CGP Centre of Genomics and Policy
Centre de génomique et politiques

HUMAN CELL ATLAS

The Human Cell Atlas (HCA)

Tissue Provenance Primers - Introduction

The 'Human Cell Atlas Tissue Provenance Primers' were developed by the Centre of Genomics and Policy (McGill University), as background research to support the development of consent and recruitment guidance tools (Human Cell Atlas Ethics Toolkit).

The intent of these three high-level documents is to survey a sample of jurisdictions representative of general models of tissue sampling and consent requirements in the following scenarios:

1. Post-mortem sampling of tissue and organs from deceased donors;
2. Sampling of fetal and embryonic tissue; and
3. Sampling of tissue from live research participants and research use of leftover clinical tissues from patients;

While this research helps in the development of generalizable tissue acquisition, consent and recruitment models, it does not address all possible models, worldwide. It is understood that certain jurisdictions may have different regulatory requirements, or socio-cultural expectations for certain tissue acquisition or use scenarios. Therefore, the HCA Ethics Toolkit, including proposed recruitment strategies or templates, should always be implemented in accordance with local specificities and requirements.

The Ethics Working Group of the HCA welcomes collaboration with members from different jurisdictions and countries, in view of further refining this background research and models, in view of the eventual development of additional templates and guidance.

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HUMAN CELL ATLAS – LAW & POLICY: DRAFT PROVENANCE PRIMER

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TISSUE SOURCE: ORGANS/POST-MORTEM
UPDATED: DECEMBER 2018

METHODOLOGY

We begin this basic primer on *post-mortem* tissue, organ and whole-body donation for research purposes with definitions (I), followed by a brief overview of selected recent applicable international and regional norms/guidelines that govern this type of donation (II). We then examine legislation and policy regarding *post-mortem* donation for research purposes in seven countries, namely: Canada, the U.S., Mexico, the UK (England, Wales, Scotland, Northern Ireland), France, Singapore and Australia (III).[1] In the interests of brevity, only a few selected legal cases and articles from the literature were included. More specifically, this basic primer answers the following questions:

- In the countries under study, what laws apply to the use of a body, or to the removal and use of tissue or organs from a deceased individual, for research purposes?
- What consent approach applies to such research uses of a body or body parts from a deceased individual?
    - Who has the authority to consent?
    - What consent standard must be met?
    - What are the procedural requirements?
    - Can family members override the deceased person's *ante-mortem* objection or consent?
- In addition to laws, are there regulations or guidelines regarding biomedical research involving human subjects that apply to *post-mortem* tissue, organ and whole-body donation for research purposes?
- Which acts are prohibited?

In addition to our analysis of the normative context in the countries under study, we offer a summary of selected case law on the ownership of deceased individual's bodies, as well as on the ownership of body parts collected from living or deceased individuals (IV). Finally, we end this primer with some conclusions about consent requirements for tissue, organ and body donation for research purposes in the countries of interest (V).

[1] For comparison purposes, we sometimes refer to legislation on organ donation for transplant. Also, some jurisdictions, such as the UK, make a distinction between tissue donation for research and whole-body donation to medical schools for anatomical examination (educational purposes). However, legislation regarding body donation for educational purposes is not the focus of this primer.

I. DEFINITIONS

Death

Generally accepted medical practice recognizes two ways of establishing death: cardiorespiratory death or brain death. In all of the jurisdictions studied, cardiorespiratory death and brain death have been specifically recognized either in the law or by the Courts. Also, in some countries (e.g. the U.S. and Singapore), the legislative definition of a deceased individual or "decedent" includes a stillborn infant and a dead fetus.

Tissue/Organ

The WHO defines human tissue as "all constituent parts of the human body formed by cells", and defines organs as "differentiated and vital part[s] of the human body, formed by different tissues, that [maintain their] structure, vascularisation and capacity to develop physiological functions with an important level of autonomy" (WHO, 2009). It is important to note, however, that not all jurisdictions define "tissue" and "organs" the same way. For example, while some laws exclude "organs" from the definition of "tissue", others include "organs" but exclude other anatomical structures or biological substances such as eyes, fetuses, blood, placenta, spermatozoa, ova, etc.

II. INTERNATIONAL/REGIONAL NORMS/GUIDELINES

A. INTERNATIONAL

[UNESCO] *Human Genetic Data: Preliminary Study by the IBC on its Collection, Processing, Storage and Use*, "Post-mortem samples", Guideline 17 (2002)

- The taking of samples from the dead for purposes other than criminal or civil justice has to be authorized by the next-of-kin of the deceased person and there has to be no evidence that the deceased person might have objected to the purpose for which the sample is sought.

[CIOMS/WHO] *International Ethical Guidelines for Health-related Research Involving Humans*, "Commentary on Guideline 11", General considerations (2016)

- Ethical guidelines that apply to research participants also apply in cases where the research uses samples and data from deceased individuals.

[ISBER] *Best Practices for Repositories I: Collection, Storage and Retrieval of Human Biological Materials for Research,* "Section K: Specimen Collection, Processing, Receiving, and Retrieval" and "Section L: Legal and Ethical Issues for Biospecimens" (2018)

- "Remnant samples may be collected from autopsy/necropsy procedures consistent with relevant regulations."
- "Full consent or authorization should be obtained from the deceased individual (e.g., a signed agreement to donate their body for scientific research), the next of kin, or a legally authorized representative."
- "Specimens that are not removed as part of the routine autopsy procedure (i.e., leg, arm, hand, foot, face tissue) are not usually available as their procurement may result in disfigurement of the body. There may be exceptions allowing procurement of such specimens if a specific consent has been obtained from a donor and/or the next of kin as appropriate under specific laws of the country or region of the acquisition."
- "Occasionally, organs that are inappropriate for transplant may be offered or made available to a repository for research purposes. Information about the donor from whom the organ was procured should be obtained from the transplant center and recorded."

It is worth noting that a number of international guidelines on biomedical research involving humans, such as the World Medical Association's *Helsinki Declaration*, do not specifically address deceased individuals, which can be explained by the fact that the deceased are not legally considered "persons".

B. REGIONAL

[COUNCIL OF EUROPE] *Additional Protocol to the Convention on Human Rights and Biomedicine Concerning Transplantation of Organs and Tissues of Human Origin* (2002)

- Article 16 – Certification of death

  "Organs or tissues shall not be removed from the body of a deceased person unless that person has been certified dead in accordance with the law."

- Article 17 – Consent and authorisation

  "Organs or tissues shall not be removed from the body of a deceased person unless consent or authorisation required by law has been obtained.

The removal shall not be carried out if the deceased person had objected to it."

[EUROPEAN PARLIAMENT AND COUNCIL OF THE EUROPEAN UNION] *Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on Setting Standards of Quality and Safety for the Donation, Procurement, Testing, Processing, Preservation, Storage and Distribution of Human Tissues and Cells* (2004)

- Annex: Information to be Provided on the Donation of Cell and/or Tissues

  "**B.** Deceased donors

  1. All information must be given and all necessary consents and authorisations must be obtained in accordance with the legislation in force in Member States."

[COUNCIL OF EUROPE] *Convention Against Trafficking in Human Organs* (2015)

- Article 4 – Illicit removal of human organs

  "**1.** Each Party shall take the necessary legislative and other measures to establish as a criminal offence under its domestic law, when committed intentionally, the removal of human organs from living or deceased donors:

  a. where the removal is performed without the free, informed and specific consent of the living or deceased donor, or, in the case of the deceased donor, without the removal being authorised under its domestic law;

  […]

  c. where in exchange for the removal of organs from a deceased donor, a third party has been offered or has received a financial gain or comparable advantage."

III. COUNTRY-SPECIFIC LAWS/GUIDANCE

First, we determine which laws, enacted by what order of government (territorial, state, provincial, etc.) apply to tissue, organ and whole-body donation for research in the countries under study (A). We then compare the different consent approaches to *post-mortem* donation (B). We also examine if certain regulations or guidelines regarding biomedical research apply to such donation (C). Finally, we identify which acts related to

the sale, purchase, ownership or analysis of tissue, organs and bodies are prohibited in the countries studied (D).

A. JURISDICTION

In some countries (Canada, USA, Australia), tissue, organ and whole-body donation for research is governed by state, territorial or provincial law. In Canada and Australia, for example, each province, territory or state has its own human tissue donation law, although they are all quite similar. In the USA, most states (but not all of them) have adopted the *Revised Uniform Anatomical Gift Act* (2006)[2]. In other countries, such as France, Mexico and Singapore, national laws apply across the country. In the UK, the *Human Tissue Act (2004)* governs tissue, organ and whole-body donation for research in England, Wales[3] and Northern Ireland, but in Scotland, this type of donation is governed by the *Human Tissue (Scotland) Act.*

B. CONSENT APPROACHES FOR TISSUE, ORGAN AND BODY DONATION

The different consent approaches found in the legislation of the countries under study can be grouped into three categories: situations where the law requires explicit *ante-mortem* consent by the individual or consent by the legally authorized representative (I); exceptional situations where no explicit consent is required (II); situations where consent is presumed by law (III).

I. *Explicit ante-mortem consent by the individual or consent by the legally authorized representative* ["Opt-in" system]

In Canada, Australia, Singapore, the UK and the U.S., there is legislation that requires explicit consent for the use of a body, or the removal and use of tissue or organs from a deceased individual for research purposes. The use of a body or body parts will be possible either with the *ante-mortem* consent of the deceased, or, in the absence thereof, with the consent of the deceased person's legally authorized representative. When the wishes

[2] When we refer to the USA in the primer, we refer to the states that have adopted the *Revised UAGA*: Alabama, Alaska, Arizona, Arkansas, California, Colorado, Connecticut, District of Columbia, Georgia, Hawaii, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, U.S. Virgin Islands, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, Wyoming (+ Introduction in Pennsylvania in 2018) (Uniform Law Commission, 2018)

[3] In Wales, the *Human Transplantation (Wales) Act* provides that consent is presumed for deceased organ donation for the purpose of transplantation. However, deemed consent does not apply to the donation of organs for research purposes, which is governed by the *Human Tissue Act (2004)*.

of the deceased are unknown, the law provides a list of who can provide consent and in what hierarchical order. Sometimes, the list will include individuals who are not necessarily a spouse or a relative of the deceased (e.g., the person who is lawfully in possession of the body). Also, the law will not allow the removal and use of tissue if there is reason to believe that the deceased has (or, in some jurisdictions, would have) objected to such removal or use, or if consent was withdrawn before death.

