics and Health. It is anticipated that the findings will facilitate the development of interoperable models for data sharing within the genomics and 'omics' related research communities.

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