Supplemental Table 1: Analysis of policy frameworks

Country-Specific Provisions
UNITED STATES
The Food and Drug Administration have formally proposed an amendment to its regulations to allow an alteration or waiver of consent for FDA-regulated clinical investigations, thereby harmonizing provisions for non-regulated and regulated trials. **Simplified consent** No requirement to include all elements of Good Clinical Practice in either the Common Rule or Food and Drug Administration (FDA) regulation. No requirement for written informed consent. Ethics committees may separately waive the requirement to document consent for both non-regulated[1] and regulated[2] trials. **Alteration/waiver of consent** For non-regulated trials, alteration and waiver of consent is permitted under the Common Rule.[3] For regulated trials, a proposed rule in the Federal Register harmonizes the requirements with the Common Rule under the 21st Century Cures Act.[4] These provisions are promulgated in Food and Drugs Administration Guidance which may be applied before its regulations are revised.[5] **Waiver of consent to use/disclose protected health information:** Permitted under the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule if: The use or disclosure involves no more than minimal risk, is impracticable without access to protected health information and there are adequate provisions to protect the privacy and maintain the confidentiality of data.[6]
AUSTRALIA
Provisions for non-regulated and regulated trials appear to permit harmonization through *de facto* provisions promulgated by the Therapeutic Goods Administration that permit regulated trials to default to the National Statement on Ethical Conduct in Human Research (the National Statement)[7] if Good Clinical Practice requirements conflict with the National Statement.[8] **<u>Provisions for both regulated and non-regulated trials</u>** **Simplified consent:** No requirement in the National Statement to include all elements of Good Clinical Practice or for consent to be written, signed and dated as long as participants' decisions are clearly established.[7] **Alteration/waiver of consent:** In the absence of research-specific regulation, investigators must consider separate sources of information: • **Alteration/waiver of consent to disclose trial participation:** The National Statement makes provision for waiver under (2.3.10); alteration through limited disclosure (2.3.1) and through opt-out (2.3.5).[7] • **Waiver of consent to receive a treatment:** Common law requires disclosure of the nature and purpose of the treatment and the material risks, benefits and reasonable alternatives.[9] • **Waiver of consent to collect/use/disclose data**: Permitted under Commonwealth privacy legislation[10] if: Privacy risks are low, it is impracticable to seek consent, the research could not be carried out using de-identified information, and the public interest in the collection of

health information substantially outweighs the public interest in maintaining the level of privacy protection afforded by the Australian Privacy Principles.[11]

ENGLAND

The requirements for non-regulated and regulated trials differ markedly and are detailed separately.

Provisions for non-regulated trials

Simplified consent: No legal requirement to include all elements of Good Clinical Practice and no requirement for written, signed consent.[12]

Alteration/waiver of consent: In the absence of research-specific regulation, investigators must consider separate sources of information:

- **Alteration/waiver of consent to disclose trial participation:** National guidance currently does not endorse or prohibit alteration or waiver of consent.[12]
- **Waiver of consent to receive treatment:** Common law requires disclosure of the nature and purpose of the treatment and the material risks, benefits and reasonable alternatives.[13,14]
- **Waiver of consent to process data:** The General Data Protection Act 2018[15] implementing the General Data Protection Regulation (GDPR)[16] requires a legal basis to process personal data. Although consent is one possible legal basis, an alternative legal basis may be used such as 'task in the public interest' or 'legitimate interests'.[17] In addition, for the common law duty of confidentiality to be set aside, support under Section 251 of the NHS Act (2006)[18] must be obtained. Support may be granted if: It is impracticable to seek consent, the research cannot be carried out using de-identified information, and the research is in the public interest or in the interests of improving patient care.

Provisions for regulated medicinal product trials - European Regulation No 536/2014[19]

Existing clinical trials regulation for medicinal products will be replaced with European Regulation No 536/2014 in 2019/20[19] so we focus on the latter. If adopted 'post Brexit', this regulation will apply to all medicinal product trials, including products used within the terms of their marketing authorization.

Simplified consent: No requirement to include all elements of Good Clinical Practice. All trials will require written, signed and dated informed consent (with the exception of a sub-set of cluster trials under Article 30).

Waiver of consent: Not permitted.
Alteration (of consent content): Not permitted. Must include elements listed in Article 29.
Alteration (of consent process): Not permitted - except for a sub-set of cluster trials under Article 30 where an opt-out approach is permitted.

References

1. U.S. Department of Health and Human Services website: Office for Human Research Protections (OHRP), Code of Federal Regulations. 45 CFR 46.117(c). [Accessed 25 February 2019], 2018.

2. U.S. Food and Drug Administration website: Code of Federal Regulations. 21 56.109.c Institutional Review Boards. Subpart C - IRB functions and operations. [Accessed 25 February 2019], 2018.

3. U.S. Department of Health and Human Services website: Office for Human Research Protections (OHRP), Code of Federal Regulations. 45 CFR 46.116(f). Requirements for waiver and alteration. [Accessed 25 February 2019], 2018.

4. U.S. Food and Drug Administration website: Institutional Review Board Waiver or Alteration of Informed Consent for Minimal Risk Clinical Investigations, Federal Register / Vol. 83, No. 221 / Thursday, November 15, 2018 / Proposed Rules. [Accessed 25 February 2019], 21 CFR Parts 50, 312, and 812 2018.

5. U.S. Food and Drug Administration website: IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects. Guidance for Sponsors, Investigators, and Institutional Review Boards. [Accessed 25 February 2019], 2017.

6. U.S. Department of Health and Human Services website: The HIPAA Privacy Rule, [Accessed 25 February 2019], 2019.

7. National Health and Medical Research Council: The National Statement on Ethical Conduct in Human Research (2007) Updated 2018.

8. Therapeutic Goods Administration: ICH Guideline for Good Clinical Practice: Introductory comments of the TGA, Accessed 25th February 2019, 2019.

9. Australia High Court: Rogers v. Whitaker. Aust Law J 1993; 67: 47-55.

10. Australian Government: Privacy Act 1988, No. 119 Compilation No.80. Canberra, 1988, pp 380.

11. Office of the Australian Information Commissioner: Australian Privacy Principles [Accessed 13th March 2019], 2014.

12. National Health Service: UK Policy Framework for Health and Social Care Research. Edited by Authority HR, 2018.

13. Chatterton vs Gerson: QB 431 1 All ER 257 (QBD), 1981.

14. The Supreme Court of the United Kingdom: Montgomery (Appellant) v Lanarkshire Health Board (Respondent) [2015] UKSC 11. On appeal from [2013] CSIH 3. London, The Supreme Court of the United Kingdom, pp 2.

15. UK Government: Data Protection Act, 2018.

16. European Parliament: 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), 2016.

17. NHS Health Research Authority: GDPR guidance for researchers, 2018.

18. National Health Service: NHS Act, 2006.

19. European Parliament: REGULATION (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC 2014.