In Mexico, the law also requires explicit consent, but consent requirements vary depending on the identity of the person or institution wishing to use the body. The general rule is that the *ante-mortem* consent of the individual is required to use a body or body parts for research purposes. However, educational institutions who wish to use bodies or parts thereof for research can do so either with the *ante-mortem* consent of the individual, or with the consent of family members[4]. Mexican law also makes a distinction between the bodies of identified individuals, and those of unidentified individuals. In the case of unidentified individuals' bodies, laws regarding missing persons apply. In France, while the law provides that consent is presumed for **organ donation** for research purposes, research institutions will only be allowed to accept a **whole-body donation** with the *ante-mortem* consent of the deceased.

i. ELEMENTS OF CONSENT

Usually, the person consenting will only need to specify what is being donated (the whole body or only certain tissues or organs), and the purpose of the donation (medical education, scientific research, transplant or other therapeutic purposes, etc.). Generally, the law does not require a legal informed consent standard to be met for tissue, organ or whole-body donation for research (the risks, benefits or nature of the research project do not need to be discussed). In certain jurisdictions however, such as in some Canadian provinces, the law will require that the person consenting understand the nature and consequences of removing organs from the body after death for the purposes specified in the consent. Also, a higher informed consent standard may be required by policy (e.g. research ethics).

ii. PROCEDURAL REQUIREMENTS

Procedural requirements vary by jurisdiction. The laws from the countries studied provide different requirements for recording a person's valid consent to tissue or body donation for research: in writing, orally

[4] While Mexican law provides a hierarchical list of family members who can consent for donation for transplant, we were not able to find such a list for donation for research purposes.

(with the presence of two or more witnesses), by telephone or recorded message, by signing a donor card or placing a symbol/sign on a driver's license, in a will, etc.

iii. FAMILY OVERRIDE OF FIRST PERSON REFUSAL OR CONSENT

In most of the countries studied[5], the *ante-mortem* **objection** of the deceased will preclude family members from authorizing the donation of the deceased person's tissue, organs or whole-body. Regarding the deceased individual's *ante-mortem* **consent**, the legislation in the jurisdictions under study either provide that: (1) the prior consent of the deceased individual is full authority and binding for the removal and use of body parts for research purposes (most Canadian provinces); (2) that family override is not legally permissible (most American states); or (3) the law simply does not contain any legal basis for family veto (UK, France, Mexico, Singapore, Australia).

II. *No explicit consent required* [Certain circumstances]

There are three jurisdictions in which the law generally requires explicit consent for tissue, organ or whole-body donation for research purposes, but where in certain circumstances, such donation will be possible without the explicit consent of either the deceased or the deceased's legally authorized representative. In the Australian states of Victoria and South Australia, the law provides that when a deceased person's wishes are unknown (and the person had never expressed an objection to the removal of tissue for research purposes in their lifetime), the removal of tissue may be authorized if, after making reasonable inquiries, there is no reason to believe that the senior next of kin has an objection to the removal of the tissue or if it is not possible to ascertain whether any next of kin has an objection to the removal. In Singapore, the law also states that when a body has not been claimed from an approved hospital or from an institution maintained on public funds within 24 hours after death, its use for research or advancement of medical science may be authorized by the Director of Medical Services.

III. *Legislated presumed consent* ["Opt-out" system]

While a number of the countries studied have a legislated presumed consent system ("opt-out") for organ donation for transplant purposes, or are considering the implementation of such a system, it is only in France that legislated presumed consent was also introduced for organ donation for research (but not for whole-body

[5] Mexican law does not specify if the person's *ante-mortem* objection precludes family members from authorizing the donation.

donation). Its public health legislation (*Code de la santé publique*) provides that the removal of organs from a deceased individual for scientific purposes can only be done as part of a research protocol previously transmitted to and approved by the *Agence de la Biomédicine*. In the other countries where consent is presumed for organ donation for transplant purposes, such as Wales and Singapore, the law distinguishes donation for transplant from donation for research, the latter requiring explicit consent (except for unclaimed bodies in Singapore).

C. Biomedical Research Involving Human Subjects – Regulations & Guidelines

In addition to legislation, some countries also have regulations or guidelines that apply specifically to biomedical research involving human subjects. However, it is important to note that in certain countries, those research guidelines do not apply to either anonymized tissue or to tissue obtained from deceased individuals (e.g. the US Common Rule). In contrast, Canada's *Tri-Council Policy Statement* applies to research involving biological materials derived from deceased individuals, and requires research ethics review, as well as the *ante-mortem* consent of the participant or in the absence thereof, the consent of an authorized third party, for such research. Likewise, Australia's *National Statement on Ethical Conduct in Human Research* specifies that human biospecimens include material collected *post-mortem*, and provides that researchers seeking to use such specimens should obtain the consents required by law, that is, the *ante-mortem* consent of the participant or in the absence thereof, the consent of a legally authorized representative (except in certain circumstances discussed above).

D. Prohibited Acts

All of the countries studied have legislation that either restricts or prohibits the sale or purchase of organs and other human tissue. In Canada, Mexico, France and Singapore, the sale, purchase or dealing for valuable consideration of either organs, tissue or both is prohibited. In the USA and the UK, those acts are prohibited if the tissue or organs are destined for transplant or therapy. However, the legislation in some countries (US, UK, Singapore, Australia) provides that individuals can be reimbursed for expenses related to the removal, transport, processing, preservation, preparation, quality control, storage, or disposal of a part, or that the prohibition on sale and purchase does not apply to tissue that has been subjected to some treatment or processing (some Australian states). Additionally, in the UK, the non-consensual analysis of DNA is a criminal offence under the *Human Tissue Act 2004*. In Mexico, the public health law specifies that cadavers cannot be an object of property.

IV. SELECTED CASE LAW

Selected case law demonstrates that in certain common law jurisdictions, the Courts have accepted the idea that body parts can be an object of property, or at least that patients, research participants or families of deceased individuals can retain "property-like" interests in excised tissue, biological materials or cadavers.

A. OWNERSHIP OF BODY PARTS COLLECTED FROM A LIVING RESEARCH PARTICIPANT/PATIENT

While the use of gametes and embryos for research is the subject of another primer, it bears noting that in both Canadian and English case law, it has been recognized that sperm may be an object of property, even if the law restricts the owner's ability to sell it (*Lam v. University of British Columbia* (2015)*; J.C.M. v. A.N.A* (2012).; *Yearworth v. North Bristol NHS Trust* (2009)). Moreover, a 2018 case awarded property rights in a frozen, purchased embryo to one of the parties in a divorce proceeding (neither party had contributed the gametes) and ordered the wife ("the patient") to reimburse the ex-husband for this transfer of property to her (*S.H.* v. *D.H*).

American and Canadian Courts have stated that tissue excised for diagnostic purposes is owned by the hospital or institution, but that the patient retains certain rights, such as the right to have "reasonable access" to the tissue or the right to order its destruction (*Piljak Estate v. Abraham* (Ontario, Can: 2014); *Moore v. Regents of U. of California* (USA: 1990)*; Greenberg v. Miami Children's Research Hospital Institute* (USA: 2003)*; Washington U. v. Catalona* (USA: 2007)).

The same does not hold true for France (or Quebec) where the human body, its parts, and tissues are "hors commerce" (cannot be property that is owned or sold). Nevertheless, in a 2006 divorce case in Quebec (Canada's only province where civil matters are regulated by the civil law) involving a dispute over two placentas, the Court based its ruling on considerations of dignity, autonomy and privacy, as opposed to considerations of ownership or property (*Droit de la famille – 061409*). It ruled that the woman could take possession and determine the fate of the two frozen placentas for burial purposes.

B. OWNERSHIP OF WHOLE BODY/BODY PARTS COLLECTED FROM A DECEASED INDIVIDUAL

American, Australian and British case law has addressed the issue of ownership of a whole body or body parts collected from a deceased individual. In the USA, the court has at times concluded that the body of a

deceased individual could constitute an object of property (*Mansaw v. Midwest Organ Bank* (1998)), and at other times concluded that while a family can have an interest in the proper treatment of the body, there is no property interest (*Adams v. King County* (2008)). In the UK, the *Haynes' case* first stated in 1614 that a human cadaver could not be owned. However, the Australian case of *Doodeward v. Spence* in 1908 contributed to the development of the common law on this topic, creating an exception for body parts that have been processed or modified in any way, after which they can be considered property. That approach was followed in subsequent cases, such as the Royal College of Surgeons case (1998) and *AB and Others v. Leeds Teaching Hospital NHS Trust* (2004), that involved the theft of body parts and the preservation of organs, respectively.

V. CONCLUSION

- Generally, human tissue legislation requires the ***ante-mortem*** **consent** of the **individual while alive** for the use of tissue, organs or bodies for research purposes after death.
- In the absence of such first-person consent, legislation usually requires the consent of the deceased person's **legally authorized representative**.
- Generally, the *ante-mortem* **objection** of the deceased will preclude family members from authorizing the donation of the deceased person's tissue, organs or whole-body.
- In certain jurisdictions (Victoria (Australia), South Australia (Australia), Singapore) and only in **specific circumstances**, explicit consent of the person or the legally authorized representative is not required for the use of tissues, organs or whole bodies for research purposes.
- Amongst the countries studied, **France** is the only jurisdiction where there is a legislated presumed consent for **organ** donation both for transplantation and for research purposes.

VI. SOURCES

A. LEGISLATION

[REGIONAL]

COUNCIL OF EUROPE (2002) *Additional Protocol to the Convention on Human Rights and Biomedicine Concerning Transplantation of Organs and Tissues of Human Origin*

COUNCIL OF EUROPE (2015) *Convention Against Trafficking in Human Organs*

EUROPEAN PARLIAMENT AND COUNCIL OF THE EUROPEAN UNION (2004) *Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on Setting Standards of Quality and Safety for the Donation, Procurement, Testing, Processing, Preservation, Storage and Distribution of Human Tissues and Cells*

[CANADA]

Human Organ and Tissue Donation Act, SNS 2010, c 36 (Nova Scotia)

Human Tissue Act, RSNL 1990, c H-15 (Newfoundland and Labrador)
Human Tissue Act, RSNWT 1988, c H-6 (Nunavut)
Human Tissue Gift Act, RSS 1978, c H-15 (Saskatchewan)
Human Tissue Donation Act, RSPEI 2011, c H-12.1 (Prince Edward Island)
Human Tissue Donation Act, SNWT 2014, c 30 (Northwest Territories)
Human Tissue Gift Act, CCSM 1987, c H180 (Manitoba)
Human Tissue Gift Act, RSBC 1996, c 211 (British Columbia)
Human Tissue Gift Act, RSNB 2014, c 113 (New-Brunswick)
Human Tissue Gift Act, RSY 2002, c 117 (Yukon)
Human Tissue and Organ Donation Act, SA 2006, c H-14.5 (Alberta)
Quebec Civil Code (1991)
Trillium Gift of Life Network Act, RSO 1990, c H.20 (Ontario)

[USA]
Federal Policy for the Protection of Human Subjects ("Common Rule"), 45 CFR Part 46
Revised Uniform Anatomical Gift Act (2006), National Conference of Commissioners on Uniform State Laws
Uniform Determination of Death Act (1980), National Conference of Commissioners on Uniform State Laws

[MEXICO]
Ley General de Salud, Diario Oficial, 1984-02-07, N. 27 (Ultima Reforma DOF 12-07-2018)

[UK]
Human Tissue Act 2004 (UK), c 30
Human Tissue (Scotland) Act 2006 (asp 4)
Human Transplantation (Wales) Act 2013 (anaw 5)

