1. Australia

In Australia, the main bodies involved in regulation and oversight of clinical trials include the Therapeutic Goods Administration (TGA)[1] and the National Health and Medical Research Council (NHMRC)[2] both agencies of the Department of Health and Ageing. The TGA is responsible for regulating therapeutic goods, including pharmaceuticals and medical devices, while the NHMRC sets the ethical standards for medical and biological research involving human subjects. The key relevant regulations for clinical trials are the Therapeutic Goods Act (1989), the Therapeutic Goods Regulations (1990), and the Therapeutic Goods (Medical Devices) Regulations (2002). Clinical trials conducted using unapproved therapeutic goods in Australia – that is, therapeutic goods that have not been evaluated by the Therapeutics Goods Administration (TGA) for quality, safety and efficacy and entered into the Australian Register of Therapeutic Goods (ARTG) for general marketing – are required to make use of the Clinical Trial Notification (CTN) or Clinical Trial Approval (CTA) schemes. Under the CTN scheme, scientific and ethical review is provided by a human research ethics committee (HREC), with subsequent notification to the TGA. In the CTA scheme, the TGA has a direct role in the review of trial scientific data and must give an 'approval' for the proposed trial program to go ahead; however, HREC review is still required. Trials conducted under the CTA or CTN schemes need to comply with Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice ICH E6(R2) annotated with TGA comments[3].

The key guidelines are the National Statement on Ethical Conduct in Human Research (2007, updated 2018) which sets national standards for conducting human research in Australia. The National Statement is developed jointly by the National Health and Medical Research Council (NHMRC) together with the Australian Research Council (ARC) and Universities Australia and consists of a series of guidelines made in accordance with the National Health and Medical Research Council Act 1992 that are applicable to research with human participants. The National Statement is the Australian ethical standard against which clinical trials are reviewed. In addition, the NHMRC, together with the ARC and Universities Australia, has also issued the Australian Code for the Responsible Conduct of Research. Ethical conduct in research with Aboriginal and Torres Strait Islander Peoples and communities: Guidelines for Researchers & Stakeholders (2018) provides a set of principles to ensure research is safe, respectful, responsible, high quality and of benefit to Aboriginal and Torres Strait Islander people and communities.

Applications for permissions/approvals for health and social care research are via the Human Research Ethics Application (HREA)[4] system managed by NHMRC. All states have signed an MoU for a mutual acceptance of scientific and ethical review of multi-centre human research projects undertaken in Public Health Organisations. Currently Australian Capital Territory (ACT), New South Wales (NSW), Northern Territory (NT), Queensland (QLD), South Australia (SA), Tasmania (TAS), Victoria (VIC) and Western Australia (WA) participate in National Mutual Acceptance (NMA). It is to be noted several Australian states and territories may have additional requirements under one or more specific regulatory areas. In VIC and WA, there are state specific modules that must be completed as part of the ethics application process. Applications in VIC and QLD must be made through the Ethics Review Manager[5] (ERM). In NSW, Tasmania and the ACT, the HREA is accessed via a system called REGIS[6]. In SA and WA, applications should be to the Certified HREC associated with the site at which the applicant is conducting the research and if this is not applicable, the selection of a suitable Certified HREC is at the discretion of the applicant.

[1] Australia Therapeutic Goods Administration (TGA): http://www.tga.gov.au
[2] Australian National Health and Medical Research Council (NHMRC): http://www.nhmrc.gov.au/
[3] ICH Guideline for Good Clinical Practice: https://www.tga.gov.au/resources/publication/publications/ich-guideline-good-clinical-practice and https://www.tga.gov.au/resources/resource/guidance/australian-clinical-trial-handbook
[4] Human Research Ethics Application (HREA) portal: https://www.hrea.gov.au/
[5] Ethics Review Manager (ERM) portal: https://au.forms.ethicalreviewmanager.com/
[6] REGIS: https://regis.health.nsw.gov.au/

It is a requirement of the NHMRC that all clinical trials are registered. If the trial is only being done in Australia and/or New Zealand, trials are typically registered on Australian New Zealand Clinical Trials Registry (ANZCTR)[7]. Multinational trials are typically registered on clinicaltrials.gov.

The key authority with regards to privacy and data protection is the Office of the Australian Information Commissioner. Researchers must comply with the Australian Privacy Principles (APPs) outlined in the Privacy Act 1988 when handling and protecting personal information collected during research.

