A recent Organisation for Economic Co-Operation and Development (OECD) survey demonstrated that an internationalization of genetic laboratory services currently emerged from the rarity of certain genetic abnormalities and from the small of laboratories performing specialized testing. When DNA samples cross national boundaries for genetic testing services to be performed in another country, the heterogeneity of national legal frameworks raises important questions regarding quality of genetic services available internationally.

Some aspects of the genetic laboratories’ services are abundantly discussed by the literature, among which most prominent are quality control standards and patients rights. Firstly, a 2003 study identified key distinctions between the different legal frameworks for genetic services. While some countries impose exhaustive regulatory requirements, others favor guidelines for good practices. Moreover, proficiency assessment, clinical validity, retention of laboratory records and test reports are not dealt with uniformly.

Secondly, a number of international laboratory accreditation standards, including International Standard Organization (ISO) norms 17025 and 15189, play an essential role in the standardization of practices. The same holds true with regard to external quality assessment programs, including those offered by the United Kingdom National External Quality Assessment Service (UK NEQAS), the European Molecular Genetics Quality Network, and the College of American Pathologists. Furthermore, professional associations play an important role, supervising the activities of professionals working in genetics. However, these various standardization attempts run parallel to one another. In order to clarify the situation, the OECD recently published an exhaustive set of guidelines for quality assurance in molecular genetic testing. These guidelines aim to standardize quality assurance practices in order to foster mutual recognition of the various national supervision methods for genetic laboratories. However, the implementation of these standards is not mandatory.

Thirdly, the variety of national legislations overseeing the medical laboratories also influences the international exchanges of the genetic samples. This aspect is rarely considered by the literature, although it can affect the internationalization of genetic services. Despite these attempts to bring together the laboratories’ quality control standards, no literature notes the impact of different national frameworks governing genetic laboratories on the internationalization of genetic services.

For example, American legislation requires that all laboratories wishing to analyze samples from U.S. citizens must be certified under the Clinical Laboratory Improvement Amendments (CLIA) from the U.S. Food and Drug Administration. This regulation might curb access to certain laboratories located outside the

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**Differences in Regulatory Frameworks Governing Genetic Laboratories in Four Countries**

**Anne Marie Tassé, Élodie Petit, and Béatrice Godard**

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This qualitative research aims to compare the differences in national frameworks governing genetic laboratories and examine their key components. Such an analysis is necessary to determine whether the heterogeneity of control structures hinder the internationalization of genetic services.

Materials and Methods
This comparative research studies the legislation regulating genetic laboratory services in four countries: Australia, France, the United Kingdom, and the United States. These countries were selected because they illustrate a range of structures governing genetic laboratories. We conducted a structured analysis of American, Australian, British, and French legislation and regulation in force by September 30, 2007, and available on the following official Web sites: ComLaw (Australia), LegiFrance (France), OPSI (United Kingdom), and FirstGov (United States). Articles comparing national control standards for genetic laboratories, published from 1987 to December 2007, were also researched in PUBMED using the following key words: (certificate OR license OR accreditation OR quality) AND (laboratory OR genetic) AND (legislation OR regulation OR control). We also searched the standards and guidelines of professional associations and recognized accreditation bodies, as listed in the legislation, regulation, standards, guidelines, or statements emanating from national or international organizations. Documents were eligible if they were national legislation or regulation, or if they were standards, guidelines, or statements emanating from national or international organizations and professional associations. We included in our research only documents written or translated in English or French. The comparative analysis of these documents was performed rationally and in detail, following a three-step process called the Three Cs Rule.

Results
In order to determine if heterogeneity of the different regulatory frameworks governing genetic laboratories in the four countries studied affect the international availability of genetic tests, an overview of the regulatory frameworks for genetic laboratories is necessary.

Australia
The federal Australian state partially controls genetic laboratory services. Only laboratories accredited under the Health Insurance Act may benefit from public reimbursement of their expenses by the Medicare program. This accreditation is strictly regulated, both by legislation and regulations general to all medical laboratories as well as by standards and guidelines specific to genetic laboratories.

The Health Insurance (Accredited Pathology Laboratories – Approval) Principles require that laboratories applying for federal accreditation undergo a preliminary audit by an independent body. This accreditation process imposes the application of standards issued by the National Pathology Accreditation Advisory Council (NPAAC), an organization governed in part by the Royal College of Pathologists of Australia. The Standards for Pathology Laboratories are the primary source of information for laboratories wishing to meet NPAAC standards. These standards are also defined, for genetic laboratories, by the Laboratory Accreditation Standards and Guidelines for Nucleic Acid Detection Techniques and the Guidelines for Cytogenetics Laboratories. It should be noted, however, that only public laboratories are required to apply these standards and guidelines.