[FRANCE]
Code général des collectivités territoriales
Code de la santé publique

[SINGAPORE]
Human Organ Transplant Act, Chapter 131A (Act 15 of 1987)
Medical (Therapy, Education and Research) Act, Chapter 175 (Act 23 of 1972)

[AUSTRALIA]
Human Tissue Act 1983 (New South Wales)
Human Tissue Act 1982 (Victoria)
Human Tissue Act 1985 (Tasmania)
Human Tissue and Transplant Act 1982 (Western Australia)
Transplantation and Anatomy Act 1979 (Queensland)
Transplantation and Anatomy Act 1983 (South Australia)

B. GUIDELINES

[INTERNATIONAL]
UNESCO (2002) *Human Genetic Data: Preliminary Study by the IBC on its Collection, Processing, Storage and Use*, "Post-mortem samples", Guideline 17

CIOMS/WHO (2016) *International Ethical Guidelines for Health-related Research Involving Humans*, "Commentary on Guideline 11", General considerations

ISBER (2018) *Best Practices for Repositories I: Collection, Storage and Retrieval of Human Biological Materials for Research*, "Section K: Specimen Collection, Processing, Receiving, and Retrieval" and "Section L: Legal and Ethical Issues for Biospecimens"

WORLD MEDICAL ASSOCIATION (WMA) (2013) *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects*

[CANADA]
Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada & Social Sciences and Humanities Research Council of Canada. *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans 2014*, (Ottawa: Secretariat on Responsible Conduct of Research, 2014) online: TCPS 2 <http://www.pre.ethics.gc.ca/pdf/eng/tcps2-2014/TCPS_2_FINAL_Web.pdf> [TCPS 2].

[USA]
American Association of Anatomists, *The Donation of Bodies for Education & Biomedical Research* (2009), http://www.anatomy.org/body-donation-policy.html

Consensus Panel on Research with the Recently Dead (CPRRD) – *Ethics guidelines for research with the recently dead,* (2005) http://www.nature.com/articles/nm1105-1145.pdf

[UK]
Human Tissue Authority, *Body, Brain and Tissue Donation Pack: Information on donating your body, brain or tissue for anatomical examination, research or education and training*,

https://www.hta.gov.uk/sites/default/files/BBT%20Donation%20Pack%20Nov%2015.pdf

Human Tissue Authority, *Code A: Guiding principles and the fundamental principle of consent*, https://www.hta.gov.uk/sites/default/files/files/HTA%20Code%20A_0.pdf

Human Tissue Authority, *Code E: Research (Practice and Standards)*, https://www.hta.gov.uk/sites/default/files/Code%20E.pdf

Human Tissue Authority, *Code F: Donation of solid organs and tissue for transplantation*, https://www.hta.gov.uk/sites/default/files/files/HTA%20Code%20F.pdf

Nuffield Council on Bioethics, *Human Bodies: Donation for Medicine and Research: An Ethical Framework*, http://nuffieldbioethics.org/wp-content/uploads/Donation_Chapter5_Ethical_framework1.pdf

[AUSTRALIA]
National Health and Medical Research Council (2007: updated 2018) *National Statement on Ethical Conduct in Human Research*, https://www.nhmrc.gov.au/_files_nhmrc/file/publications/national-statement-2018.pdf

C. SELECTED CASE LAW

[CANADA]
Droit de la famille – 061409, 2006 QCCS 7871
J.C.M. v. A.N.A., 2012 BCSC 584
Lam v. University of British Columbia, 2015 BCCA 2
McKitty v. Hayani, 2018 ONSC 4015
Piljak Estate v. Abraham, 2014 ONSC 2893
S.H. v. *D.H.*, 2018 ONSC 4506

[USA]
Adams v. King County, No. 81828-1 (Wash Sup Ct 2008)
Greenberg v. Miami Children's Research Hospital Institute, 264 F Supp. 2d 1064 (SD Fla 2003)
Lovato v. District Court in & for Tenth Jud., 601 P. 2d 1072 (1979)
Mansaw v. Midwest Organ Bank, No. 97-0271-CV-W-6 (U.S. Dist. 1998)
Moore v. Regents of University of California, 793 P.2d 479 (Cal 1990)
People v. EULO, 63 N.Y. 2d 341 (1984)
Re: The Welfare of William Matthew Bowman, Wash. 617 P. 2d 731
Washington University v. Catalona, 490 F.3d 667 (8th Cir 2007), cert. denied, 128 S Ct. 1122 (2008)

[UK]
AB and Others v. Leeds Teaching Hospital NHS Trust [2004] EWHC 644 (QB)
Doodeward v. Spence, 6 CLR 406 (1908)
Haynes' case (1614) 12 Co Rep 113 77ER
Re: A (A minor), [1992] 3 Med LR 303 (Fam. Div.)
Re: T.C. (A minor), [1994] 2 Med LR 376
Re: A (A child), [2015] EWCA 443 (Fam.)
R. v. Kelly & Lindsay, Q.B. 621 (1999)
Yearworth v. North Bristol NHS Trust [2009] EWCA Civ 37

D. LITERATURE (SELECTED ARTICLES)

Amy L. McGuire, Mary A. Majumder, Scott D. Halpern et al. (2010) *Taking DNA From the Dead* 11 Nat Rev Genetics 318

Andreas Winkelmann, Anne-Kathrin Heinze, Sven Hendrix (2016) *Acknowledging Tissue Donation: Human Cadaveric Specimens in Musculoskeletal Research* 29 Clinical Anatomy 65

Maeghan Toews and Timothy Caulfield (2016) *Evaluating the "family veto" of consent for organ donation* 188 CMAJ 17

Rebecca L. Walker, Eric T. Juengst, Warren Whipple, Arlene M. Davis (2014) *Genomic Research with the Newly Dead: A Crossroads for Ethics and Policy* 42 JL Med & Ethics 220

E. ONLINE RESOURCES

Uniform Law Commission, *Anatomical Gift Act – Fact Sheet*, http://www.uniformlaws.org/LegislativeFactSheet.aspx?title=Anatomical%20Gift%20Act%20(2006) (Accessed June 20th 2018)

World Health Organization (WHO) (2009) *Global Glossary of Terms and Definitions on Donation and Transplantation*, http://www.who.int/transplantation/activities/GlobalGlossaryonDonationTransplantation.pdf

HUMAN CELL ATLAS – LAW & POLICY: DRAFT PROVENANCE PRIMER

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TISSUE SOURCE: HUMAN EMBRYONIC AND FETAL TISSUE
UPDATED: DECEMBER 2018

METHODOLOGY

We begin this basic primer on human embryonic and fetal tissue collection and transfer for research purposes with definitions (I), followed by a brief overview of selected recent applicable international and regional norms/guidelines (II). We then examine legislation and policy regarding the collection and transfer of human embryonic and fetal tissue for research purposes in seven countries: Canada, the United States (U.S.), Mexico, the United Kingdom (UK), France, Singapore and Australia (III). In the interests of brevity, only a few selected legal cases and articles from the literature were included. More specifically, this basic primer answers the following questions:

- In the countries under study, what laws apply to the collection and transfer of human embryonic and fetal tissue for research purposes?
- What consent approach applies to such collection and transfer of human embryonic and fetal tissue? Specifically: 1) who has the authority to consent? 2) what consent standard must be met? and 3) what are the procedural requirements?
- In addition to laws, are there regulations or guidelines regarding biomedical research involving human subjects that apply to the collection and transfer of human embryonic and fetal tissue for research purposes?
- Which acts are prohibited?

In addition to our analysis of the normative context in the countries under study, we present selected case law on the right to donate embryos for research; the resolution of disagreements over the disposition of embryos; the ethical procurement of fetal tissue for research; prohibitions of embryonic/fetal tissue donation; and administrative decision-making (IV). Finally, we end the primer with some conclusions on consent requirements for the collection and transfer of human embryonic and fetal tissue for research purposes in the countries of interest (V).

I. DEFINITIONS

Across the jurisdictions examined, the legal definitions of ***embryo*** and ***fetus*** form a patchwork. These terms are either 1) not statutorily defined, 2) statutorily, yet inconsistently defined, or 3) statutorily and consistently defined. This patchwork might be of concern. Indeed, since a term's definition affects downstream interpretation and attendant recommendations, terminology might be "manipulated to achieve certain ends indirectly which could not be achieved directly."[1]

Gamete

The term is not always defined in legislation, and where definition is provided, statutes typically define sperm and ova separately. In turn, these definitions often appeal to biological definitions (e.g., in Canada, "sperm" means "a human sperm, whether mature or not.")

Embryo

Three jurisdictions have no legislative definition (i.e., France, Mexico, and Singapore). In Canada, embryo is defined as a human organism during the first 56 days of development following fertilization or creation (or the first mitotic division). By contrast, UK and Australian laws define the term more broadly. There, "embryo" can include seminal human entities undergoing "any […] process" that "initiates organised development," or is "capable of resulting in an embryo." It is nevertheless interesting to note that Canada emphasizes *chronology* whereas the UK and Australia pay mind to *potentiality*.

Moreover, statutes are generally silent on the question of viability. This "void" is generally filled by definitions given in ethical guidelines which themselves are biological in orientation.[2]

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[1] See Knowles, LP. International Perspectives on Human Embryo and Fetal Tissue Research (https://bioethicsarchive.georgetown.edu/nbac/briefings/may99/ip.pdf); at p. 11.

[2] See, for example, the Council of Europe's *Recommendation 1100 (1989) of the Parliamentary Assembly of the Council of Europe on the use of human embryos and fetuses in scientific research*, Appendix (Scientific research and/or experimentation on human gametes, embryos and foetuses and donation of such human material), at para 25.

Fetus

As above, neither France, Mexico, nor Singapore provide a statutory definition for the term. In addition to these three jurisdictions, statutes in Australia and the UK are silent as to the legal definition of fetus in the context of research. By contrast, Canadian legislation defines fetus as "a human organism during the period of its development beginning on the fifty-seventh day following fertilization or creation […]."

The U.S. stands in contrast to all the other jurisdictions in that the legal definition of fetus may or may not include the embryo as defined in other jurisdictions above. Specifically, the *Common Rule (2018)* defines "fetus" as "the product of conception from implantation until delivery."

II. INTERNATIONAL/REGIONAL NORMS/GUIDELINES

A. INTERNATIONAL

[ISSCR] *Guidelines for Stem Cell Research and Clinical Translation* (2016)

- Oversight of procurement, Recommendation 2.2.1: "Rigorous review [by a specialized process] must be performed prior to the procurement of all gametes, embryos, or somatic cells that are destined for use in human embryo and stem cell research [in order to ensure that vulnerable populations are not exploited]."
- Consent for biomaterials, Recommendation 2.2.2: "Explicit and contemporaneous informed consent for the provision of all biomaterials for embryo and embryonic stem cell research is necessary, including from all gamete donors. Informed consent should be obtained at the time of proposed transfer of any biomaterials to the research team or during the time that biomaterials are collected and stored for future research use."
- Review for biomaterials collection for embryo and stem cell research, Recommendation 2.2.3: "Review of procurement protocols must ensure that biomaterials donors are adequately informed about the specific aspects of their voluntary research participation."
- Payments to individuals providing tissue for research, Recommendation 2.2.4: The ISSCR clarifies that "no payment or valuable consideration of any kind beyond out-of-pocket expenses may be offered to donors for their procurement."