2. Canada

The authority responsible for clinical trial approvals, oversight, and inspections in Canada is Health Canada (HC)[8], while the Interagency Advisory Panel on Research Ethics (PRE)[9] is responsible for addressing the needs of Canada's three federal research agencies, Canadian Institutes of Health Research (CIHR), NSERC and SSHRC, in promoting the ethics of research involving humans. Applications for permissions/approvals for health and social care research are initiated by sponsors submitting a Clinical Trial Application (CTA) for drug studies, and an Investigational Testing Authorization (ITA) for device studies, which includes information on the investigational product and proposed clinical trial. Approval is also required from a Research Ethics Board (REB). The site of the clinical trial will dictate which REB is relevant[10].

PRE has defined key standards in the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans, 2nd Edition (2018)[11]. HC's Health Products and Food Branch (HPFB) coordinates the CTA approval process. Prior to initiating the trial, the sponsor must file a CTA to the appropriate HPFB Directorate. CTAs involving pharmaceutical drugs should be sent to the Pharmaceutical Drugs Directorate (PDD)[12]. Other relevant drug standards which need to be addressed are the Regulations Amending the Food and Drug Regulations (1024 – Clinical Trials) (2001), and HC Good Clinical Practice[13]. Regarding regulation and standards pertaining to devices, the key regulatory oversight is provided by HC's Medical Devices section[14] and standards per Medical Devices Regulations (SOR/98-282) (1998).

Also applicable are standards pertaining to Research Injury (again, covered under PRE's Tri-Council Policy Statement) and Privacy/Data Protection overseen by PRE, CIHR and the Office of the Privacy Commissioner of Canada (OPC). The relevant standards are under PRE's Tri-Council Policy and the Privacy Act, Sections 7-8 (1983), and Personal Information Protection and Electronic Documents Act, Articles 5 and 7 (2001). Regulations pertaining to Human Biological Materials also falls under the PRE Tri-Council Policy Statement. Clinical trial registries are maintained by PRE and the HC Clinical Trial Database[15].

Further, is also important to note that several Canadian provinces and territories also have human subject research standards. In particular, for the Toronto (Ontario) region, collection and/or use of personal health information must be compliant with Ontario's Personal Health Information Protection Act (PHIPA) (2004), and Research involving collection and/or use of personal information must be compliant with Ontario's Freedom of Information and Protection of Privacy Act (1990).

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[7] Australian New Zealand Clinical Trials Registry (ANZCTR): https://www.anzctr.org.au/
[8] Health Canada (HC): https://www.canada.ca/en/health-canada.html
[9] https://ethics.gc.ca/eng/home.html
[10] HC REB: https://www.canada.ca/en/health-canada/services/science-research/science-advice-decision-making/research-ethics-board.html
[11] PRE Tri-Council Policy statement: http://www.pre.ethics.gc.ca/eng/documents/tcps2-2018-en-interactive-final.pdf
[12] https://www.canada.ca/en/health-canada/corporate/about-health-canada/branches-agencies/health-products-food-branch/therapeutic-products-directorate.html
[13] HC Good Clinical Practice: https://www.canada.ca/en/health-canada/services/drugs-health-products/compliance-enforcement/good-clinical-practices.html
[14] HC Medical Devices: https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices.html
[15] HC Clinical Trial Database : http://www.hc-sc.gc.ca/dhpmps/prodpharma/databasdonclin/index-eng.php

3. European Union (France, Germany, Italy, Netherlands)

The regulation of clinical trials within the European Union is harmonised under EU Clinical Trial Regulation 536/2014 (EU-CTR)[16] . EU-CTR facilitates an authorisation procedure based on a single submission via a single EU portal and an assessment procedure leading to a single decision (per Member State Concerned (MSC)) via the Clinical Trials Information System (CTIS)[17] portal operated by the European Medicines Agency (EMA). It is mandatory for all new applications to be submitted through CTIS, and multinational clinical trials applications require to be led by one Reporting Member State (RMS) throughout a trial's life cycle – which means a crucial step in multinational trial applications is the careful selection of the RMS. The application content and assessment are divided into two parts: Part I consists of the evaluation of scientific documentation related to the trial on the anticipated therapeutic and public health benefits, risks and inconveniences for the subject, manufacturing and import requirements, labelling requirements, and completeness and adequateness of the investigator's brochure as outlined in Article 6 of EU-CTR. Part II consists of the evaluation of the application by each MSC, for their own territory, regarding the aspects set out in Article 7 of EU-CTR and the General Data Protection Regulation (GDPR).

