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Clinical Trial Supply in the U.S. and Europe: What International Sponsors Need to Plan For – Part I

Regulatory Authorization, GMP Requirements, Packaging, Labeling, Blinding, and Comparator Sourcing Considerations

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The United States (US) is the largest pharmaceutical market and offers significant opportunities for both domestic and international sponsors. However, with current tariffs and the current administration's emphasis on expanding domestic manufacturing and strengthening national supply-chain resilience, the greatest opportunities lie with sponsors capable of manufacturing final products in the country rather than importing them. Similar dynamics exist in the European Union (EU) and the United Kingdom (UK), which are also major pharmaceutical markets.

For non-US/EU/UK companies seeking to capitalize on these markets, access to local manufacturing capacity is essential. However, general drug product manufacturing capacity won't be sufficient. Working with an outsourcing partner that has expertise in specialty products, such as dry powders for inhalation, and the ability to package and label them in compliance with specific US/EU/UK regulatory requirements provides a significant advantage. Traceability and serialization expectations, as well as product recall processes, can be challenging for international sponsors unfamiliar with them.

In the US in particular, international sponsors should also be aware of the highly litigious nature of American society. Any issues with the safety of drug products will immediately result in lawsuits. Meanwhile, failure to comply with US Food and Drug Administration (FDA) regulations can lead to significant penalties and potentially block the entry of drug products into the country.

Given the many factors to consider, this discussion has been broken into two parts. Part I addresses regulatory authorization, Good Manufacturing Practices (GMP) in the US and Europe, packaging operations, labeling, blinding considerations for randomized trials, and comparator sourcing.

Regulatory Authorization: IND vs. CTA

Authorization for initiation of a clinical trial involving humans for an investigational medicine is required in the US, EU, and UK.[1-3] Sponsors must submit an Investigational New Drug (IND) Application according to 21 CFR (Code of Federal Regulations) Part 312[4] to FDA in the US and a Clinical Trial Application (CTA) under Regulation (EU) No 536/2014[5] to the European Medicines Agency (EMA) in the EU. In the UK, a CTA is submitted to the Medicines and Healthcare products Regulatory Agency (MHRA) as required by the Medicines for Human Use (Clinical Trials) Regulations 2004[6] and amended by the Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025.[7]

INDs for small-molecule drugs (biological license applications, or BLAs, are required for biologic drugs) are submitted to the FDA in electronic Common Technical Document (eCTD) format. Approvals are based on chemistry, manufacturing, and controls (CMC), non-clinical (stability, quality, purity, toxicity, etc.), and clinical (obtained in relevant animal models) data reported in separate documents. FDA has 30 days to respond, and trials may proceed if the agency has no objection.

CTAs containing the same information are submitted as a single Investigational Medicinal Product Dossier (IMPD) through the EMA's centralized Clinical Trials Information System (CTIS) in the EU. The sponsor must nominate a Reporting Member State (RMS). The EMA has 45-120 days to respond, during which the assessment is coordinated among the RMS, other Concerned Member States (CMS), and various ethics committees. In the UK, CTAs are also submitted as single documents through the Integrated Research Application System (IRAS), and the MHRA has 30 days to respond.[8]

Note that the CTD format, established by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), is used in EU and UK submission dossiers, enabling harmonized electronic submissions of quality, safety, and efficacy information for new drug applications across ICH regulatory authorities.[9]

Importantly, INDs are product-specific, while CTAs are protocol-specific. This means that additional data and study information for a specific investigational drug are handled differently. In the US, such information is submitted as an addition to the existing IND. In the UK and Canada, CTAs must be resubmitted whenever protocols change or a new trial is initiated.

Despite these differences, because all clinical trials must be conducted in accordance with Good Clinical Practice (GCP) guidelines, trial data collected in the US and EU are often accepted as part of submissions to both regulatory agencies.

Good Manufacturing Practice (GMP) Requirements in the US and EU

GMP requirements must be met to ensure the production of safe, high-quality drug products, including clinical trial materials. Manufacturers are expected to be proactive in ensuring safety and quality and to demonstrate compliance through detailed documentation. Implementation varies slightly but importantly across regions, particularly with respect to labeling, testing, and enforcement approaches.[10,11]

For non-US/EU/UK companies seeking to capitalize on US and EU pharma markets, access to local manufacturing capacity is essential

Manufacturing and supplying clinical trial materials for the US, EU, and UK markets requires sponsors to navigate significant differences in regulatory pathways, GMP expectations, packaging rules, labeling formats, and comparator sourcing

- In the US, GMP requirements are established by 21 CFR Parts 210[12] and 211[13] and enforced by the FDA. In the EU, they are outlined in EudraLex Volume 4[14] and different product- and process-specific Annexes, including specific guidance for investigational medicinal products.[15]
- US manufacturers must have a Quality Control Unit (QCU) to oversee final product release, with release authority within the general Quality Assurance structure. EU manufacturers must have a Pharmaceutical Quality System (PQS) in place that manages a formal risk management program, and a designated Qualified Person (QP) (usually a trained pharmacist or scientist) must certify and release each production batch.[16]
- The US FDA does not issue any formal GMP certificates. EU competent authorities do, and they must be logged in the centralized EudraGMDP database.
- Non-EU companies involved in the manufacture and/or importation of human or veterinary pharmaceutical products in the EU, including investigational medicinal products, must also obtain a Manufacturer's/Importation Authorization (MIA),[17] sometimes referred to as a GMP license.[18] MIAs are issued following registration with the local regulatory authority and after passing a facility inspection.