Recommendation 2.2.5: "For provision of oocytes for research, when oocytes are collected outside the course of clinical treatment, compensation for non-financial burdens should not constitute an undue inducement." The ISSCR goes on to add that "[b]ecause women carry more burdens than men during the procurement of their gametes, [their] efforts should be acknowledged fairly and appropriately [while avoiding the potential for exploitation]." To that end, the ISSCR recommends that there be a review committee that assesses "the safety and the voluntary and informed choice of women" according to specific standards.

- Separating research consent from treatment, Recommendation 2.2.6: "Informed consent for research donation must be kept distinct from informed consent for clinical treatment."
- Informed consent for biomaterials procurement, Recommendation 2.2.7: "The informed consent process and study design of human biomaterials procurement should be robust." "The informed consent document alone can never take the place of a dialogue between research staff and providers of human biomaterials."

[INTERNATIONAL BIOETHICS COMMITTEE, UNESCO] *The Use of Embryonic Stem Cells in Therapeutic Research* (April 2001)

- "If research is allowed on human embryos […], then it must be subjected to strict supervision and to severe basic constraints [such as the obtaining of full donor consent]" (para 51).
- When authorizing embryo donation for therapeutic stem cell research, attention should be paid to the dignity and rights of donors. This entails disclosure of full information (purposes and execution of research), and prior, free, and informed consent (para 55B).

[FIGO] *Ethical Issues in Obstetrics and Gynecology*, Embryo Research (2012)

- "It is essential that neither men nor women should be coerced or unduly induced into donating sperm, oocytes or embryos for research."
- "In IVF programmes, recipients of resulting embryos may shall [sic] be asked for consent to the use of their supernumerary embryos for research."
- "Women must be protected from coercion or undue inducement to donate oocytes, especially when they are vulnerable medically, psychologically or socio-economically."

- "Because oocytes are a [sic] scarce resources for infertile women and research, their allocation to one or the other requires ethical justification."
- "The physicians providing pregnancy terminations should not be allowed to benefit from the subsequent use of the embryonic or fetal tissue. Informed consent should be obtained from the woman alone for the use of embryonic or fetal tissue for research or for therapeutic clinical applications. Any proposed research must be conducted under the direct review of any local or national ethics committees."

B. REGIONAL

[COUNCIL OF EUROPE] *Recommendation 1100 (1989) of the Parliamentary Assembly of the Council of Europe on the use of human embryos and fetuses in scientific research*, Appendix – Scientific research and/or experimentation on human gametes, embryos and foetuses and donation of such human material (1989)

- On gametes

  "1. Gametes may be used independently for purposes of basic or experimental investigation, subject to the provisions of the following paragraphs;"

  "3. The human gametes employed for investigation or experimentation shall not be used to create zygotes or embryos in vitro for the purpose of procreation."

- On dead pre-implantation embryos

  "8. Investigation of and experimentation on dead embryos for scientific, diagnostic, therapeutic or other purposes shall be permitted subject to prior authorisation."

- On post-implantation embryos or live fetuses in utero

  "9. The removal of cells, tissues or embryonic or foetal organs, or of the placenta or the membranes, if live, for investigations other than of a diagnostic character and for preventive or therapeutic purposes shall be prohibited."

- On post-implantation embryos or live fetuses outside the uterus

"14. Experiments on living embryos or foetuses, whether viable or not, shall be prohibited. None the less [sic], where a state authorises certain experiments on non-viable foetuses or embryos only, these experiments may be undertaken in accordance with the terms of this recommendation and subject to prior authorisation from the health or scientific authorities or, where applicable, the national multidisciplinary body."

- On dead embryos or fetuses

"16. The use of biological matter from dead embryos or foetuses for scientific, preventive, diagnostic, therapeutic, pharmaceutical, clinical or surgical purposes shall be permitted within the framework of the rules governing investigation, experimentation, diagnosis and therapy, in accordance with the terms of this recommendation."

- Donation of human embryological material

"20. The donation of human embryological material shall be authorised solely for scientific research on diagnostic, prevention or therapeutic purposes. Its sale shall be prohibited."

"22. The donation and use of human embryological material shall be conditional on the freely given written consent of the donor parents."

"23. The donation of organs shall be devoid of any commercial aspect. The purchase or sale of embryos or foetuses or parts thereof by their donor parents or other parties, and their importation or exportation, shall also be prohibited."

"24. The donation and use of human embryological material for the manufacture of dangerous and exterminatory biological weapons shall be forbidden."

[EUROPEAN GROUP ON ETHICS IN SCIENCE AND NEW TECHNOLOGIES TO THE EUROPEAN COMMISSION] *Opinion No. 15: Ethical Aspects of Human Stem Cell Research and Use* (2000)

- 2.4 Principal requirements according to the diverse sources of stem cells

"The retrieval of foetal tissues to derive stem cells requires, besides informed consent, that no abortion is induced for the purpose of obtaining the tissues and that the termination timing and the way it is carried out are not influenced by this retrieval."

- 2.9. Stem cell research and the rights of women

"Women who undergo infertility treatment are subject to high psychological and physical strain. The Group stresses the necessity to ensure that the demand for spare embryos and oocyte donation does not increase the burden on women."

- 2.10. Free and informed consent [Clinical research on human stem cells]

  "Free and informed consent is required not only from the donor but also from the recipient as stated in the Group's opinion on Human Tissue Banking (21/07/1998). In each case, it is necessary to inform the donor (the woman or the couple) of the possible use of the embryonal cells for the specific purpose in question before requesting consent."

III. COUNTRY-SPECIFIC LAWS/GUIDANCE

A. JURISDICTION

Embryo and gamete collection and transfer is governed by national assisted human reproduction legislation in almost all the jurisdictions examined (i.e., Australia, Canada, France, Singapore, the UK). As to fetal tissue collection, the U.S.[3] and France are the only jurisdictions with explicit and specific national and federal statutory governance. In the other jurisdictions, fetal tissue donation is generally governed by a composite of national ethical guidelines and/or general tissue donation regulation (provincial, state, etc.).

While Mexico does not currently have any federal law governing collection and transfer, "supernumerary IVF embryos are often used for basic science research in private health research setting[s]."[4] Still, in 2012, a National Consensus document was issued by a group of researchers and professionals calling for more specific and permissive rules to govern embryo and gamete donation.[5]

[3] As indicated in the above Definitions section, the U.S. definition of "fetus" may include embryos.
[4] Kably-Ambe AC et al. Consenso Nacional Mexicano de Reproduccion Asistida. Rev Mex Reprod 5:2 (2012); 68-113.
[5] Kably-Ambe AC et al. Consenso Nacional Mexicano de Reproduccion Asistida. Rev Mex Reprod 5:2 (2012); 68-113.

B. CONSENT APPROACHES

1. Who has authority to consent?

a. Embryos and gametes

In Australia, Canada, France, Singapore, the UK and the U.S., the authority to consent to donate embryos for research purposes is limited to the members—or a surviving member—of a couple who had been seeking assisted reproduction technology (ART), but are no longer interested in the pursuit of pregnancy. Indeed, it appears that only embryos deemed to be excess (or surplus) ART embryos may be donated for research. This proposition is supported by the fact that in certain jurisdictions (e.g., France), embryos must be destroyed if the consent of the donor couple cannot be obtained—for instance, when both members of the couple are deceased. Comparatively, in Australia, the limitation is only that the embryos "not be used in research" if a dispute arises, or, a "responsible person" dies without leaving directions.

Interestingly, some jurisdictions such as the U.S. appear to give normative precedence to the consent of "the woman" (presumably, over the consent of the partner). Under the U.S. *Public Health Service (PHS) Act* (amended Sept. 2018), the minimal requirement is that it be the woman who provides consent. Still, in other U.S. policy documents (e.g. Ethics Committee for the American Society for Reproductive Medicine 2009), emphasis is placed on the "joint agreement" between the male and female partner. In Singapore, this normative precedence might be reflected in the fact that the ambit of "restricted research" is limited to oocyte (i.e., to the exclusion of sperm) and embryo research.

As to gamete donation for research, authority to consent typically falls on the donors by default. In some jurisdictions, such as the UK, consent authority may, in limited circumstances, extend to the parents of minors. For adults lacking capacity, UK law grants the regulator the power to waive the requirement of consent (under strict conditions). Even so, in this latter case, UK law imposes a duty on the researcher to make reasonable efforts to identify, and consult with, a person who is engaged in caring for the adult lacking capacity.

b. Fetus

In all the jurisdictions examined, the use of fetal tissue for research purposes is contingent upon the prior consent of the woman whose pregnancy was terminated (and from whom the fetal tissue is to be derived).

2. What consent standard must be met?

The scope of consent standards varies across the jurisdictions examined. In Australia, consent must be "informed, competent, voluntary […] specific [and] in writing."[6] Importantly, the consent form must be specific as to the purpose, nature, rationale and scope of the research. The process must also allow for withdrawal. In the context of embryo-destructive research, a two-week reflection period must also be given to the prospective donor. As to the researcher's obligations—in addition to being sensitive to the needs of the potential donor, the researcher must disclose the proposed research, its aims, its potential impact (commercial, scientific, technological, etc.), the donor's right to withdraw consent, as well as the possibility to store tissues for later use. In the context of embryo-destructive research, the researcher must also inform the donor that it may not be possible to report outcomes for individual embryos.

In Singapore, the legislative requirements are only that the donors (both the embryo donor and partner) confirm in writing that the consent is taken that: 1) they have each been informed of the full implications of the donations; and 2) they do not require the embryo for future reproductive use.

As to UK law, a requirement of the consent to the use of embryos is that it be in writing, in person to the extent possible, and that it specify "use for the purposes of any project of research." The donor must also be informed of—and consent to, as applicable—whether the gametes or embryos are to be exported. The consent should also be voluntary (without pressure to accept treatment or agree to donation). UK authorities generally recommend that consent for use be given at the same time as consent for storage. For the latter end, UK law requires, among other things, that the consent: 1) specify the maximum period of storage (if less than the statutory period); and

[6] National Health and Medical Research Council. 2017. Ethical guidelines on the use of assisted reproductive technology, at paragraph 13.16.

2) state what is to be done with the gametes or embryo if the person who gave the consent dies or is unable (for lack of capacity), to vary the terms of the consent or to withdraw it.

In the U.S., in addition to the individual State law requirements, the *Public Health Service Act* requires that the consent establish, in writing, that: a) the woman donates the fetal tissue for use in research; b) the donation is made without any restriction regarding the identity of individuals who may be the recipients of transplantations of the tissue; and c) the woman has not been informed of the identity of any such individuals.

