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Position on Consent/Assent in Compassionate Use/Expanded Access

GE2P2 Global Foundation

CURRENT AT 02 April 2026

Context

Compassionate use/expanded access (CU/EA) programs – including those operating under titles such as managed access, cohort programmes, named patient or individual patient request (IPR) programs, pre-approval access, and others – have evolved to become more global over the last decade. At least one program has served patients in 100+ countries [1].

Generally, CU/EA interventions are not licensed in the jurisdiction relevant to a given patient; they may still be investigational and be undergoing clinical trials; and they may not be approved for marketing or be reimbursable in any jurisdiction.

Historically, CU/EA interventions have been considered therapeutic rather than clinical research intended to produce generalizable evidence. But as a growing number of CU/EA programs now collect RWD/RWE [real world data/evidence] about patients from the requesting physicians, this boundary between treatment and research is becoming blurred, raising ethical implications as discussed below.

Further, the use of collected patient RWD/RWE data, genomic sequencing, biospecimens or other evidence in "secondary" or additional research, or for other purposes, including publication, **is often unaddressed, or is inadequately addressed, in country laws and regulations.**

In the global arena, role of ethics review bodies [ERCs/ERBs/IRBs, clinical ethics review bodies] in providing review and continuing oversight of CU/EA interventions **– including consent/assent processes – is often unspecified, or otherwise not fit-for-purpose.**

We project that AI will increasingly become a dimension of CU/EA – including in program administration, how RWD/RWE is collected and analyzed, and how consent/assent documentation is generated, and how consent/assent transactions are conducted.

There has been recent progress involving consent/assent for some types of EA/CU interventions. For example, the International Society for Cell & Gene Therapy [ISCT] Expanded Access Working Group has released an important position paper on expanded access involving cell and gene therapies [CGT]. The paper helpfully addresses a number of issues including consent and assent generally, and with specific relevance to CGT programs [3].

Overall, however, laws and regulations at country level often do not address compassionate use/expanded access adequately, if at all, resulting in a fragmented landscapes of practices. We believe that these programs should operate under a robust, viable, harmonized global framework of norms and standards to guide responsible CU/EA administration and that protect the rights and welfare of the patients they serve.[4,5]

We are issuing this position to help advance such a normative framework by addressing consent/assent in these programs.

Key Observation/Position Argument

We anchor this position with the observation that the investigational/pre-approval status of CU/EA interventions means that patients receiving them may face risks and potential harms at least comparable to those faced by participants in clinical trials. Indeed, the risks and potential harms of a CU/EA intervention may, in some instances, be amplified, insofar as patients receiving CU/EA interventions could have a more advanced stage of disease, are more likely to have comorbidities, be taking concomitant medication, and not enjoy the support capabilities inherent in clinical trial infrastructures.

Reflecting these risks and potential harms, we argue that informed consent/assent in CU/EA should meet standards at least as rigorous and robust as those required for clinical investigations involving human participants and be well-aligned to the ecology of norms and standards which currently guide clinical research [2].

Implications for/Obligations of Organizations, Institutions, Individuals involved in CU/EA

Recognizing the importance of extending the general position outlined above into specific action, we outline below what we consider to be affirmative obligations and other imperatives associated with consent/assent for various actors across the CU/EA life cycle:

CU/EA Program Sponsors [sometimes referenced as "manufacturers" or "developers"] should act on affirmative obligations to:

:: Specify transparently and publicly – including on organization websites and trial registries – the processes, documentation, attestations and ethical review of consent and assent that will be required before providing CU/EA interventions to treating physicians and patients under their CU/EA programs,

:: Specify that country laws and regulations and ethical oversight mechanisms [where they are established at national and local institutional levels] must be fully adhered to,

:: Specify the minimum information elements required to be addressed by the requesting physician or health care provider securing consent/assent [including elements reflecting unique characteristics of the CU/EA intervention or program, such as cohort programs],

:: Support development of robust CU/EA consent and assent templates and other support to help ensure patient understanding and autonomous decision-making. Such supports could include IC content enriched by different forms of media and graphical design, and consent/assent templates and other IC content with versions adapted to:

- :: cultural, linguistic and other contextual factors,
- :: pediatric patients,
- :: patients with varying cognitive capacity and/or accessibility challenges, and,
- :: patients whose CU/EA disease condition may require special adaptions or other accommodations,

:: Specify conditions that would trigger securing re-consent/assent of a patient continuing an intervention, such as the emergence of safety signals, serious adverse events, or the availability of new information relevant to the assessment of risks and benefits.