There is currently no dedicated procedure foreseen in EU regulations and therefore, no harmonized procedure for combined medicinal product and medical device trails. Sponsors of such clinical trials are required to consult national guidance documents and contact National Competent Authorities prior to clinical trial submission[18].

In Ireland, which has been identified as the RMS for this proposed study, as in the rest of the EU, clinical trial applications are submitted via CTIS. This process is managed by the National Office for Research Ethics Committees (NREC)[19]. The separate medical device trial application process is also administered by NREC, which allows sequential or parallel submissions to the CTIS-routed trial application for medicinal product studies.

3.1 France

The key regulators in France are the Ministry of Solidarites and Health[20] and the National Agency for Medicines and Health Products Safety (ANSM)[21], with the National Consultative Bioethics Committee for Health and Life Sciences (CCNE)[22] playing an advisory role in the management of laws on bioethics. The French Ethics Committees (Comités de Protection des Personnes – CPP) are responsible for decisions concerning interventional studies, standard of care studies, medical and other health products. Clinical trial sponsors must submit their protocols to the relevant competent authority – here, ANSM[23], after which a regional CPP is picked at random to evaluate the trial protocol and procedures. The authorisation to conduct a trial requires both the Ethics Committee (CPP) approval and the ANSM authorization.

Clinical trials and medical research involving human subjects are governed by 'Code de la santé publique: *Titre II: Recherches impliquant la personne humaine (Articles L1121-1 à L1128-12)'*. Additionally, the CCNE provides ethical guidelines for medical and biological research involving human subjects. The

[16] EU Clinical Trials regulation 536/2014: https://health.ec.europa.eu/medicinal-products/clinical-trials/clinical-trials-regulation-eu-no-5362014_en
[17] Clinical Trials Information System (CTIS) of the European Medicines Agency (EMA): https://euclinicaltrials.eu/
[18] EU Medical Device Coordination Group Document 2022-10: https://health.ec.europa.eu/system/files/2022-05/mdcg_2022-10_en.pdf
[19] Ireland National Office for Research Ethics Committees (NREC): https://www.nrecoffice.ie/about/national-office/
[20] France Ministry of Social Affairs and Health: http://www.sante.gouv.fr/
[21] National Agency for Medicines and Health Products Safety (ANSM): https://ansm.sante.fr/
[22] National Consultative Bioethics Committee for Health and Life Sciences (CCNE): http://www.ccne-ethique.fr/en
[23] France CPPs: http://www.eurecnet.org/information/france.html#:~:text=These%20Committees%20of%20Protection%20of,competent%20for%20the%20whole%20region.

regulations concerning drugs, medical devices, and other therapeutic products fall under the responsibility of ANSM and CPP, with their standards specified within the publications 'Medications for Human Use, Articles 5111-1' and 'Decision on Good Clinical Practices' available on the relevant websites. Further, researchers in France must comply with the relevant law (Code de la santé publique: *Titre II: Recherches impliquant la personne humaine (Articles L1121-1 à L1128-12*)).

Regarding privacy and data protection, researchers must comply with the General Data Protection Regulation (GDPR) and the French Data Protection Act (2018). The French National Commission on Informatics and Liberty (CNIL)[24] is responsible for overseeing data protection in France and has issued the Practical Guide on the Protection of Personal Data: What Framework Applies to Research? (2018) for guiding research. Clinical trial registrations are maintained by ANSM through the Clinical Trials Registry (Base de données publique des essais cliniques - BDP-EC).

3.2 Germany

The key German regulatory agencies for healthcare and clinical standards are the Federal Ministry of Health (Bundesministerium für Gesundheit - BMG)[25], the Paul-Ehrlich-Institut (PEI)[26], and the German Medical Association (BÄK)[27]. The PEI and BÄK work closely with the Ministry of Health, alongside other relevant agencies such as the German Ethics Council (Ethik-Kommission)[28]. Clinical trials and medical research involving human subjects are governed by the German Medicines Act (Arzneimittelgesetz - AMG) and the Medical Devices Act (Medizinproduktegesetz - MPG). The BÄK has identified standards under the 'Professional code for Physicians in Germany, Article 15 (2018)' which are relevant to clinical trials. Additionally, the Federal Institute for Drugs and Medical Devices (BfArM)[29] plays a significant role in overseeing clinical trials and ensuring compliance. The Ethik-Kommission provides ethical guidelines and approval for medical and biological research involving human subjects, and researchers must seek approval from these committees before conducting clinical trials.