3. What are the procedural requirements?

For gamete, embryo or fetal tissue donation, the basic procedural requirements for obtaining consent are largely similar across the different jurisdictions examined. In addition to giving consent in writing and in person, the potential donor must generally be informed of the specific purpose of the research, as well as any risks involved. In situations where the donor is a minor or an adult lacking the capacity to consent, basic protective measures—such as the requirement of the written consent of a legal representative, or the prior consultation of a carer—are set out in legislation and regulations in the various jurisdictions.

For embryos and fetuses, there appears to be an additional procedural element: the separation between consent for procedures related to fertility care (ART, pregnancy termination, miscarriage, etc.), and consent related to the donation of tissue for research. This separation of consent likely emerged from the apparent consensus among the different jurisdictions that donation is only permissible in the context of abandoned/aborted fertility procedures. To illustrate this separation, Australian legislation provides that researchers may not seek consent to use an embryo in research until the prospective donor independently declares that the embryo is no longer needed for fertility purposes. Moreover, those involved in embryonic or fetal tissue research should not be involved in the clinical care of the woman. The strictness of this separation may vary in degree and execution across different jurisdictions.

In addition to the separation of the individual consents for clinical care and donation toward research, respectively, the consent process must generally include a "cool-off period." This period is intended to provide the potential donor a period of independent reflection. The precise parameters (i.e., length, timing, etc.) of this cool-off period are jurisdiction-dependent. For

instance, France sets out a three-month reflection period from the time of initial consent (research cannot commence until this period has elapsed). In contrast, Singapore provides for an eight-day reflection period after the initial consent documents were transmitted to the potential donor; while the UK requires only that the cool-off period be "suitable."

C. BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS – REGULATIONS AND GUIDELINES

While the majority of jurisdictions examined have legislation governing embryo and gamete donation, most also have applicable supplementary ethical guidelines. As noted above, guidelines are especially relevant in the fetal context, given the absence of specific and explicit legislation. In Australia, for example, fetal tissue procurement is guided by the *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research*. Still, the same document may also govern both embryonic and fetal tissue research—as is the case for both Australia and Canada (*Tri-Council Policy Statement*).

D. PROHIBITED ACTS

The prohibitions against commencement of research without the consent of the potential donor (s), or the implantation of embryos on which research has been conducted, are universal.

In most jurisdictions, *in vitro* creation of embryos for research or commercial purposes is prohibited. This harkens back to the general restriction on embryo or fetal tissue donation to the context of abandoned or aborted assisted reproduction procedures.

Moreover, tying back to one of the above procedural requirements, prospective researchers must not be involved in oocyte, embryo or fetus research if they were involved in the assisted reproduction treatment or other therapeutic treatment of the person from whom the tissue is obtained.

IV. SELECTED CASE LAW

Embryo donation and the right to respect for private life

At present, one of the highest profile cases is *Parrillo v Italy* (2015). In this case, the Grand Chamber of the European Court of Human Rights ruled that Italy's ban against experiments on human embryos (and by extension, the donation of embryos), does not violate Article 8 of the *European Convention on Human Rights* (right to respect for private life). In its ruling, the Court considered that Italy had not overstepped the wide margin of appreciation enjoyed by it in this case, and that the ban in question had been "necessary in a democratic society."

By contrast, the decision to donate one's embryos for research could possibly be a constitutionally protected right in Mexico. This proposition is based on the fact that Mexico's Constitution gives international treaties and international human rights norms constitutional status. As such, Mexico might be constitutionally bound by a decision rendered by the Inter-American Court of Human Rights (whose jurisdiction it has accepted).[7] In this decision, the Court held that Costa Rica's ban of IVF violated multiple provisions of the *American Convention of Human Rights*. One such provision is the prohibition of arbitrary interference with "private life, family, home […]" (art. 11.2). Per the court, the right to private life includes "reproductive autonomy and access to reproductive health services." If a parallel is drawn with the European Court of Human Right's interpretation of the right to privacy as including the decision to donate one's embryos for research, an argument could subsequently be made that Mexico's Constitution may protect the autonomy of such a decision.

Disagreement within couples over embryo disposition

Somewhat related to the question of embryo and gamete donation is the resolution of disputes between the members of a couple regarding supernumerary IVF embryos. In *Davis v Davis* (1995), the Supreme Court of Tennessee adjudicated one such dispute.[8] The holding in this case is that courts should 1) follow the wishes of gamete providers; and that 2) in case of dispute, to enforce prior agreements between gamete providers; and 3) if no such agreement exists, to weigh individual interests of the providers. Among other observations, the court posited that truly

[7] See *Artavia Murillo v Costa Rica*. Inter-American Court of Human Rights. 2012.
[8] It must be noted that this case is only explicitly connected to the donation of supernumerary IVF embryos to other couples—not necessarily to research.

informed consent over supernumerary embryos could be difficult to secure (given the emotional nature of the proceedings, as well as changes in one's life circumstances). Because of this, the Court proposed that couples should be permitted to modify their initial IVF contracts by mutual agreement (and, failing this, that couples be bound by prior agreements). Additionally, while the court reaffirmed the inextricability of procreational autonomy (right to procreate and not to procreate) from the right to privacy (as envisaged by the 14th amendment of the U.S. Constitution), it held that in IVF, providers of gametes have equal rights to make decisions over the supernumerary embryos (as opposed to abortion, where the woman's decision generally prevails). In the end, the Court resolved this dispute in an ad hoc manner, weighing each party's individual interests over the supernumerary embryos. As such, this case provides no bright-line rule or judicial test. Still, the decision offers potentially valuable pronouncements, especially on the question of informed consent.

In 2018, the Supreme Court of Colorado in the U.S. set out a largely contiguous framework for resolving disputes over embryo disposition.[9] Notably, the Court spells out which factors to consider (and which to exclude) when balancing the providers' individual interests. Of note, however, is the Court's rejection of the first step in the *Davis* framework because "it injects legal uncertainty" by "allow[ing] one party to change [his] mind about disposition up to the point of use or destruction of any stored [embryo]."

Similarly, a 2018 Canadian decision also suggested that courts should resolve couples' disputes with a contractual approach (*SH v DH*).[10] There are, however, critical differences—both in *fact* and in *law*—with *Davis v Davis*. In *fact*, the scope of *SH v DH* is limited to the disposition of embryos biologically *unrelated* to the parties in dispute. In *law*, the Canadian court adopted the view that "[i]t would be contrary to contract law were [courts] to decide that the wishes of the parties at the time of entering [embryo disposition contracts] were other than what they agreed to." Surprisingly, this is a marked departure from the approach adopted in the U.S. by the Supreme Court of Tennessee. Ultimately though, the extent to which biological relatedness can explain the differences in contractual interpretation between these cases remains unclear.

[9] *In re Marriage of Rooks* (Colorado Supreme Court; 2018; 2018 CO 85).
[10] *SH v DH* (Ontario Superior Court of Justice; 2018; 2018 ONSC 4506).

Ethical procurement of fetal tissue

In 2017, in the U.S. a group of planned parenthood organizations brought an action[11] against the State of Texas—the action was motivated by the decision of the state to disenroll planned parenthood services from a medicaid program. The disenrollment, for its part, resulted from an investigation of a secretly recorded conversation between an undercover anti-abortion activist and the head of the research department of one of the planned parenthood service providers. Specifically, the investigation had led to allegations that the planned parenthood service provider was procuring fetal tissue for research unethically. In its ruling, the court rejected the allegations, holding that there was no credible evidence that the provider breached procurement ethical obligations. Still, with the recent announcement of a "comprehensive review" of human fetal tissue research by the Trump administration, and attendant contract cancellations due to concerns over procurement of fetal tissue,[12] as well as the intensification of anti-abortion activism, the current U.S. context is such that more legal actions might be launched in the future.

Prohibition against the donation of fetal and/or embryonic tissue

In a 2017 case,[13] in the U.S., the Louisiana District Court dismissed an action[14] that was brought by a provider of reproductive health services for lack of standing. In their initial action, the plaintiffs sought to challenge the constitutionality of seven new bills restricting abortion passed by the Louisiana Legislature. Figuring among those two bills were House Bill 815 (HB 815), and Senate Bill 33 (SB 33). Cumulatively, these bills prohibited post-abortion donation of embryonic and/or fetal tissue. The court dismissed the action on the basis that the plaintiff lacked standing (as they failed to show "the required injury in fact to confer standing because [they] have not alleged that they engage in or would engage in the conduct prohibited by S.B. 33").

The take-away from this case is that adjudication of fetal tissue donation has so far seemingly proceeded solely on procedural grounds. As such, the question is yet to be decided on

[11] *Planned Parenthood of Greater Texas Family Planning and Preventative Health Services, Inc v Smith* (2017; case no. A-15-CA-1058-SS; U.S. District Court for the Western District of Texas Austin Division).
[12] Wadman, M. NIH says cancer study also hit by fetal tissue ban. (Dec 2018). *Science*. Available at: http://www.sciencemag.org/news/2018/12/trump-administration-has-quietly-barred-nih-scientists-acquiring-fetal-tissue.
[13] *June Medical Services LLC v Gee* (US District Court, Louisiana) (280 F.Supp.3d 849 (2017))
[14] https://www.reproductiverights.org/sites/crr.civicactions.net/files/documents/june-medical-services-v-gee-complaint-16-CV-444.pdf

substantive grounds. Still, while dismissing the plaintiff action, the court opened the door to future substantive litigation by stating that "[the dismissal] is not to say that Plaintiffs could never plead that S.B. 33 violates their Due Process or Equal Protection rights, only that at this point in time, Plaintiffs have failed to do so."

Example of an administrative authorization of research using donated embryonic material by the *Agence de la biomédecine*[15]

"Considering therefore that the applicant sufficiently establishes the scientific relevance of the research project on the one hand, and its conditions of implementation with regard to ethical principles on the other hand; that it justifies that the project will be carried out in accordance with ethical principles relating to embryonic and embryonic stem cell research and that these cells were obtained in the respect of the fundamental principles set out in articles 16 to 16-8 of the Civil Code, and with the prior consent of the parent couple, and without any payment, in whatever form, being made to them;

[...]

This authorization is granted for a period of five years. It may be suspended at any time [...] in the event of a breach of laws or regulations [...]." (Our translation)

V. CONCLUSIONS

- Statutory governance of fetal tissue collection and/or transfer is not as comprehensive as that for gametes/embryonic tissue donation. National and professional guidelines typically fill this statutory void.
- Consent authority generally rests on the provider of gametes and/or the conceiving couple.
- Consent for donation of tissue (embryonic or fetal) must be i) specific and in writing; ii) distinct and separate from consent for clinical treatment; and iii) include a cool-off period.
- International courts are willing to recognize the decision to donate one's embryo or fetal tissue as protected under the right to privacy and/or autonomy (constitutionally protected in some jurisdictions). Recent developments (legal actions, political appointments and

[15] *Décision du 13 octobre 2015 portant autorisation de protocole de recherche sur les cellules souches embryonnaires humaines en application des dispositions de l'article L. 2151-5 du code de la santé publique*

surging activism), suggest that courts will be seized with disputes related to gametes, embryonic or fetal tissue collection and transfer (research).