By virtue of their constitutional powers, Australian states can also require that genetic laboratories obtain a state accreditation in order to offer services in their territory. However, since late 2003, no Australian state requires a local accreditation.

When DNA samples cross national boundaries for genetic testing services to be performed in another country, the heterogeneity of national legal frameworks raises important questions regarding quality of genetic services available internationally.

LegiFrance (France), OPSI (United Kingdom), and FirstGov (United States). Articles comparing national control standards for genetic laboratories, published from 1987 to December 2007, were also researched in PUBMED using the following key words: (certificate OR license OR accreditation OR quality) AND (laboratory OR genetic) AND (legislation OR regulation OR control). We also searched the standards and guidelines of professional associations and recognized accreditation bodies, as listed in the legislation, regulation, standards, guidelines, or statements emanating from national or international organizations.
France
In France, only certain types of laboratories may offer genetic testing, and these laboratories must also be individually authorized to do so by the State.21 As such, testing can only be conducted by clinical laboratories at public health institutions, cancer treatment centers, the Établissement français du sang [French blood institution], and some private laboratories.22
Currently, the regional prefect authorizes laboratories to perform genetic testing, subject to the opinion of the Commission consultative nationale en matière d’examens des caractéristiques génétiques à des fins médicales [national advisory board on genetic testing for medical purposes].23 In addition to laboratory authorization, French law provides for the accreditation of practitioners responsible for overseeing genetic testing in a laboratory. Only they can comment on and sign reports on genetic tests.24 This accreditation may only be granted for certain types of genetic testing. The Loi relative à la bioéthique, 2004 [Bioethics act, 2004]25 transfers the issuance of this accreditation to the new Agence de la biomédecine [biomedical agency].26 However, since all the decrees necessary for applying the legislative provisions concerning human genetics are being drafted, the regional prefect continues to have jurisdiction for new applications and applications to amend practitioner accreditation.27
Quality controls for genetic services are tied to a laboratory’s authorization to dispense genetic testing. Thus, the Code de la santé publique28 [public health act] stipulates that authorization may be revoked on the grounds of failure to comply with the obligations under the Guide de bonne exécution des analyses de biologie médicale29 [guide for the proper execution of laboratory testing] and refusal to participate in national quality controls for biomedical analysis.

The United Kingdom
The public health services in the United Kingdom are controlled by the Department of Health (DOH), which delegates its authority in matters of health care organization to the National Health Service (NHS) in England, Scotland, and Wales.30 In Northern Ireland (NI), the Health and Care NI holds a mandate similar to the NHS. These health services are funded by the state through the NHS trusts, which determine where public funds are spent. Currently, genetic testing is offered mainly by regional centers specializing in genetics.31 These laboratories usually offer testing services in cytogentic and molecular genetics. Other genetic testing may also be conducted outside the regional centers, some of which occurs in biochemistry or pathology laboratories.32
Since June 2003, the Department of Health’s Genetic White Paper33 requires that all English laboratories be accredited by an independent body, such as Clinical Pathology Accreditation (U.K.) Ltd (CPA). The Scot-
atory Systems of the Centers for Disease Control and Prevention (CDC).

Under the CLIA, a laboratory that applies for federal certification must show that it operates in accordance with specific standards or that is accredited by a recognized independent body. The requirements for federal certification are set out in the Laboratory Requirements. Under these Laboratory Requirements, genetic testing may be categorized as high complexity. A laboratory certified to perform high-complexity testing must commit to an exhaustive quality control process specific to its specialty. However, the CLIA does not recognize genetics as a specialty. Without a specialty, a laboratory certified for high-complexity testing must establish and maintain satisfactory quality control processes, as well as proficiency testing at least twice a year.

American states may also benefit from a CLIA exemption that allows them to control laboratory services in their territory. To do so, the state must show that it has a quality control program at least as rigorous as the federal program. Currently, only the states of New York and Washington benefit from such an exemption.

Discussion
The four jurisdictions chose different ways to control genetic laboratory services. These different options result in three important distinctions, regarding the choice of a mandatory vs. voluntary approach, general vs. genetic-specific requirements, and the vocabulary used. These distinctions interfere with uniformity of standards and the internationalization of genetic services.

The Choice of Different Standards
The comparison of the different regulatory frameworks for genetic laboratories reveals the various structural options available to States that wish to control the delivery of genetic laboratory services. Table 1 summarizes the components of the control systems for genetic laboratories in the four countries studied. It shows the source of the laboratories’ obligation with respect to control (regulations or recommendation), as well as whether a general standard (*) or a specific standard (\(\checkmark\)) applies to genetic laboratories.