Clinical trial applications must be submitted via the German Medical Devices Information and Database System (DMIDS)[30], a portal operated by BfArM. The application then must first be forwarded to the competent ethics committee and can only be transmitted to the competent federal higher authority after its approval (all via DMIDS).

For the regulation of drugs, medical devices, and other therapeutic products, the German Medicines Act (AMG) and the Medical Devices Act (MPG) outline the requirements and standards. The Ordinance for Good Clinical Practice (Gute Klinische Praxis - GCP-Verordnung) provides guidelines for conducting clinical trials in accordance with good clinical practices. Relevant standards for drugs, devices and biologics are set out by PEI, BfArM under the legislature specified above in the '2020 English version: Medicinal Products Act, Division 6 (2020)', the '2021 German version: Medicinal Products Act, Division 6 (2021)', the Promulgation on the Principles of the Conduct of Clinical Trials of Drugs According to the Rules (1987), the Second Promulgation on the Clinical Trial of Drugs in Human (1997), and the Medical Device Law Implementation Act, Division 4 (2021). Standards for research injury are prescribed within the Medicinal Products Act, Section 40(3) (2020), and the Medical Device Law Implementation Act, Section 26 (2021). Clinical trial registrations in Germany are maintained by the German Clinical Trials Register (DRKS)[31], which is operated by the German Institute of Medical Documentation and Information (DIMDI).

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[24] French National Commission on Informatics and Liberty (CNIL): https://www.cnil.fr/en/home
[25] Germany Federal Ministry of Health: https://www.bundesgesundheitsministerium.de/en/index.html
[26] Paul-Ehrlich-Institut: https://www.pei.de/EN/home/home-node.html
[27] German Medical Association (BÄK): https://www.bundesaerztekammer.de/weitere-sprachen/english/german-medical-association/
[28] German Ethics Council: https://www.ethikrat.org/en/
[29] Federal Institute for Drugs and Medical Devices (BfArM): https://www.bfarm.de/EN/Home/_node.html
[30] BfArM medical devices information and database system (DMIDS): https://www.bfarm.de/EN/Medical-devices/Portals/DMIDS/_node.html;jsessionid=ED324A95EA7BE4DA2EE390CF53C30FD4.internet272
[31] German Clinical Trials Register (DRKS): https://www.drks.de/drks_web/setLocale_EN.do

In terms of privacy and data protection, researchers in Germany must adhere to the General Data Protection Regulation (GDPR) and the German Federal Data Protection Act (BDSG). The German Federal Commissioner for Data Protection and Freedom of Information (BfDI) oversees data protection in Germany. In addition to the federal data protection laws, the Data Protection Conference – Datenschutzkonferenz (DSK) – has prescribed standards under 'DSK, Short Paper No. 4: Data Transmission to Third Countries' which are relevant for this project.

3.3 Italy

In Italy, healthcare and medical research are regulated by several key agencies. The main regulatory bodies include the Ministry of Health[32], the Italian Medicines Agency (AIFA)[33], the National Health Institute (ISS), the National Bioethics Committee (CNB)[34] and the National Observatory on Clinical Trials (OsSC)[35]. The Ministry of Health plays the central role in shaping and overseeing policies with the support of ISS and works with the other regulatory bodies. AIFA is responsible for regulating pharmaceuticals and medical devices in Italy, while the CNB advices on bioethical issues and the OsSC monitors the conduct of clinical trials in Italy.

OsSC manages the authorisation process of clinical trials that are conducted in Italy. The OsSC e-platform[36] allows the submission of applications for clinical trials and for substantial amendments to initiated clinical trials, including all related documentation, at the same time to AIFA, as the competent authority, and to the coordinating ethics committee for each trial.

The Italian legislative framework for clinical trials is outlined in the Decree of the President of the Republic No. 189/2001, which implements the provisions of Directive 2001/20/EC. Standards are provided within the Good Clinical Practice Guidelines for Drugs and Medical Devices issued by AIFA. Research involving human subjects is guided by the ethical principles set forth in the Declaration of Helsinki. Additionally, the Code of Ethics of ISS and CNB provide further guidance on conducting ethical research. There are multiple decrees specifying the standards for drugs, biologics and devices including the Legislative Decree No. 211 (2003), 200 (2007), Ministerial Decrees of 21 Dec 2007, 31 March 2008, and 2 August 2005. Further, the Ministerial Decree of 14 July 2009 specifies the minimum standards pertaining to research injury in participants of clinical trials.