:: Specify the mechanisms by which supply or other programmatic issues involving the CU/EA intervention – and mitigation strategies – will be communicated to the treating physician,

:: Specify the mechanisms by which patient data, genomic sequencing, biometrics and/or biospecimens will be collected and how such information is controlled and under what terms it might be used for future research and/or publication, how the patient will be informed, and how health authorities will be informed as part of any review/approval process,

:: Specify the mechanisms for informing EA/CU patients who may have concluded treatments of any relevant SAE/ADR or other information that would be reasonably understood to be relevant to their ongoing health decisions,

:: Specify in its public CU/EA program information the roles and accountabilities of any third-party contractors or non-sponsor organizations which are supporting any aspect of the CU-EA program, including provision of independent ethics review and support for consent/assent processes,

:: Continuously and rigorously assess their program's consent and assent processes and effectiveness to support refinement and strengthening.

Physicians [who request CU/EA access for and treat patients receiving the intervention] should act on affirmative obligations to:

:: Ensure that the patient understands that the CU/EA intervention is still not approved in the patient's country, and whether it is still investigational, with ongoing clinical trials,

:: Secure all information and support from the program sponsor required to fully and effectively communicate the relevant risks, potential harms and benefits of the proposed EA/CU intervention to the patient and their legal representatives and caregivers as relevant,

:: Fully assess and effectively present to the patient the relevant potential risks, harms, and benefits of initiating, continuing, and potentially interrupting or extending the EA/CU intervention for any reason, and the mechanism by which patients will be informed of a change in the benefit-risk balance, adverse events and safety signals in the program that would be material to assessing risks, potential harms, and potential benefits,

:: Fully assess and effectively present to the patient how their data, genomic information, and biometrics/biospecimens will be collected and how such information is controlled and under what terms it might be used for future research and/or publication,

:: Ensure that the patient [and/or their legal representatives and caregivers as relevant] have the time and privacy to make an independent, voluntary decision to proceed or not to proceed with the proposed EU/CU intervention before completing the informed consent process, and,

:: Recognize the patient's right to withdraw from, or modify consent/assent to continue, the CU/EA intervention, and respond to such a decision in a timely and medically responsible manner.

Patients, and their legal representatives and caregivers as relevant, approved to receive the CU/EA intervention should act on affirmative obligations to:

:: Secure any information and continuing support from the treating physician [and associated health care institutions where relevant] necessary to fully understand the risks, potential harms and benefits of the proposed EA/CU intervention and the alternative options available. This includes understanding the current regulatory status of the treatment, relevant potential risks, harms, and benefits of potentially interrupting the EA/CU intervention for any reason; the mechanism by which patients will be informed of adverse events and safety signals in the program that might affect their decision to continue treatment, as well as how potential supply interruptions will be communicated and mitigated,

:: Secure any information and continuing support from the treating physician (and associated health care institution[s] where relevant) required to fully understand whether and how their data, genomic information, and biometrics/biospecimens will be collected and controlled, and under what terms it might be used for future research, secondary use, and/or publication,

:: Secure the time and privacy to make an independent, voluntary decision to proceed or not to proceed with the proposed EA/CU intervention before completing the informed consent process,

:: Understand and commit to the compliance-related dimensions of the EA/CU intervention's course of treatment as appropriately informed by their individual response to the treatment (including dosing and any necessary restrictions of diet, concomitant medication, and activities) as well as timely and transparent reporting of adverse events and treatment experience.

:: Understand and commit to complying with the conditions required for the intervention – as appropriately informed by their individual response to the treatment and unless they elect to withdraw for reasons of adverse effects, new information, or personal choice.

While CU/EA program sponsors/manufacturers, requesting physicians and patients represent the primary implementing context for consent/assent, we recognize that other institutions/organizations/ roles have authority and are otherwise critical to achieving the intended standard of consent as below.

Health Authorities [HA]/country regulatory authorities should act on affirmative obligations to:
:: Ensure that, where informed consent and assent requirements in current law and regulation that apply to clinical research involving human participants, they also apply to CU/EA programs and individual instances of health interventions under such programs,

:: Consider appropriate legislative and regulatory action to achieve appropriate harmonization between current law and regulation on informed consent and assent in clinical research involving human participants, treatment with investigational interventions under CU/EA, and core global ethics guidance [2],

:: Ensure that health care institutions which may be treating patients receiving CU/EA interventions are operating under regulations and practices which align with the above.

Health Care Institutions should act on the affirmative obligation to:
:: Ensure there is robust ethics review and continuing oversight of CU/EA interventions made available to patients being cared for in their institutions, aligned with country laws and regulations.