Mandatory Versus Voluntary Implementation of Standards
The OECD defines accreditation as a “procedure by which an authoritative body gives formal recognition that a body is competent to carry out specific tasks.” This is public acknowledgement of a laboratory’s ability to perform certain tests. Obtaining this recognition involves an exhaustive assessment of the laboratory infrastructure, internal quality control and external assessment through participation in a recognized laboratory proficiency testing scheme. It is noteworthy that all regulatory systems analyzed in the present study are based on quality control requirements. However, standards differ from a country to another.

In Australia, only public genetic laboratories must be accredited by the National Association of Testing Authorities (NATA). Private laboratories are currently not regulated by federal or provincial legislation.

In France, the Code de la santé publique provides for the obligation to comply with the Guide de bonne exécution des analyses de biologie médicale and to participate in national quality controls for laboratory testing.

In the United Kingdom, accreditation is not mandatory by law. Nevertheless, the Department of Health’s guideline requires laboratory accreditation by Clinical Pathology Accreditation (U.K.) Ltd (CPA) or another equivalent body. This accreditation is the main control framework for laboratories in the United Kingdom. Northern Ireland, although favorable to the process

<table>
<thead>
<tr>
<th>Table 1 Comparison of Legal Frameworks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
</tr>
<tr>
<td>Right to perform genetic tests (licence, permit, certificate, etc.)</td>
</tr>
<tr>
<td>Accreditation</td>
</tr>
<tr>
<td>External quality assessment (or proficiency testing)</td>
</tr>
</tbody>
</table>

Rec indicates jurisdictions where genetic laboratories are governed by recommendations; Reg indicates jurisdictions where genetic laboratories are governed by regulations; * indicates areas covered by general regulations or recommendations; \(\checkmark\) indicates areas covered by regulations or recommendations specific to genetic laboratories.
established in Great Britain, has not yet imposed a strict obligation in this regard.

Finally, in the United States, all laboratories, private and public, must prove that they meet the standards set by legislation or show that they are accredited by an independent body whose program is recognized by Health and Human Services.49

**General Versus Specific Requirements**

Despite the omnipresence of rules concerning quality controls for medical laboratories, few specifically apply to genetic laboratories. Table 2 shows that each jurisdiction studied generally deals with the same aspects of the quality control process. However, there is a distinction between countries that impose a special scheme of provisions for genetic laboratories (√) and those that impose a general standard (*) to all medical laboratories.

In Australia, genetic laboratories that wish to receive accreditation must comply with standards developed by the National Pathology Accreditation Advisory Council (NPAAC) for quality controls at genetic laboratories. Australia is unique in its implementation of accreditation standards specific to genetic laboratories. In fact, the National Pathology Accreditation Advisory Council (NPAAC) has created an exhaustive set of standards and guidelines exclusive to laboratories that use nucleic acid detection and cytogenetic techniques.50

In France, there are a few provisions concerning molecular genetics in the *Guide de bonne exécution des analyses de biologie médicale*.51 There is also quality control specific to genetic fingerprinting for identification purposes as well as to genetic testing for medical purposes.52 Moreover, the *Guide de bonne exécution des analyses de biologie médicale* recommends that all laboratories participate in other external assessment offered by scientific organizations.53

In the United Kingdom, CPA standards impose general rules for internal quality controls at genetic laboratories.54 However, a special proficiency assessment program is available to laboratories that conduct cytogenetic and molecular genetic testing.55

In the United States, the *Laboratory Requirements* impose only a few specific obligations for genetic laboratories, particularly in cytogenetics, leaving a vast area of genetics that is not subject to specific provisions. It should also be noted that laboratories certified for complexity testing must commit to a quality control process specific to their specialty, when their specialty is included in the CLIA. These areas of specialty are subject to quality control requirements that are more exhaustive than the CLIA’s general requirements. There is currently no specialty specific to genetics under the CLIA. While there is no specialty for laboratories that are certified

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**Table 2**

<table>
<thead>
<tr>
<th>Comparison of Quality Control Standards</th>
<th>Australia</th>
<th>France</th>
<th>United Kingdom</th>
<th>United States</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control of laboratory management (role and training of staff in charge of laboratory)</td>
<td>√</td>
<td>√</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Control of equipment and testing material (purchase, maintenance, repairs, calibration, etc.)</td>
<td>√</td>
<td>√</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Control of pre-testing process (patient reception, genetic counselling, consent)</td>
<td>√</td>
<td>√</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Control of testing process (recognized testing procedures)</td>
<td>√</td>
<td>√</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Control of post-testing process (treatment of results, test report, genetic counselling, etc.)</td>
<td>√</td>
<td>√</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Control of premises (number, use of rooms, ventilation, etc.)</td>
<td>√</td>
<td>√</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Control of staff members (training, experience, professional accreditation, etc.)</td>
<td>√</td>
<td>√</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Control of documentation (equipment control manuals, testing procedures, staff records, etc.)</td>
<td>√</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Skills assessment program</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>*</td>
</tr>
</tbody>
</table>

* √ indicates requirements specific to genetic laboratories.
* * indicates requirements general to all medical laboratories;
for high-complexity testing, the CLIA stipulates that laboratories must establish and maintain appropriate quality control processes as well as proficiency testing at least twice a year.\textsuperscript{57}

The efforts to create uniform quality control standards for genetic laboratories are essential but are dependant upon each country’s situation, which have varying degrees of standards that specifically address genetic laboratories. The ease of implementing the OECD’s harmonization proposals depends on the choice of standardization the normative instrument used by the countries. It is easier to amend an administrative guideline than a legislation.