Several laws and regulations govern the protection of personal data in Italy, including the General Data Protection Regulation (GDPR), the General Principles of Processing Personal Data (2018), and the Privacy Code (Codice Privacy). For medical data, the Code of Medical Deontology and the Medical Records Management Guidelines outline specific measures for protecting patient information.
Clinical trial registration is overseen by AIFA through its publicly accessible national clinical trial registry. OsSC ensures the transparency and compliance of clinical trial data reporting.

3.4 Netherlands

The key regulator in the Netherlands is the Central Committee for Research Involving Human Subjects (CCMO)[37] under the Ministry of Health, Welfare, and Sport (VWS). Another regulator relevant for this work, also operating under VWS is the Medicines Evaluation Board (MEB)[38].

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[32] Italy Ministry of Health: http://www.ministerosalute.it
[33] Italian Medicines Agency: http://www.agenziafarmaco.it/
[34] National Bioethics Committee (CNB): http://www.governo.it/bioetica/eng/index.html
[35] National Observatory on Clinical Trials (OsSC): https://www.aifa.gov.it/en/osservatorio-nazionale-sperimentazione-clinica
[36] OsSC access: https://servizionline.aifa.gov.it/jam/UI/Login?goto=https://servizionline.aifa.gov.it%2Fportale%2F%23/ossc/home
[37] The Netherlands Central Committee for Research Involving Human Subjects: https://english.ccmo.nl/
[38] Medicines Evaluation Board (MEB): http://english.cbg-meb.nl/

CCMO has provided detailed guidance on the application processes pertaining to clinical trials with medicinal products (CTR)[39] and for clinical investigations with medical devices (MDR)[40]. CTR application dossiers must be submitted via CTIS.

There are multiple relevant standards pertaining to the development of drugs, biologics and devices including the VWS Medicines Act (2007), VWS Medicines Act Decree (2007), VWS Medicines Act Regulation (2007), CCMO Clinical Research with Medicinal Products in the Netherlands: Instructional Manual (2005), and CCMO Memorandum, Definition of Medical Research.

Also applicable are standards pertaining to Research Injury – i.e. the Medical Research Involving Human Subjects Act Article 7 (1998), CCMO Decree of 2014 containing rules for compulsory insurance in medical research involving human subjects and explanatory memorandum; standards pertaining to Privacy and Data Protection – i.e. Law for the Protection of Personal Information (2000), General Data Protection Regulation (2016); and standards pertaining to Human Biological Materials – i.e. Civil Code, Article 467 (1994) and Human Tissue and Medical Research: Code of Conduct for responsible use (2011). The relevant bodies regulating clinical trial registries are the Netherlands Trial Register[41] and the CCMO Register[42].

4. Japan

The key regulators in Japan are the Ministry of Health, Labor, and Welfare (MHLW)[43] and the Ministry of Education, Culture, Sports, Science, and Technology (MEXT)[44]. The PMDA (Pharmaceuticals and Medical Devices Agency)[45] is another important regulator, which is independent of but works closely with MHLW. The relevant standards operated by MHLW are identified within the Clinical Trials Act (2009), while MEXT's standards are covered under the Ethical Guidelines for Medical and Biological Research Involving Human Subjects (2021).

The application process for clinical trials is initiated by securing approval from one of the PMDA-recognised Institutional Review Boards (for the relevant site this would be IMSUT Hospital, the Institute of Medical Science at the University of Tokyo). The sponsor is then required to submit a trial notification and study protocol along with supporting documents to PMDA for assessment and approval.
The key standards covering the regulation of drugs and devices are the Pharmaceuticals, Medical Devices, and Other Therapeutic Products Act (2016), the Clinical Trials Act (2017), and the Ministerial Ordinance on Good Clinical Practice for Drugs (2020). The above standards also cover requirements relevant to Research Injury, in addition the Ethics Guidelines for Medical and Health Research Involving Human Subjects, Chapter 2, 3, and No. 6 (2021) is also applicable. Additionally, the guidance under On Research and Development Utilizing Human Tissues Removed for Surgery and Other Procedures (1998) covers standards under Human Biological Materials.

Clinical trial registries are maintained by MHLW as well as the National Institute of Public Health[46] and the Japan Registry of Clinical Trials (JRCT)[47].