National Ethics Committees [where they exist and which may operate under various titles in different jurisdictions] should act on the affirmative obligation to:
:: Consider the arguments in this position and act, under their remit/terms of reference, to support evolution of their country's laws, regulations and frameworks guiding ethics review committees/ ERCs/IRBs such that ethics review and consent standards in CU/EA interventions align with ethical standards associated with clinical research involving human participants,

Organizations and initiatives issuing normative/ethics guidance involving medical/health interventions should act on affirmative obligations to:

:: Ensure that their respective guidances, frameworks and policy instruments, wherever relevant, address informed consent/assent in CU/EA aligned with how it is addressed for clinical research involving human participants,

:: Actively explore harmonization of their relevant guidance with rigorous guidance issued by other organizations to evolve towards robust and more uniform treatment of informed consent/assent in CU/EA that is well-aligned to those standards applying to clinical research involving human participants.

Revisions/Updates to this Position

We anticipate that CU/EA programs will continue to expand their global impact, and that issues and solutions to ensure their responsible administration will evolve. We will review and refresh this position at least annually, and as otherwise indicated by developments in the field.

# # # #

References

[1] **International Country-Level Trends, Factors, and Disparities in Compassionate Use Access to Unlicensed Products for Patients With Serious Medical Conditions**
Original Investigation
Paul Aliu, PharmD, MRPharmS, G.Dip (Law), MBA1; Séverine Sarp, MD, PhD, MSc1; Ramona Reichenbach, MBA1; et al.
JAMA Health Forum, Published Online: April 15, 2022 2022;3;(4):e220475. doi:10.1001/jamahealthforum.2022.0475
Key Points
Question What are the key factors associated with the significant disparity in compassionate use (CU) activity across countries?
Findings In this cohort study of 31 711 CU requests received from 110 countries, the presence of CU regulations and their public availability, as well as local clinical trial activity, were positively associated with higher request rates. Despite generally free provision of unlicensed therapeutic products, there was an association between a country's economic development and its request activity for unlicensed compounds via CU.
Meaning Existence and public availability of CU regulations and an increase in local clinical trial activity are modifiable country-level factors that could potentially facilitate patient access to novel lifesaving medicines.

[2] The ethical requirements for a patient's informed consent to a medical intervention and for a research subject's informed consent to social, behavioral, or biomedical research are almost universal: Valid informed consent is a prerequisite and must be individual, knowing, voluntary, and in circumstances conducive to voluntariness. Only a legally valid, morally valid representative may proxy consent for an individual who lacks ability to make an informed decision.

Contexts, rules, regulations and interpretations differ but are well articulated across the current "ecology" of international declarations, covenants, conventions, guidances, frameworks, codes and similar instruments referencing consent/assent/agency/ autonomy.

The guidance instruments listed below comprise a variety of forms and formats, are for the most part non-binding, and proceed from a diverse range of sources. This list is evolving and indicative, not exhaustive.

Nuremberg Code [1947]

Universal Declaration of Human Rights [1949]
International Covenant on Social, Economic and Cultural Rights [1966]
International Covenant on Civil and Political Rights [1966]
Convention on the Rights of the Child [1989]
Belmont Report [1979]
Universal Declaration on Bioethics and Human Rights [2005]
WMA – Declaration of Helsinki [2024 revision integrating Declaration of Taipei [2016]
CIOMS – International ethical guidelines for health-related research involving humans [2016]
CIOMS – Clinical research in resource-limited settings [2021]
CIOMS – Patient involvement in the development, regulation and safe use of medicines [Oct 2022]
INSERM – Global Ethics Charter for the Protection of Healthy Volunteers in Clinical [2024]
WHO – Guidance for best practices for clinical trials [25 September 2024]
UNESCO – First Draft of the Recommendation on the Ethics of Neurotechnology [October 2024]
WHO – Guidance for human genome data collection, access, use and sharing [20 November 2024]
ICH E6(R3) [GCP] Principles, Annex 1 [January 2025]
ICH: ICH E6(R3) [GCP] Annex 2 [[in development – Feb 2025]
WHO guidance on the ethics of health research priority setting [in development – Feb 2025]

[3] **International Society for Cell & Gene Therapy Expanded Access Working Group position paper: key considerations to support equitable and ethical expanded access to investigational cell- and gene-based interventions**

ISCT Committee Statements

Elena Maryamchik1 maryame@mskcc.org · Laertis Ikonomou2 · Beth E. Roxland3 · … · Bruce L. Levine5 · Bambi J. Grilley6,7 for the ISCT Committee on the Ethics of Cell and Gene Therapy Expanded Access Working Group …