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- Overall, the US GMP guidelines tend to be more flexible, while those in the EU are more proscriptive, particularly with respect to the manufacture of sterile products via aseptic processes.[19]

In addition to FDA and EMA, the World Health Organization (WHO) also has GMP guidelines. ICH and the Pharmaceutical Inspection Co-operation Scheme (PIC/S) work to harmonize GMP regulations and inspection protocols.

Packaging Operations

Effective packaging of clinical trial materials, both primary (immediate, including vials and other containers containing the drug product) and secondary (e.g., cardboard boxes or cartons containing the primary container), is essential to protect the identity, quality, and safety of investigational medicines. The US, EU, and UK require that packaging of clinical trial materials comply with GMP requirements, including expectations for container closure integrity, material compatibility, tamper-evident packaging, data integrity, and serialization and traceability. Serialization and traceability are governed by the Drug Supply Chain Security Act (DSCSA) in the US and the Falsified Medicines Directive in the EU.[20]

Equipment for packaging investigational medicinal products includes not only packaging operations but also serialization/coding and inspection systems, all of which must be validated and revalidated if changes occur. Equipment must be easily cleanable and designed to prevent contamination. Cleaning must be performed and validated using established, well-documented procedures. Specific data integrity requirements also apply.

Labeling: Two Sets of Rules

Different labeling requirements can challenge international sponsors looking to manufacture clinical trial materials in the US and EU, particularly regarding shelf life and product expiry. Labeling of investigational medicines is regulated in the US under 21 CFR Part 312[4] and in the EU since 2022 under the amended Clinical Trials Regulation (Annex 6).[5]

Clinical trial material labels (immediate packaging) in the US must include a statement that the product is only for investigational purposes and the drug name or code, dosage form, route of administration, storage conditions, and an identifier for traceability.[21] Sponsor information is required on the secondary packaging. Labels on primary packaging for investigational medicinal products in the EU must also include a statement that they are for clinical trial use only, along with the trial reference code, name and address of the sponsor, batch number, expiration date, unique patient identification code, protocol number, and instructions for use.

Unlike in Europe, the FDA does not require an expiration date on clinical trial material labels if the information is provided elsewhere, such as in trial protocols or investigator brochures. Shelf life and product expiry pose issues because clinical trial materials typically have limited stability data to support long shelf lives. Limitations on allowable shelf lives mean investigational drug products often expire while a clinical trial is still underway, creating the need for extensions. In the EU, because the expiration date must be placed on the primary packaging label and relabeling involves breaking tamper seals and repackaging kits, updates can pose a safety risk, particularly for light-sensitive products.[22] It also increases supply-chain complexity. The amended CTR allows, in certain cases where relabeling may impact quality and safety, for expiry information to be included on the secondary rather than the primary product packaging.

Blinding Considerations

For randomized trials, both the FDA and the EMA require investigational medicinal product labels to be similar for active drug products and placebos.[23] Generic terms such as "Study Medication" are used instead of the active ingredient name, which must be maintained elsewhere as part of a tracking system. Secure interactive response technology (see below) links patient numbers to blinded treatment kits, and regular integrity checks are required at depots and clinical trial sites. Systems that enable immediate unblinding of a specific product without affecting overall trial blinding must also be implemented in emergencies.

Comparator Sourcing Challenges

Clinical trials investigating the safety and efficacy of investigational medicines intended to offer improved performance over existing therapies often require testing one or more of those existing medicines alongside the new drug candidate. Sourcing comparator (benchmark, reference) drugs for clinical studies can be challenging. Manufacturers often limit the use of their drug products as comparators. Investigational products are even more difficult to acquire.[24]

Sponsors must also comply with labeling, traceability, and chain-of-custody requirements that vary by region and country. In the US, the DSCSA applies to comparators brought into the US for use in clinical trials. Products must be traceable from the manufacturer to the dispenser, and sourcing partners (brokers, wholesalers) must meet US standards.[25] The challenges are magnified for specialty drugs with short shelf lives and complex handling requirements, limited supplies, and more complicated documentation for cross-border movement.[26]

Working with outsourcing partners who already operate within these regulatory systems provides international sponsors with a practical way to manage the complexity without building that expertise in-house

Proactive comparator sourcing strategies should account for the level of complexity, leverage experienced sourcing partners, establish those relationships early in protocol development, and include appropriate timelines.

Planning Ahead Pays Off

Manufacturing and supplying clinical trial materials for the US, EU, and UK markets requires sponsors to navigate significant differences in regulatory pathways, GMP expectations, packaging rules, labeling formats, and comparator sourcing. None of these differences are minor, and none can be addressed with a single global playbook.