\textit{The Vocabulary in Question}

Although the vocabulary used by these countries is highly similar, their different interpretation is likely to result in difficulties with regard to assessing the equivalency of official national recognitions. For example, the \textit{OECD Guidelines for Quality Assurance in Molecular Genetic Testing} define licensing as being a legal permit or formal authorization to operate a laboratory.\textsuperscript{58}

However, this obligation is referred to differently in the various countries, i.e., “accreditation” in Australia, “certification” in the United States and “autorisation,” or “authorization,” in France. The United Kingdom does not require such a national recognition.

In Australia, the term “accreditation” is used to identify an official document, issued by a government body, attesting compliance with national legislation. This accreditation is mandatory for all laboratories that wish to receive payment for their services through the public Medicare plan.\textsuperscript{59} Besides, the use of the term accreditation in two different situations — one referring to the OECD definition of accreditation and the other referring to a license — can lead to confusion for foreign health professionals when choosing laboratories.

In the United States, the term “certification” is used for identifying the procedure for obtaining a legal permit or formal authorization to operate a laboratory. The CLIA requires all laboratories to be certified.\textsuperscript{60}

Although most of the countries studied require genetic laboratories to obtain recognition by a public or para-public authority, only France has created a license specific to genetic laboratories.\textsuperscript{61}

The use of a different vocabulary can result in confusion that can now be partially clarified through implementation of the \textit{OECD Guidelines for Quality Assurance in Molecular Genetic Testing}. But despite the usefulness of a common vocabulary, the particularities for obtaining a license in each country remain. This means that the different licenses cannot be claimed to be equivalent to one another, particularly due to the disparate requirements concerning genetic laboratories. Then, should Australian Medicare recognize genetic tests performed in the United-States? And should American laboratories recognize tests performed in Canada, when the Canadian laboratory is not CLIA certified?

In conclusion, an overview of the main features of the legal frameworks governing genetic laboratories shows different — sometimes even opposing — choices. In all four jurisdictions, genetic laboratories are subject to more or less exhaustive control of their services. In fact, none of the jurisdictions really functions like any other, since each assigns the State and professional associations a different role.

The complete harmonization of these legal frameworks is not a realistic, effective solution. However, geneticists should be informed that when DNA samples cross national boundaries for genetic testing services to be performed in another country, they are governed by the legal framework of this jurisdiction. Therefore, in order to protect the patient’s best interests, and prior to transferring genetic material to another country, geneticists might want to verify not only if the foreign laboratory is accredited, but also under which standards or legal framework. To do so, it is essential to develop easy-to-use mechanisms giving researchers access to this information.

\textbf{Acknowledgements}

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5. \textit{Id.}
6. \textit{Id.}
18. Australian Government, National Pathology Accreditation Advisory Council, Standards for Pathology Laboratory (Canberra: Publications Production Unit, 2002).
35. Id., at 4.
41. Laboratory Requirements, 42 C.F.R. § 493.17.
44. See OECD Biotechnology Division, supra note 9, at 24.
45. Id., at 25.
47. See Code de la santé publique, supra note 21, § L.6213-3; Guide de bonne exécution des analyses de biologie médicale, supra note 29.
48. See Department of Health, supra note 33.
49. See Clinical Laboratory Improvement Amendments of 1988 (CLIA), supra note 38; Laboratory Requirements, supra note 41.
50. See Australian Government, National Pathology Accreditation Advisory Council, supra note 19; Australian Government, National Pathology Accreditation Advisory Council, supra note 20.
51. See Guide de Bonne Exécution des Analyses de Biologie Médicale, supra note 29.
53. See Guide de Bonne Exécution des Analyses de Biologie Médicale, supra note 29, § V.2.2.
54. See Clinical Pathology Accreditation (UK), supra note 34.
55. See U.K. NEQAS, supra note 36.
56. See Hudson, Murphy, and Kaufman et al., supra note 42.
57. Id.
58. See OECD Biotechnology Division, supra note 9, at 25.
60. See Clinical Laboratory Improvement Amendments of 1988 (CLIA), supra note 38.