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PDF download here

Abstract

This position paper reviews the Expanded Access pathway for cell and gene therapies, examining its critical role at the nexus of patient need, regulatory frameworks, and scientific advancement. Spearheaded by the International Society for Cell & Gene Therapy's Expanded Access Working Group, it explores how investigational therapies are accessed outside of clinical trials for patients with serious or life-threatening conditions when no approved alternatives exist. Access to cell and gene therapy products are of specific interest to patients because many times the products are bespoke, being used to treat serious and/or incurable conditions, and are potentially curative. As the field of cell and gene therapy rapidly progresses, healthcare professionals face mounting challenges in navigating the balance between access and oversight. Key considerations include transparent communication with patients, robust data reporting, and a discussion of cost recovery models and their implications for long-term commercialization strategies. Equity and inclusivity are central themes, highlighting the need to design pathways that are accessible to diverse patient populations while upholding high scientific and ethical standards. This position paper is presented as a resource for clinicians, researchers, and policymakers navigating the evolving landscape of investigational cell and gene therapies. It emphasizes the importance of ethical frameworks and equitable practices in delivering transformative treatments to patients in need.

[4] **Therapeutic Innovation & Regulatory Science**

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Review

An Industry Perspective on Compassionate Use in Europe: A Call for Change

Philipp Schlatter, Nina Heiss, Pedro Franco, Annie O'Keefe Martin, Susan Robson & Ramona Reichenbach

Abstract

Background

Options for patients to receive unauthorised medicines through compassionate use (CU) in Europe vary greatly. There are two CU pathways: cohort programmes, regulated uniformly by the Regulation across EU member states, and individual patient requests (IPRs) governed by the Directive. The latter allows member states to determine their own laws, resulting in heterogeneous regulatory requirements and challenges in operationalization. Consequently, patients may experience delays in accessing CU medicines depending on their country of residence. To compare CU availability across European countries and formulate recommendations for improvement, we analyzed 8,934 patient requests from 30 European countries.

Methods

An exploratory post-hoc analysis was conducted using pooled collaborative data from 8,934 patient requests provided by Merck KGaA, Novartis, Roche, and Sanofi, tracked from January 1, 2020 to April 30, 2023 across 30 countries. All requests with complete dates for submission, company approval, relevant Ethics Committees or Health Authorities, and shipment dates were included.

Results

While internal company CU approval steps were found to be similar with a median approval time of 5 days (median interquartile range (IQR) of 1 (0–6) for cohorts; median IQR 4 (1–8) for IPRs), the time from company approval until shipment varied between cohort requests (median IQR 5 (1–16) days) and IPRs (median IQR 8 (1–22) days). Challenges experienced included differences in the use of CU terminologies, scope, settings, regulatory, and operational requirements.

Conclusion

Our findings indicate that differing national requirements across Europe lead to operational challenges and inter-country variability in CU implementation posing operational challenges for stakeholders, highlighting the need for improved harmonization.

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[5] **Journal of Pharmaceutical Policy and Practice**

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Article

Factors influencing pharmaceutical companies' decisions to pursue compassionate use programs in the EU: a qualitative study in The Netherlands

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ABSTRACT

Background
Access to unauthorized medicines in the EU is legally restricted, except in certain cases such as clinical trials, magistral preparations, hospital exemptions, and early access programs, including compassionate use programs (CUPs) and named patient use (NPU). CUPs, regulated under Article 83 of Regulation (EC) No 726/2004, are intended for a group of patients with an unmet medical need. Despite this EU-wide regulation, the implementation of CUPs varies among member states, and the factors driving pharmaceutical companies to pursue them are poorly understood.
Methods
This study conducted semi-structured interviews with pharmaceutical companies that had applied for CUPs in the Netherlands, as well as those with potentially eligible medicines that had not pursued CUPs. The interviews explored the decision-making processes and factors influencing CUP applications. Transcripts were analyzed using Atlas.ti software, with coding categories derived from the interview guide and emerging themes.
Results
Ten interviews were conducted. Factors influencing CUP applications were classified into four categories: regulatory, medical, operational, and financial. Regulatory factors included recommendations from the Health and Youth Care Inspectorate (IGJ) and European Medicines Agency (EMA), concerns about post-marketing authorization uncertainties, and timelines for CUP approval. Medical factors involved unmet medical needs, patient numbers, and the alignment of CUP indications with authorized indications. Operational factors included prior experience with CUPs, supply availability, and the appeal of NPU due to faster approval times. Financial factors centered on reimbursement expectations and decisions by company headquarters on the free provision of medicines.
Conclusion
The decision to pursue CUPs is influenced by multiple factors, with regulatory uncertainties and operational complexities playing significant roles. Improving clarity concerning CUP regulations, particularly data collection and the post-marketing phase, could encourage more pharmaceutical companies to apply for CUPs, which would provide patients with earlier access to potentially promising treatments.