Lastly, there are numerous standards to be adhered to pertaining to Privacy/Data Protection including the Act on the Protection of Personal Information (2020), the Act Regarding Anonymized Medical Data to Contribute to R&D in the Medical Field (2017), the Amendment to the Cabinet Order to Enforce the Act on the Protection of Personal Information (2016), the Enforcement Rules for the Act on the Protection of

[39] CCMO CTR applications: https://english.ccmo.nl/investigators/clinical-trials-with-medicinal-products-ctr
[40] CCMO MDR applications: https://english.ccmo.nl/investigators/clinical-investigations-with-medical-devices
[41] Netherlands Trial Register: http://www.trialregister.nl/trialreg/index.asp
[42] CCMO Register: https://www.toetsingonline.nl/to/ccmo_search.nsf/Searchform?OpenForm
[43] Japan Ministry of Health, Labor, and Welfare (MHLW): http://www.mhlw.go.jp/english/index.html
[44] Ministry of Education, Culture, Sports, Science, and Technology (MEXT): http://www.mext.go.jp/english/
[45] Japan Pharmaceuticals and Medical Devices Agency (PMDA): https://www.pmda.go.jp/english/index.html
[46] https://www.niph.go.jp/index_en.html
[47] Registry of Clinical Trials: https://jrct.niph.go.jp/

Personal Information (2016), the International Compilation of Human Research Standards (2021 Edition) and the Regulation for Enforcement of the Clinical Trials Act, Article 20 (2018).

5. United States

In the United States, the process of submitting a clinical trial application for approval is primarily overseen by the Food and Drug Administration (FDA) and the Office for Human Research Protections (OHRP). Key standards are set out by the Department of Health and Human Services (HSS) and OHRP regulations under 45 CFR 46[48] and OHRP, Human Research Protections Guidance[49]. A number of additional standards set out by different US Federal departments and agencies may be relevant depending on the nature of the studies, such as the Environmental Protection Agency, Program in Human Research Ethics[50].

Before submission to the FDA for approval, the clinical trial protocol must undergo review and approval by an Institutional Review Board (IRB) or Ethics Committee (EC). The next step after receiving IRB/EC approval is to apply for FDA Investigational New Drug (IND)[51] or Investigational Device Exemption (IDE)[52] – it is also possible to apply to FDA for a combined IND/IDE[53] study. Specific standards which need to be adhered to for drugs, biologics and devices include the Good Clinical Practice (GCP) and Human Subject Protection in FDA-Regulated Clinical Trials[54]; the Food, Drug, and Cosmetic Act, 21 USC Sections 355 and 371 (2012); Public Health Service Act, 42 USC Section 262 (1998); 21st Century Cures Act, Section 3024 (2016). In addition to GCP, FDA has issued guidelines specific to drugs[55] and devices[56]. Standards pertaining to research injury are prescribed under the HSS Sections 116(a)(6) and (7) of the Common Rule. Privacy/data protection standards are mainly prescribed within 45 CFR 46 and the 21st Century Cures Act sections both covered above, however there are additional HHS, NIH and other departmental/agency requirements that may be relevant depending on the specific studies in question.

While federal regulations provide the baseline standards for clinical trials, individual states may have additional regulations or requirements that pertain to research activities. These additional state-specific regulations typically focus on aspects such as patient rights, informed consent, and data privacy. Clinical trial registrations are maintained by the FDA, the National Institutes of Health[57], and the Office of Research Oversight[58].

[48] HHS 45 CFR 46: https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html
[49] OHRP, Human Research Protections Guidance: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/index.html
[50] EPA Program in Human Research Ethics: https://www.epa.gov/osa/basic-information-about-human-subjects-research-0
[51] FDA IND application: https://www.fda.gov/drugs/types-applications/investigational-new-drug-ind-application
[52] FDA IDE application: https://www.fda.gov/medical-devices/investigational-device-exemption-ide/ide-application
[53] FDA combined IND/IDE application: https://www.fda.gov/combination-products/about-combination-products/frequently-asked-questions-about-combination-products#CP
[54] FDA GCP: https://www.fda.gov/science-research/science-and-research-special-topics/clinical-trials-and-humansubject-protection
[55] FDA, Drugs, Guidance, various: https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs
[56] FDA, Devices, Guidance, Various: https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/guidance-documents-medical-devices-and-radiation-emitting-products
[57] NIH ClinicalTrials.gov: https://www.clinicaltrials.gov/ct2/home
[58] ORO: http://www1.va.gov/oro/