Sponsors who plan for these differences early, rather than discovering them mid-program, avoid costly delays and rework. Working with outsourcing partners who already operate within these regulatory systems provides international sponsors with a practical way to manage the complexity without building that expertise in-house.

Part II of this article addresses cross-border logistics, customs declarations, clinical trial supply management, temperature-controlled logistics, and more.

REFERENCES

1. Mahin Arastu, "3 Key Differences between Investigational New Drug (IND) Applications and Clinical Trial Applications (CTA) Regulatory Submissions," Feb 28 2026. https://www.acumenmedcom.com/acumen-blog/3-key-differences-between-investigational-new-drug-ind-applications-and-clinical-trial-applications-cta-regulatory-submissionsnbspnbsp

2. Worldwide Clinical Trials, "Navigating the Global Clinical Landscape: CTA or IND for Your First-in-Human Study?" Blog, March 7, 2024. https://www.worldwide.com/blog/2024/03/ind-or-cta-for-first-in-huma-study/

3. Zermeena, "IND vs CTA: Complete FDA and EMA Clinical Trial Authorization Guide July 2026," Assyro blog, May 1, 2026 https://www.assyro.com/blog/ind-vs-cta

4. 21 CFR Part 312 - Investigational New Drug Application

5. EU Clinical Trials Regulation 536/2014

6. https://www.legislation.gov.uk/uksi/2004/1031/contents

7. https://www.legislation.gov.uk/uksi/2025/538

8. MHRA, "Guidance: Clinical trials for medicines: apply for authorisation in the UK," June 25, 2026. https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk

9. https://www.ich.org/page/ctd

10. CFPIE, "Global GMP Standards Demystified: Comparing FDA, EU, WHO, and Beyond," April 21, 2025. https://www.cfpie.com/global-gmp-standards-demystified-comparing-fda-eu-who-and-beyond

11. Siegfried Schmitt, "Complying with European versus US GMPs," BioPharm International 48 (4), p 26 (2025). https://www.biopharminternational.com/view/complying-with-european-versus-us-gmps

12. https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-210

13. https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-211

14. EC. EudraLex–Volume 4–Good Manufacturing Practice (GMP) Guidelines. https://health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-4_en

15. https://www.gmp-compliance.org/files/guidemgr/guideline_adopted_1_en_act_part1_v3.pdf

16. EC. Annex 16–Certification by a Qualified Person and Batch Release. EudraLex–Volume 4, https://health.ec.europa.eu/document/download/20c41532-33d5-4635-ae80-8735d3d09fe0_en?filename=v4_an16_201510_en.pdf

17. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/interpretation-union-format-manufacturer-importer-authorisation_en.pdf

18. PCS Netherlands, "What is a Manufacturing and Import Authorization in pharma?" February 23, 2024. https://www.pcs-nl.com/en/post/what-is-a-manufacturing-and-import-authorization-in-pharma

19. EC. Annex 1–Manufacture of Sterile Medicinal Products. EudraLex–Volume 4. https://health.ec.europa.eu/document/download/e05af55b-38e9-42bf-8495-194bbf0b9262_en?filename=20220825_gmp-an1_en_0.pdf

20. Petty Fu, "Pharma Packaging Standards: FDA, EU GMP, ISO & Serialization Requirements Explained," JINLU Packaging Blog, May 12, 2026. https://www.jinlupacking.com/blogs/pharma-packaging-standards-guide/

21. Inbal Hacmon, "Differences in Investigational Product Labeling for Clinical Trials Requirements Between the US and the EU," January 9, 2024. https://adres.bio/differences-in-investigational-product-labeling-for-clinical-trials-requirements-between-the-us-and-the-eu/

22. Lotte K. McNamara, "Practical Considerations for EU Labeling Requirements of Investigational Drug Products following Annex VI Adoption and Amended CTR regulation No 536/2014," BDO Insights, May 09, 2024. https://www.bdo.com/insights/industries/life-sciences/practical-considerations-for-eu-labeling-requirements-of-investigational-drug-products-following-ann

23. Freyr, "Designing Packaging Labels for Blinded Clinical Studies," Blog, July 11, 2025. https://www.freyrsolutions.com/blog/designing-packaging-labels-for-blinded-clinical-studies

24. Hector Oyarzun and Salman Pathan, "Evolving Needs for Comprehensive Clinical Comparator Sourcing Strategies," Pharma's Almanac, July 1, 2020. https://www.pharmasalmanac.com/articles/evolving-needs-for-comprehensive-clinical-comparator-sourcing-strategies

25. World Courier, "New U.S. rules for comparator sourcing and what trial sponsors need to know," Insights, September 10, 2025. https://www.worldcourier.com/insights/new-us-rules-for-comparator-sourcing-what-trial-sponsors-need-to-know

26. World Courier, "High-demand, hard to access — how to source specialty drugs for global trials," Insights, June 10, 2025. https://www.worldcourier.com/insights/how-to-source-specialty-drugs-for-global-trials

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