- In matters related to embryo disposition disputes, courts prefer a contractual approach—though their approaches to contractual interpretation may differ.

VI. SOURCES

A. LEGISLATION

[AUSTRALIA]
Research Involving Human Embryos Act 2002 (No. 145, 2002)

[CANADA]
Assisted Human Reproduction Act (S.C. 2004, c.2)

[FRANCE]
Code civil
Code de la santé publique

[REGIONAL]
American Convention on Human Rights "Pact of San Jose, Costa Rica" (B-32)
European Convention on Human Rights

[SINGAPORE]
Human Biomedical Research Act 2015
Human Biomedical Research Regulations 2017
Human Cloning and Other Prohibited Practices Act

[UK]
Human Tissue Act 2004 (c. 30)
Human Fertilisation and Embryology Act 1990 (c. 37)

[US]
Public Health Service Act, 42 U.S.C. ch. 6A §201 et seq.
Common Rule, 45 C.F.R. §46.202(c) 2018

B. GUIDELINES

[AUSTRALIA]
National Health and Medical Research Council (2017) *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research*

[CANADA]
Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada & Social Sciences and Humanities Research Council of Canada (2014) *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans*

[INTERNATIONAL]
CIOMS/WHO (2016) *Ethical Guidelines for Health-related Research Involving Humans*

FIGO (2012) *Ethical Issues in Obstetrics and Gynecology*

International Bioethics Committee (2011) *The Use of Embryonic Stem Cells in Therapeutic Research*

ISSCR (2016) *Guidelines for Stem Cell Research and Clinical Translation*

[MEXICO]
Ambe AK et al. *Consenso Nacional Mexicano de Reproduccion Asistida*. Rev Mex Med Repro (2012); 4.5 (2).

[REGIONAL]
Council of Europe (1989) *Recommendation 1100 (1989) of the Parliamentary Assembly of the Council of Europe on the use of human embryos and fetuses in scientific research (Appendix)*

Council of Europe (1997) *Council of Europe Convention on Human Rights and Biomedicine ("Oviedo Convention")*

European Group on Ethics in Science and New Technologies to the European Commission (2009) *Opinion 15: Ethical Aspects of Human Stem Cell Research and Use*

[SINGAPORE]
Bioethics Advisory Committee (2015) *Ethics Guidelines for Human Biomedical Research*

[UK]
Human Fertilisation & Embryology Authority (2018) *Code of Practice (9th ed.)*

[US]
Ethics Committee of the American Society for Reproductive Medicine (2009) *Donating spare embryos for stem cell research*

National Institutes of Health (2009) *Guidelines for Human Stem Cell Research*

NIH Human Embryo Research Panel (1994) *Report of the Human Embryo Research Panel (Volume I)*

C. SELECTED CASE LAW

[CANADA]
SH v DH (Ontario Superior Court of Justice; 2018; 2018 ONSC 4506)

[FRANCE]
Décision du 13 octobre 2015 portant autorisation de protocole de recherche sur les cellules souches embryonnaires humaines en application des dispositions de l'article L. 2151-5 du code de la santé publique

[REGIONAL]
Artavia Murillo et al. ("In Vitro Fertilization") v Costa Rica (Inter-American Court of Human Rights; 2012)
Parrillo v Italy (European Court of Human Rights; 2015; Application no. 46470/11)

[US]
Davis v Davis (Supreme Court of Tennessee, at Knoxville; 1992; 842 S.W.2d 588)
In re Marriage of Rooks (Colorado Supreme Court; 2018; 2018 CO 85)
June Medical Services LLC v Gee (US District Court, Louisiana; 2017; 280 F.Supp.3d 849)
Planned Parenthood of Greater Texas Family Planning and Preventative Health Services, Inc v Smith (US District Court for the Western District of Texas Austin Division; 2017; case no. A-15-CA-1058-SS)

D. LITERATURE

See Knowles LP. *International Perspectives on Human Embryo and Fetal Tissue Research*. Available at: https://bioethicsarchive.georgetown.edu/nbac/briefings/may99/ip.pdf; at p. 11.

E. ONLINE RESOURCES

June Medical Services LLC v Gee (Complaint for Declaratory and Injunctive Relief) (US District Court for the Middle District of Louisiana; 2016; 3:16-cv-00444-BAJ-RLB)

Wadman M. *Trump Administration to review human fetal tissue research*. (2018). Science. Available at: https://www.sciencemag.org/news/2018/09/trump-administration-review-human-fetal-tissue-research.

HUMAN CELL ATLAS – LAW & POLICY: DRAFT PROVENANCE PRIMER

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TISSUE SOURCE: RESEARCH AND CLINICAL (RESIDUAL)TISSUE
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METHODOLOGY

We begin this basic primer on the collection and use of research and clinical (residual) tissues with definitions (I), followed by a brief overview of selected recent applicable international and regional norms/guidelines that govern consent for theuse of research tissue and the secondary use of clinical (residual) tissues (II). We then examine legislation and policy regarding these topics in seven jurisdictions that represent a topology of approaches: Canada, the United States, Mexico, the UK (England, Wales, Scotland, Northern Ireland), France, Singapore and Australia (III). More specifically, this basic primer answers the following questions:

- In the countries under study, what laws apply to the use of tissue obtained explicitly for research purposes?
- In the countries under study, what laws apply to the secondary research use of tissue originally collected for clinical purposes (residual tissues)?
- What consent approaches apply to such research uses?
    - What consent standard must be met?
    - What information should be included in the consent?
    - How consent should be obtained?
- In addition to laws, are there regulations or guidelines that apply to the collection and use of both research and clinical (residual) tissues?
- What are the major conclusions found in the studied laws and regulations?

In addition to our analysis of the normative context in the countries under study, we offer a summary of selected case law on the use of clinical (residual) tissues that address patient's rights and institutional responsibilities (IV). In the interest of brevity, only a few selected legal cases were included. Finally, we end this primer with some conclusions about consent requirements for the collection and use of research tissue as well as the secondary use of clinical (residual) tissues for research purposes in the countries of interest (V).

Of note, this primer will only cover legislation and other normative documents pertaining to competent adult patients and research participants. Our discussions will, therefore, not include considerations related to the use of research or clinical (residual) tissues collected from minors and incompetent adults or other populations deemed vulnerable.

I. DEFINITIONS

Biological materials, tissues, and cells

The World Medical Association (WMA) defines biological material as any "sample obtained from an individual human being, living or deceased, which can provide biological information, including genetic information, about that individual" (WMA 2016). Research on human biological materials can make use of a variety of type of samples, including "tissues, organs, blood, plasma, skin, serum, DNA, RNA, proteins, cells, hair, nail clippings, urine, saliva, or other bodily fluids" (CIOMS/WHO 2016). The 2004 EU Directive on setting standards forthe quality and safety of the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cellsrefers to 'tissue' as "all constituents parts of the human body formed by cells" (Directive 2004/23/EC). The same directive defines 'cell' as an "individual human cell or a collection of human cells when not bound by any form of connective tissue" (Directive 2004/23/EC). That being said, these definitions are not universal across jurisdictions: 'tissue', for example, may not be defined in a consistent way. Indeed, while some legislation will include anatomical structures (e.g. organs, fetuses) and/or biological substances (e.g. blood, spermatozoa) in the definition of 'tissue', others will exclude them. In this primer, we will exclude fetal/embryonic tissues as well as gametes (for more information on these, consult the primer written specifically on this specific topic).

Clinical (Residual) tissue

A clinical, residual or diagnostic tissue refers to a sample that was "taken in the course of clinical care and is leftover (e.g. a diagnostic biopsy or therapeutic removal of tissue)" (Giesbertz et al. 2012). These stored tissues are particularly valuable for research if they remain linked to other information about the patient, such as their clinical record. These are initially stored to satisfy regulatory requirements, calling for the tissues to "be sent to the clinical laboratory for analysis, reporting, retention and ultimately, disposal in an appropriate safe manner" (Cheung et al. 2014). A tissue is considered 'clinical' or 'residual', when it has been excised with a therapeutic or diagnostic intent, regardless of its final use, including research.

Research tissue

In contrast to clinical (residual) tissue, 'research tissue' is any tissue that is collected explicitly for research purposes (Cheung et al. 2014). While clinical tissues may end up being used for research, the distinction between these two categories is important, as the associated consent requirements may differ.

Secondary use

Secondary use "refers to the use in research of human biological materials originally collected for a purpose other than the current research purpose" (Canada, TCPS 2 – 2014). The concept of secondary use can apply to research tissue collected for a specific research project and then used for another project, as well as situations where clinical (residual) tissue is subsequently used for research purposes.

II. INTERNATIONAL/REGIONAL NORMS & GUIDELINES

A. CONSENT FOR THE COLLECTION AND USE OF RESEARCH TISSUE

[WMA] *Declaration of Helsinki* (2013)

- Informed consent is required before samples are collected and research is done using them. Research must be well designed, conducted by people with expertise in the area, and aim to lead to meaningful conclusions. Risks to the subject should be minimized and should not exceed the benefit of the expected findings.
- "Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information" (Article 24).
- "For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable to obtain for such research. In such situations the research may be done only after consideration and approval of a research ethics committee" (Article 32).

[WMA] *Declaration of Taipei on ethical considerations regarding health databases and biobanks* (2016)

- For consent to multiple and indefinite uses to be considered valid, participants will need to be informed of the following: purpose of the repository; risks and burden associated with the collection, storage, and use of material; procedures for return of results including incidental findings; rules of access to the repository; privacy measures; governance arrangements; and, when applicable, commercial use and benefit sharing; intellectual property issues; and, the transfer of data or material to other institutions or third countries. (Article 12)
- "[I]n case the data and material are made non-identifiable the individual may not be able to know what is done with their data/material and that they will not have the option of withdrawing their consent." (Article 12)

[ISBER] *Best Practices for Repositories I: Collection, Storage and Retrieval of Human Biological Materials for Research,* "Section L: Legal and Ethical Issues for Biospecimens" (2018):

- "Informed consent for the collection, retention, and use of specimens is a process that offers donors information sufficient to allow them to make an informed choice about whether to donate specimens and data to the repository and agree, where applicable, to future research use. Consent should only be obtained under circumstances that provide the prospective donor or the donor's representative sufficient opportunity to consider whether or not to donate and minimizes the possibility of coercion or undue influence. The information that is given to the donor or the representative should be under- standable to the subject or their representative." (Section L2.2)
- "Known restrictions on specimen use, including use in future studies, should be documented and associated with the specimen(s)/collection within the repository. A separate consent for research purposes other than those originally outlined may be required." (Section L2.2)

[CIOMS/WHO] *International Ethical Guidelines for Health-related Research Involving Humans*, "Commentary on Guideline 11" and "Commentary on Guideline 12" (2016)

- "When specimens are collected for research purposes, either specific informed consent for a particular use or broad informed consent for unspecified future use must be obtained from the person from whom the material originally is obtained."