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Public Consultation Process

Development of this position benefitted from a public consultation period which ran from 31 July 2025 through 30 September 2025. We greatly appreciate the many thoughtful insights and suggestions received during this comment period.

Conflicts of Interest

The Foundation's affiliate, GE2P2 Global Advisory Services pbc, provided advisory support involving assessment of ethical issues for a limited number of CU/EA requests before and during the development period of this position. No other conflicts/potential conflicts are reported.

Additional Resources

Global Regulatory Frameworks: Informed Consent & Assent in Expanded Access / Compassionate Use Programs

Utilizing Claude [AI tool], we requested an inventory of global and jurisdiction-specific guidance, regulations or laws which address consent and/or assent in compassionate use/expanded access programs. This interrogatory was conducted on 24 February 2026 by David Curry, GE2P2 Global. We assess the results to be indicative but may not be exhaustive, and have explored the embedded links to confirm relevance.

European Union / EMA

The overarching EU framework is found in two instruments:

- **Regulation (EC) No 726/2004, Article 83** — establishes the legal basis for EU-level compassionate use programs and requires compliance with member state rules on consent.
- **Directive 2001/83/EC, Article 5** — governs the named-patient/special-needs exemption and also defers to national consent laws.
- **EMA Guideline on Compassionate Use of Medicinal Products (EMEA/27170/2006)** — the CHMP guidance document that frames conditions for compassionate use under Article 83, noting that informed consent must follow applicable national legislation and GCP.
- **EMA Compassionate Use Overview Page** — landing page with links to current CHMP opinions and further guidance.

As noted in a helpful comparative overview, **EU member state implementation varies considerably**, and the EMA's role is advisory, not binding, on consent procedures. A broad cross-country comparison of EU member state CUP approaches (Belgium, France, Germany, Italy, Spain, UK) is available via **Lexology**.

France restructured its ATU (*autorisation temporaire d'utilisation*) system into *accès précoce* in 2021 under the *Loi de financement de la sécurité sociale*; consent requirements fall under the **Code de la Santé Publique** (Articles L. 1111-4 and related).

UK (Post-Brexit) — MHRA

- **Early Access to Medicines Scheme (EAMS) — Guidance for Applicants** — the primary MHRA operational guidance, which requires patients to be informed the medicine is unlicensed and to provide informed consent; notes that consent forms are the prescribing physician's responsibility and need not be submitted to the MHRA.
- **EAMS Overview** — general scheme description.
- **EAMS Operational Guidance (PDF)** — the joint MHRA/NICE/NHS England operational document.
- For pediatric patients and adults lacking capacity, consent hierarchies are governed by national law: the **Mental Capacity Act 2005** (England & Wales) and the **Children Act 1989**.
- The **Medicines for Human Use (Clinical Trials) Regulations 2004** also apply where compassionate use programs resemble structured trials, as discussed in this Clinical Research Made Simple overview.

Canada — Health Canada

- **Special Access Program (SAP) — Overview** — top-level Health Canada SAP page.
- **Food and Drug Regulations, Part C, Division 8 (ss. C.08.010–C.08.011)** — the statutory basis for the SAP; places responsibility on the practitioner to ensure patients are "well informed of the possible risks and benefits."
- **Draft SAP Guidance Document for Industry and Practitioners** — clarifies consent obligations in detail.
- For medical devices, consent requirements are explicitly stated in the Medical Devices SAP (Lexology summary), which notes that practitioners must obtain patient informed consent as a condition of use, though Health Canada acknowledges this is regulated at the provincial/territorial level through medical colleges.
- The ethical framework for research involving human subjects (including assent for minors) is set by the **Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2)**.
- A useful critical analysis of SAP consent ethics is available at **PMC (Montaner et al.)**.

Australia — TGA

- **Special Access Scheme (SAS) — Guidance for Health Practitioners** — the TGA's primary guidance document, which explicitly requires written informed consent as a legislative condition for SAS

supply and specifies what patients must be informed of (unapproved status, known risks and side effects, possible unknown risks, available approved alternatives).

- **TGA SAS Guidance (full HTML export)** — references the NHMRC National Statement as the applicable standard for consent in compassionate use contexts.
- **TGA — Human Research Ethics Committees and the Therapeutic Goods Legislation (PDF)** — the TGA's guidance to HRECs, noting that consent form review is an important HREC function in relation to unapproved goods.
- **NHMRC National Statement on Ethical Conduct in Human Research (2023, updated 2025)** — the governing ethics framework that includes detailed provisions on consent and assent for children, adults lacking decision-making capacity, and other vulnerable populations. The 2025 update (effective early 2026) includes updated guidance on specific population groups.
- A clinical summary of TGA SAS consent requirements is available at **PMC (Penm et al., 2017)**.