[EUROPEAN PARLIAMENT AND COUNCIL OF THE EUROPEAN UNION] *Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) (GDPR)*(2016)[1]

- The GDPR does not apply to anonymous data or data that has been anonymized or to deceased persons.
- Genetic data ("inherited or acquired genetic characteristics of a natural person which give unique information about the physiology or the health of that natural person and which result, in particular, from an analysis of a biological sample from the natural person") is considered personal data. This means the person must provide explicit consent, unless processing is for scientific research purposes that are "proportionate to the aim pursued, respect the essence of the right to data protection and provide for suitable and specific measures to safeguard the fundamental rights and the interests of the data subject" (Articles 4 & 9).

[1]The GDPR's application on the topic of collection and use of research tissue is subject to a more complex review, as it primarily applies to data protection and not regulation of research.

- "Consent should be given by a clear affirmative act establishing a freely given, specific, informed and unambiguous indication of the data subject's agreement to the processing of personal data relating to him or her, such as by a written statement, including by electronic means, or an oral statement […] Consent should cover all processing activities carried out for the same purpose or purposes. When the processing has multiple purposes, consent should be given for all of them." (Recital 32).
- "It is often not possible to fully identify the purpose of personal data processing for scientific research purposes at the time of data collection. Therefore, data subjects should be allowed to give their consent to certain areas of scientific research when in keeping with recognised ethical standards for scientific research. Data subjects should have the opportunity to give their consent only to certain areas of research or parts of research projects to the extent allowed by the intended purpose" (Recital 33).

[COUNCIL OF EUROPE] *Recommendation CM/Rec(2016)6 of the Committee of Ministers to member States on research on biological materials of human origin* (2016).

- "1. Biological materials should only be removed for storage for future research with the prior, free, express and documented consent of the person concerned that is: i. specific to the intervention carried out to remove the materials; and ii. as precise as possible with regard to the envisaged research use." (Article 11).

B. CONSENT FOR THE SECONDARY USE OF CLINICAL (RESIDUAL) TISSUE FOR RESEARCH

[ISBER] *Best Practices for Repositories I: Collection, Storage and Retrieval of Human Biological Materials for Research* (2018):

- "Remnant clinical specimens may be collected from diagnostic surgical procedures. With proper ethics committee approval and appropriate informed consent, specimens may be resected specifically for research. […]" ("Section K: Specimen Collection, Processing, Receiving, and Retrieval", K.5.1.1)
- "Some regulations and laws may permit the use of an 'opting out' principle for human tissue leftovers from diagnostic sampling. After an obligatory information of potential donors, the consent for including the leftover material in a repository is presumed to be given, unless it is actively withdrawn by the donor." ("Section L: Legal and Ethical Issues for Biospecimens", Setion L.2.2)

[CIOMS/WHO]*International Ethical Guidelines for Health-related Research Involving Humans* (2016)

- When clinical tissue is used in research, "the individual whose biological materials and related data are used in research is a study participant and ethical guidelines that apply to research participant are applicable in this situation." ("Commentary on Guideline 11")
- "An informed opt-out procedure for research on residual tissue may not be appropriate in certain circumstances, namely a) when the research involves more than minimal risks to the individual, or b) when controversial or high-impact techniques are used, for example the creation of immortal cell lines, or c) when research is conducted on certain tissue types, for example gametes, or d) when research is conducted in contexts of heightened vulnerability."("Commentary on Guideline 12")

[COUNCIL OF EUROPE] *Recommendation CM/Rec(2016)6 of the Committee of Ministers to member States on research on biological materials of human origin* (2016).

- "2. Biological materials previously removed for another purpose should only be stored for future research with the consent of the person concerned, as provided for by law. Whenever possible, consent should be requested before biological materials are removed." (Article 11)
- "3. Biological materials previously removed for another purpose and already non-identifiable may be stored for future research subject to authorisation provided for by law." (Article 11).
- "2 a. If the proposed use of identifiable biological materials in a research project is not within the scope of prior consent or authorisation, if any, given by the person concerned, consent or authorisation to the proposed use should be sought and, to this end, reasonable efforts should be made to contact the person concerned. The wish of the person concerned not to be contacted should be observed." (Article 21)
- "2 b. Where the attempt to contact the person concerned proves unsuccessful, these biological materials should only be used in the research project subject to an independent evaluation of the fulfilment of the following conditions: i. evidence is provided that reasonable efforts have been made to contact the person concerned; ii. the research addresses an important scientific interest and is in accordance with the principle of proportionality; iii. the aims of the research could not reasonably be achieved using biological materials for which consent or authorisation can be obtained; and iv. there is no evidence that the person concerned has expressly opposed such research use." (Article 21)

III. COUNTRY-SPECIFIC LAWS/GUIDANCE

A. JURISDICTION

In the United States, Canada and Australia, use of tissue or other biological materials for research is governed by state and territorial or provincial law, creating many legislative layers. In the United States, the *Common Rule* – with an updated version now in force (2019) – sets out a baseline ofprotection for research subjects. A comprehensive review of all US state legislation is beyond the scope of this primer, but it should be noted that additional requirements might exist beyond those detailed below. In France, Mexico, the United Kingdom and Singapore, national laws apply across the country. Finally, several of the countries studied supplement their state laws with national guidelines (e.g. Canada, (*Tri-Council Policy Statement* – 2014) and Australia (*National Statement on Ethical Conduct in Human Research* – 2018)).

B. COLLECTION AND USE OF TISSUE FOR RESEARCH

i. REQUIREMENT OF INFORMED CONSENT

Consent is required for the collection of tissue for research. Informed consent at the time of tissue collection should ideally include a discussion of potential future uses for the tissue and whether there is a plan to perform other procedures or to study other diseases than those described in the consent form.

Informed consent is also required when collecting tissues with the stated purpose of biobanking. Again, predicted future use as well as length of storage and use must be mentioned in the consent form (see below for a detailed discussion).

ii. ELEMENTS OF CONSENT

Across the jurisdictions studied, consent must be informed, voluntary, explicit and continuous. When donating tissue or other biological materials for research purposes, the informed consent should go over what samples or data will be collected, the nature of the research project and the risks associated with participating in research (both physical and informational risks (e.g. privacy-related)). The consent process must also allow for withdrawal of consent. Beyond these widely-accepted requirements, however, certain jurisdictions may enact additional statutory requirements. Even within Europe, where many directives and regulations of regional scope are enacted, there are and will continue to be differences in the interpretation of informed consent requirements. Some jurisdictions will have more stringent requirements for consent to research than that used in informed consent to clinical treatment. Research ethics norms may also add additional standards, such as imposition of more specific plain language requirements (e.g. TCPS 2 – 2014). Alternatively, additional oversight requirements might exist from regional data protection provisions (e.g. GDPR – 2016).

Generally, consent for research should be obtained in writing, but a growing number of normative documents now accept the use of other means to capture consent.

iii. BROAD CONSENT

Broad consent is a model in which research participants are informed that their data and samples will be used for future, as-yet unspecified research subject to ethics oversight. Indeed, broad consent is usually accompanied with oversight, governance and ongoing communication strategies. A broad consent will meet the requirements of informed consent if it includes a discussion of the goals and relevant processes involved, such as the manner in which tissues will be conserved, mechanisms for ensuring the security of data, and ongoing communication as well as governance structures for access and ethics monitoring. Additionally, while the broad consent approach privileges flexibility, owing to its ability to envision a wider set of research uses for data and samples, such flexibility does not constitute a blanket consent (i.e. use without any restrictions). Indeed, broad consent should be accompanied by additional security and governance mechanisms. Furthermore, research projects that follow participants over time often periodically re-contact donors to administer questionnaires and collect additional samples. Such re-contact with updated information presented to participants may constitute a renewal of consent. Participants are thereby given an opportunity to reassert whether they are interested in continuing their participation.

iv. WAIVER OF CONSENT

In addition, in cases where the original consent is not broad enough to cover anticipated secondary uses of research samples, waivers of consent can be sought in many jurisdictions, to enable such use, on the condition that a number of requirements are met. These generally include that: the research involves no more than minimal risk (USA Common Rule 46.116 – 2018, Canada TCPS 2 – 2016, art. 12.3A); the research cannot be practically carried out without the waiver (USA Common Rule), the researchers "will take the appropriate measures to protect the privacy of individuals and safeguard the identifiable human biological materials" (TCPS 2 – 2016, art. 12.3A) and the use of identifiable human biological materials is unlikely to adversely affect the welfare of those that have donated these tissues (TCPS 2 – 2016, art. 12.3A). The Australian *National Statement on Ethical Conduct in Human Research*, updated in 2018, has similar requirements. These conditions generally need to be established by a research ethics board or institutional review board (e.g. Singapore, Human Biomedical Research Act – 2015, art. 13).

The UK explicitly allows for the waiver of consent requirements for secondary research on 'coded' samples (where the participant information is replaced with a code). Indeed, the *Human Tissue Act* allows a waiver of consent requirement for tissues obtained prior to 2006 as well as imported coded tissues, where the recipient researcher has no access to the link (de-identified but not anonymized data). Singapore also plans to have

similar time limitation on the consent requirements to use tissues in the new version of its *Human Biomedical Research Act* (Human Biomedical Research (Exemptions) Regulations – 2018).

v. ANONYMIZATION

Anonymization of samples means that they are irreversibly delinked from any data that could lead to re-identification. Tissues can be anonymized with the goal of using them in other research projects without triggering consent requirementsas they are not considered as personal data (e.g. United States, Common Rule – 2018). Anonymization is in contrast with coding, where the key that can link samples to the person remains. In many jurisdictions, the possibility of identifying someone triggers the application of laws or guidelines specific to consent for research. For example, in Singapore, the biological material has to be individually identifiable to fall under the 'human tissue' category (Human Biomedical Research Act – 2015, art. 3).

C. SECONDARY USE OF CLINICAL (RESIDUAL) TISSUE FOR RESEARCH

i. CLINICAL CARE CONSENT VS. RESEARCH CONSENT

Tissues collected, stored and potentially studied as part of clinical care, quality review or education generally do not trigger the need for a specific written consent process, as their use is considered part of care. However, to undertake research on clinical (residual) tissues, a separate informed consent for research is generally required (unless a waiver is obtained, see section iv, below). Countries that distinguish consent in the clinical and research contexts tend to impose more stringent requirements on the latter (e.g. France). In some cases, the secondary use of clinical (residual) tissues or data for research entails the same requirements as detailed in the previous section. Informed consent for research on humans applies to both identifiable tissue from a previous research project or a biobank as well as to stored archived diagnostic tissue from clinical or diagnostic interventions.