Japan — MHLW / PMDA

Japan's compassionate use system ("*kakudai chiken*" / Expanded Access Clinical Trials, EACTs) is implemented **within the standard clinical trial framework** under the GCP Ministerial Ordinance, rather than through a separate compassionate use pathway.

- **MHLW/PMDA Notification on Clinical Trials Conducted for Humanitarian Purposes (PSEHB/ELD Notification No. 0122-7, January 22, 2016)** — the foundational notification establishing Japan's EACT/compassionate use system.
- **PMDA Overview Slide Deck on EACTs (PDF, Japanese)** — provides the regulatory rationale and conditions for the program.
- **PMDA Ministerial Ordinance on GCP (English translation)** — establishes consent requirements under Articles 50 et seq., including provisions for situations where consent is difficult to obtain and proxy consent procedures.
- **PMDA Notifications and Administrative Notices Index** — includes the PSEHB/PED Notification No. 0330-6 (March 2023) on electronic informed consent in clinical trials.
- A peer-reviewed analysis of Japan's EACT program in practice (2016–2021) is available at **PMC** and in **Clinical Pharmacology & Therapeutics**.

Brazil — ANVISA

Important update: RDC No. 204/2017 (cited in my original response as the primary reference) was **revoked as of January 15, 2026** and replaced by **RDC No. 1,001 of December 11, 2025**, which outlines the revised priority classification framework.

The underlying consent framework for expanded access/compassionate use in Brazil remains:

- **ANVISA RDC No. 38/2013** — the primary regulation governing expanded access, compassionate use, and post-study drug supply programs; requires compliance with the applicable ethics framework.
- **ANVISA RDC No. 9/2015** — the clinical trials regulation (English machine translation via ClinRegs) which governs consent processes for clinical trials and programs approved by ANVISA; Art. 80 addresses transitional consent requirements.
- **CNS Resolution No. 466/2012** — the National Health Council's foundational research ethics resolution, which is the primary framework governing informed consent (including assent for minors) in Brazilian research involving human subjects.
- **ClinRegs Brazil Profile** — a regularly updated, comprehensive English-language overview of Brazilian clinical research regulation, including the December 2025 regulatory updates.
- **Baker McKenzie Clinical Trials Handbook — Brazil (PDF)** — a useful English-language practitioner summary of the ANVISA/CEP/CONEP consent framework.

Switzerland — Swissmedic / FOPH

- **Federal Act on Research involving Human Beings (Human Research Act / HRA) — English text (PDF)** — the primary statute; Articles 16 and 22–24 govern informed consent; Articles addressing incapacitated persons and minors require representative consent and, where feasible, the individual's assent.
- **FOPH — Regulation of Human Research in Switzerland** — the government landing page with links to the HRA and all four implementing ordinances (ClinO, ClinO-MD, HRO, OrgO-HRA).
- **FOPH — Human Research: Approval of Research Projects** — explains the ethics committee approval process and written informed consent requirements.
- **Swissmedic — Clinical Trials Page** — covers Swissmedic's role alongside ethics committees and links to the November 2024 revised ordinances.
- **Swissmedic — New Implementing Regulations from November 1, 2024** — details the 2024 revisions to the HRA ordinances, including strengthened consent information requirements, e-consent provisions, and enhanced requirements for comprehensible patient-facing information.
- **EDÖB (Swiss Federal Data Protection Commissioner) — Human Research Consent Overview** — a clear explanation of how the HRA applies the informed consent principle across primary and secondary research contexts.
- **SAMS Handbook: Research with Human Subjects (PDF)** — the Swiss Academy of Medical Sciences practitioner handbook, which explains the HRA consent framework (including assent) in accessible terms and addresses the distinction between standard treatment and experimental treatment in individual cases.

United States: Informed Consent and Assent in Expanded Access Programs

The U.S. framework is one of the most detailed and explicitly codified globally, built on interlocking statutory, regulatory, and guidance layers. There are also two distinct pathways — FDA Expanded Access and the Right to Try Act — that differ meaningfully in their consent architecture.

Foundational Statutory Authority

- **Federal Food, Drug, and Cosmetic Act (FD&C Act), Section 561 / 21 U.S.C. 360bbb et seq.** — the statutory foundation for expanded access to investigational drugs. Consent is required and flows from this authority.
- **FD&C Act, Section 561B (Right to Try)** — added by the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2018 (P.L. 115-176), establishing a parallel pathway for terminally ill patients with modified consent requirements (discussed separately below).

Core Regulatory Framework: Informed Consent

Expanded access is treated by FDA as a "clinical investigation" under 21 CFR Part 50, triggering the full informed consent regulatory apparatus.

- **21 CFR Part 50, Subpart B — Informed Consent of Human Subjects** — the primary consent regulation. Key provisions include:
    - **§ 50.20**: General requirement that no investigator may involve a human subject unless informed consent has been obtained.
    - **§ 50.25**: The required *elements* of informed consent — including a statement that the study involves research; a description of reasonably foreseeable risks; a description of potential benefits; disclosure of alternatives; a statement on confidentiality; and contact information for questions about rights and research-related injuries. The consent form must also state that the drug is investigational and that FDA has not determined it is safe or effective.
    - **§ 50.23**: Exceptions to informed consent in certain life-threatening situations (e.g., emergency use where there is no time to obtain consent and no LAR is available), subject to certification by two physicians.
    - **§ 50.24**: Exception from informed consent requirements for emergency research conducted under very specific conditions.

- **§ 50.22**: An IRB may waive or alter consent elements for minimal-risk clinical investigations (added following the 21st Century Cures Act; see December 2023 final rule).

- **21 CFR Part 312, Subpart I — Expanded Access to Investigational Drugs for Treatment Use** — establishes the three categories of expanded access, each with specific consent obligations:

  - **§ 312.305** — applies to all expanded access uses; explicitly assigns investigators responsibility for ensuring Part 50 consent requirements are met, and requires IRB review consistent with 21 CFR Part 56.

  - **§ 312.310** — individual patient expanded access, including emergency use. In a genuine emergency, treatment may begin before IRB review, but the IRB must be notified within 5 working days (§ 56.104(c)).

  - **§ 312.315** — intermediate-size patient populations; requires prospective IRB approval and informed consent.

  - **§ 312.320** — treatment IND or treatment protocol (widespread use); requires prospective IRB approval and informed consent.

- **21 CFR Part 56 — Institutional Review Boards** — governs IRB review of consent documents and procedures for all expanded access uses. For individual patient expanded access, FDA permits a waiver allowing IRB chairperson (or designee) review in lieu of full board review (via Field 10.b on Form FDA 3926).

Key FDA Guidance Documents

- **Informed Consent: Guidance for IRBs, Clinical Investigators, and Sponsors (August 2023)** — the FDA's comprehensive, current guidance on all aspects of informed consent for FDA-regulated clinical investigations. It explicitly applies to expanded access and describes roles, process, content requirements, electronic consent, and ongoing consent obligations. This finalizes and supersedes the 1998 guidance. A Federal Register notice accompanied its release.

- **Expanded Access to Investigational Drugs for Treatment Use: Questions and Answers (October 2025)** — the most current version of FDA's primary expanded access Q&A guidance (replacing the 2017 version). Q12–Q14 specifically address informed consent requirements for expanded access. The guidance confirms that all categories of expanded access constitute a "clinical investigation" under 21 CFR 50.3(c), triggering full Part 50 consent requirements. It also addresses the requirement that the consent form include a statement that the treatment "involves research" under § 50.25(a)(1), even though expanded access is not primarily research in intent. A detailed analysis of what changed from 2017 to 2025 is available from WEP Clinical.

- **Informed Consent Template for Individual Patient Expanded Access** — FDA's model consent form (included as Appendix B of the Q&A guidance), introduced in the 2022 draft and finalized in 2025. Required elements include: the investigational nature of the drug; FDA's lack of safety/efficacy determination; the voluntary nature of participation; known and potential risks; the ability to

withdraw; and confidentiality provisions. This template was created to reduce back-and-forth with IRBs and facilitate faster individual patient access approvals.

- **Expanded Access: Information for Institutional Review Boards (IRBs)** — FDA's IRB-specific guidance page, which confirms that for pediatric patients, IRBs must confirm that age-appropriate assent provisions and parental/guardian permission are in place per 21 CFR 50.55.

- **IRB Review of Individual Patient Expanded Access Submissions for Investigational Drugs and Biological Products (Guidance)** — FDA's dedicated guidance on how IRBs should approach individual patient expanded access reviews, including their role in reviewing and approving consent materials.

- **Form FDA 3926 — Individual Patient Expanded Access IND Application** — the preferred submission form for individual patient requests; includes Field 10.b for requesting IRB chairperson review in lieu of full board review. Guidance on completing the form is at Form FDA 3926 Guidance (PDF).

Pediatric Assent

The U.S. framework includes explicit, binding regulations on assent — one of the most detailed treatments of this issue among the jurisdictions surveyed.