There are however very few laws specific to research on residual tissue. Some countries do not regulate the use of residual tissue and data as the scope of legislation applies only on tissue obtained for research (United States, Common Rule – 2018). Other countries treat clinical (residual) tissues to be used in research in the same manner and require the same consent dispositions noted earlier (Canada, TCPS 2 – 2014). Another possibility is the use of residual medical care tissue with a simple notification and the possibility of an opt-out (see iii, below).

ii. CONCEPT OF CONTROL ("OWNERSHIP")

"Ownership" of clinical (residual) tissues is controversial as institutions (i.e. hospitals) archive most tissues. Most countries hold that there can be no ownership of the human body or its parts. In France and in Quebec

(Canada), for example, the human body, its parts, and tissues are explicitly "hors commerce" (cannot be property that is owned or sold). Case law in other countries have likened excised tissue to medical records (discussed below, see section V), which opens the door to the notion of tissue ownership. Irrespective, where legal ownership of samples is not explicit under law, persons still retain the right to control the use of their tissue. Consequently, consent has to be obtained unless tissues and data are anonymized or a waiver is sought. Research consent typically contain clauses reminding participants that even if there may be potential commercial value (e.g. development of drugs or devices), they will not personally benefit. Patients do not retain an "ownership" interest in their excised tissue once consented for research.

iii. NOTIFICATION WITH OPT-OUT VS OPTING-IN

Reflecting the divide between clinical and research use of residual tissue and out of respect for the values of patients, a distinction is increasingly being made between notifications with possible opt-out for the research use of clinical(residual) tissues for care, research, educational purposes and quality control. If patients do not agree, they can opt-out. Under this approval patients are notified that the hospital will be storing and using their tissue. This distinction stems from the moment where consent is understood to have happened such as upon admission. The opt-out model implies consent unless the patient upon notification of this policy explicitely opt-out.

The UK and France have adopted this approach. Both jurisdictions stress the need for patients to be able to convey their wishes when it comes to the secondary uses of their clinical (residual) tissue. In Australia, the opt-out approach can also be used and is understood as constituting an informed consent, when meeting certain conditions such as being low-risk research, or research whose success depends on a near complete enrollment rate (National Statement on Ethical Conduct in Human Research – 2018, art. 2.3.5 – 2.3.8).

iv. WAIVER OF CONSENT FOR SECONDARY USE OF RESIDUAL TISSUES

In some jurisdictions, a waiver of consent is possible in situations where a patient previously donated tissue for their clinical care and cannot be consented when their tissue is being repurposed for research use because it would be impractical or impossible (France, Code de la santé publique L1211-2, Canada, TCPS 2 – 2014, art. 12.3A). In such cases, the conditions enumerated earlier in section B.iv necessary to obtaining a waiver of consent for the secondary use of research samples, also apply here.

v. BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS – GUIDELINES

As previously stated, some countries rely on guidance in addition to legislation as concerns biomedical research (e.g. Australia, Canada). In other countries, questions of secondary uses of clinical (residual) tissues have not yet been covered by law or any other guidance concerning residual tissues. Mexico is a good example; the *General Health Law (LGS)* does not offer any clarification on the use of residual clinical tissues

for research purposes. It is also unclear whether the initial consent to participate in a specific research project can be extended to further additional projects and this even in the same field (in the absence of any mention thereof). As a result, and in the absence of legislation on the matter, tissue repositories in Mexico have resorted to self-regulation via internal guidance (Gomez 2014).

IV. SELECTED CASE LAW

Selected case law illustrates that in common law jurisdictions, the Courts tend to protect research initiatives by giving ownership of clinical tissues to the institution that stores the tissues. However, they will normally allow the patient to retain certain 'property-like' interests over their tissues, in order to respect broader research ethical principles. Thus, American and Canadian Courts have both stated that tissue collected for diagnostic or therapeutic purposes is owned by the institution. A 2015 case from Canadian province British Columbia even considered stored frozen sperm to be property in the context of legislation regulating the storage of goods (*Lam v. University of British Columbia* (Canada – 2015)). As for other rights, the Courts recognized that patientsstill had the right to have "reasonable access" to their tissues (akin to the right to consult one's study file or medical records) and the right to demand its destruction (akin to the right to withdraw) (*Piljak Estate v. Abraham* (Ontario, Canada – 2014); *Moore v. Regents of U. of California* (USA – 1990)*; Greenberg v. Miami Children's Research Hospital Institute* (USA – 2003)*; Washington U. v. Catalona* (USA – 2007)).

US Courts have consistently rejected ownership by patients of excised tissues. However, the fact that the Courts do not recognize ownership interest does not alleviate the requirements of obtaining informed consent when using the tissue for research purposes afforded to patients over stored tissues. Overall, the rights protected appear to be closer to privacy rights than property rights.

V. CONCLUSION

- In all countries reviewed, consent for the collection and use of tissue for research purposes must be free and informed. A right to withdraw from research must also remain at all time unless the samples or data have been anonymized.
- International and regional norms and guidelines refer to the possibility of obtaining consent for multiple and indefinite uses (broad consent) as long as information regarding: 1) the purpose of the collection; 2) risks associated with it; 3) privacy/security measures in place to safeguard the tissues; and, 4) any information on the access mechanisms by outside researchers are given to research

participants. This is generally complemented with ethics oversight and ongoing communication. The process should also allow for withdrawal.

- In most countries, research with anonymized samples or data is not considered human research.
- For the secondary use of clinical (residual) tissues for research purposes, generally the consent of the person concerned should be sought.
- If not possible or practicable, researchers who intend to use residual tissues or research tissues beyond the original purpose can seek a waiver of consent from an ethics committee or institutional board by showing that: the proposed research involves no more than minimal risk; it could not be practically carried out without a waiver; appropriate measures to protect privacy and security have been established; and, the use of samples or data will not adversely affect the welfare of the research participant or patient.
- Notifications with opt-out is possible in France, the UK and Australia for the research use of clinical (residual) tissues.

VI. SOURCES

A. LEGISLATION

[REGIONAL]

EUROPEAN PARLIAMENT AND COUNCIL OF THE EUROPEAN UNION (2016) *Regulation 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)*

EUROPEAN PARLIAMENT AND COUNCIL OF THE EUROPEAN UNION (2004) *Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.*

[AUSTRALIA]
Human Tissue Act 1983 (New South Wales)
Human Tissue Act 1982 (Victoria)
Human Tissue Act 1985 (Tasmania)
Human Tissue and Transplant Act 1982 (Western Australia)
Transplantation and Anatomy Act 1979 (Queensland)

[CANADA]
Quebec Civil Code, 1991, article 19 and 22 (Quebec)
Public Hospitals Act, RRO 1990, Regulation 965 (Ontario)

[FRANCE]
Code de la santé publique (Consolidated version 2019)

[MEXICO]
Ley General de Salud, DiarioOficial, 1984-02-07, N. 27 (Ultima Reforma DOF 12-07-2018)

[SINGAPORE]
Human Biomedical Research Act (2015)
Human Biomedical Research (Exemptions) Regulations (2018)

[UK]
Human Tissue Act 2004 (UK), c 30
Human Tissue (Scotland) Act 2006 (asp 4)

[USA]
Common Rule (2018), 45 C.F.R. 45 Code of Federal Regulations §46

B. GUIDELINES

[INTERNATIONAL]

CIOMS/WHO (2016) *International Ethical Guidelines for Health-related Research Involving Humans*

ISBER (2018) *Best Practices for Repositories I: Collection, Storage and Retrieval of Human Biological Materials for Research*

UNESCO (2002) *Human Genetic Data: Preliminary Study by the IBC on its Collection, Processing, Storage and Use*

WORLD MEDICAL ASSOCIATION (WMA) (2013) *WMA Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects*

WORLD MEDICAL ASSOCIATION (WMA) (2016) *Declaration of Taipei on Ethical Considerations Regarding Health Databases and Biobanks.*

[REGIONAL]

COUNCIL OF EUROPE (2016)*Recommendation CM/Rec(2016)6 of the Committee of Ministers to member States on research on biological materials of human origin*.

COUNCIL OF EUROPE (1997) *Convention for the protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*[Oviedo Convention].

[AUSTRALIA]
National Health and Medical Research Council (2007: updated 2018) *National Statement on Ethical Conduct in Human Research*, https://www.nhmrc.gov.au/_files_nhmrc/file/publications/national-statement-2018.pdf

[CANADA]
Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada & Social Sciences and Humanities Research Council of Canada. *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans2014*, (Ottawa: Secretariat on Responsible Conduct of Research, 2014) online: TCPS 2 <http://www.pre.ethics.gc.ca/pdf/eng/tcps2-2014/TCPS_2_FINAL_Web.pdf> [TCPS 2].

[UK]
Human Tissue Authority, *Code A: Guiding principles and the fundamental principle of consent*, https://www.hta.gov.uk/sites/default/files/files/HTA%20Code%20A_0.pdf

Human Tissue Authority, *Code E: Research (Practice and Standards)*, https://www.hta.gov.uk/sites/default/files/Code%20E.pdf

C. SELECTED CASE LAW

[CANADA]
Droit de la famille – 061409, 2006 QCCS 7871
J.C.M. v. A.N.A., 2012 BCSC 584
Lam v. University of British Columbia, 2015 BCCA 2
Piljak Estate v. Abraham, 2014 ONSC 2893
S.H. v. *D.H.*, 2018 ONSC 4506
McInerney v. *MacDonald* [1992] 2 SCR 138

[USA]
Adams v. King County, No. 81828-1 (Wash Sup Ct 2008)
Greenberg v. Miami Children's Research Hospital Institute, 264 F Supp. 2d 1064 (SD Fla 2003)
Moore v. Regents of University of California, 793 P.2d 479 (Cal 1990)

D. LITERATURE (SELECTED ARTICLES)

Bovenberg, J. "How to Achieve 'Free Movement of Tissue' in the EU Research Area", in *Human Tissue Research: a European Perspective on the Ethical and Legal Challenges* (C. Lenk, N. Hoppe, K. Beier and C. Wiesemann eds., Oxford University Press, 2011).

Cheung, CC, et al. "The role of diagnostic tissue in research" *Pathobiology.* 81(5-6) (2014): 298-303.

Gomez, L.S. "Regulating Mexican biobanks for human biomedical research: What can be learned from the European experience?" *Mexican law review* 7(1) (2014): 31-55.

Giesbertz N.A., Bredenoord AL, van Delden JJ. "Inclusion of residual tissue in biobanks: opt-in or opt-out?" *PLoS Biology* 10(8) (2012):e1001373.

Grady, C., et al. "Broad Consent for Research With Biological Samples: Workshop Conclusions" *American journal of bioethics : AJOB* vol. 15(9) (2015): 34-42.

Kaye, J., Bell, J., Briceno, L., & Mitchell, C. (2016). Biobank Report: United Kingdom. *The Journal of Law, Medicine & Ethics*, *44*(1), 96–105.

Motta-Murguia, L., & Saruwatari-Zavala, G. (2016). Mexican Regulation of Biobanks. *The Journal of Law, Medicine & Ethics*, *44*(1), 58–67.

Rothstein, M. A., & Knoppers, B. M. (2015). Harmonizing Privacy Laws to Enable International Biobank Research. *The Journal of Law, Medicine & Ethics*, *43*(4), 673–674.