- **21 CFR Part 50, Subpart D — Additional Safeguards for Children in Clinical Investigations** — directly applicable when a child is the patient in an expanded access use. Key provisions:

    - **§ 50.55** — requires IRBs to determine whether children are capable of providing assent, taking into account their age, maturity, and psychological state. Assent is defined as affirmative agreement; mere failure to object does not constitute assent (§ 50.3(n)). The IRB may waive the assent requirement under limited conditions (§ 50.55(d)), but parental/guardian permission remains required whenever informed consent would otherwise be required. Both parents' permission is generally required for research involving greater than minimal risk that does not offer the prospect of direct benefit (§ 50.55(e)).

    - **§§ 50.51–50.54** — tiered risk categories governing what clinical investigations involving children may be IRB-approved (from no greater than minimal risk up to investigations requiring FDA Commissioner's determination after expert panel review).

- **Draft Guidance: Ethical Considerations for Clinical Investigations of Medical Products Involving Children (September 2022)** — FDA's most recent guidance document on pediatric protections, addressing the framework of Subpart D, component analysis of risk and benefit, and assent/permission requirements. See also the Federal Register notice and SACHRP commentary on the draft. Note: this remains a *draft* guidance as of February 2026 and has not yet been finalized.

- **FDA's Additional Protections for Children page** — overview of the Subpart D framework and its application.

- **Federal Register: Final Rule on Subpart D (February 2013)** — the rulemaking history finalizing the interim 2001 Subpart D rule and explaining FDA's policy rationale, including on assent documentation and waiver.

- **Process for Handling Referrals to FDA Under 21 CFR 50.54** — applies to protocols not approvable under §§ 50.51–50.53; requires FDA Commissioner's determination after expert panel review and public comment, with requirements for parental permission and child assent still intact.

The Right to Try Pathway: A Distinct Consent Architecture

The **Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2018 (P.L. 115-176)** — codified at FD&C Act § 561B — created a parallel access pathway that diverges significantly from the expanded access framework in its consent requirements:

- Written informed consent is **required** from the eligible patient or their legally authorized representative, specifically referencing "the requirements of part 50 of title 21, Code of Federal Regulations." However, the Act does **not** require IRB review or approval of the consent form, and it does not define the specific content of "written informed consent" beyond this cross-reference, leaving the content largely to the physician and manufacturer to determine.

- **No IRB review or approval** of the request or consent form is required, in contrast to expanded access.

- **No FDA review** of the individual request is required; the FDA's role is limited to receipt and posting of annual summary reports from manufacturers.

A comprehensive academic analysis of the Right to Try Act's consent provisions and their limitations is available via PMC. A useful CRS Report comparing expanded access and Right to Try is also available. Legal commentators have noted that the Right to Try Act's failure to define "written informed consent" creates ambiguity about the level of disclosure required, with some characterizing the consent provisions as "vague" compared to the expanded access framework. See Shipman & Goodwin's analysis.

HHS / Common Rule Alignment

FDA's informed consent regulations exist alongside the **Federal Policy for the Protection of Human Subjects (the Common Rule, 45 CFR Part 46)**, administered by HHS's Office for Human Research Protections (OHRP). The 2018 revisions to the Common Rule (the "Revised Common Rule") updated consent requirements — including the "key information" requirement, which asks that the most important information be presented first in a concise manner — but FDA has not yet fully harmonized its own regulations with the 2018 Common Rule. The August 2023 FDA Informed Consent Guidance notes where differences exist and references the HHS/FDA Draft Guidance on Key Information and Facilitating Understanding in Informed Consent, which addresses both sets of requirements. FDA has proposed a rule (September 2022 proposed rule, 87 FR 58733) to further harmonize its regulations with the 2018 Common Rule; this rulemaking remains pending as of February 2026.

Notable Structural Features Distinguishing the U.S. Approach

Compared to most other jurisdictions, the U.S. framework stands out in several respects. First, the FDA has published an actual **consent template** specific to individual patient expanded access, which is unusual globally and directly addresses the common complaint that practitioners find it burdensome to draft consent documents. Second, the **IRB chairperson review waiver** for individual patient expanded access is a practical mechanism found in few other systems. Third, the **Subpart D assent framework** is among the most prescriptive globally in terms of codifying when assent is required, how it is assessed, and when it may be waived. Fourth, the **Right to Try Act's reduced consent infrastructure** (no IRB review of consent form; no FDA review of request) represents a deliberate legislative choice to streamline access for terminally ill patients, at the cost of reduced oversight — a tradeoff that continues to be debated in the literature.

ICH International Guidelines

- **ICH E6(R3) — Good Clinical Practice** — the foundational GCP standard adopted by reference in most jurisdictions' compassionate use frameworks; contains core consent requirements applicable where GCP is referenced.
- **ICH E11(R1) — Clinical Investigation of Medicinal Products in the Pediatric Population** — provides guidance on assent for pediatric subjects in clinical trials and related programs.

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