Novyra eSystems

Why Your GxP System Should Start Before Your First Clinical Trial

A Strategic Brief for Pre-Clinical and Early-Stage Biotech Companies

Although regulatory frameworks differ between jurisdictions, expectations are increasingly aligned through ICH guidance. FDA submissions rely on Investigational New Drug (IND) and later New Drug Applications (NDA) or Biologics License Applications (BLA). In Europe, sponsors submit Clinical Trial Applications (CTA) through Clinical Trials Information System (CTIS) and ultimately marketing authorization applications.

Regardless of jurisdiction - whether in the US or Europe - regulatory expectations are broadly the same: data integrity, traceability, oversight, and the reliability of development data.

The Objection We Hear - and Why It's Costly

"We're too early for a GxP system. We already have a fit-for-purpose setup and we'll talk when we get to clinical stage."

It's a reasonable-sounding position. It's also one of the most expensive assumptions a small biotech can make.

By the time a company reaches IND (Investigational New Drug) submission - let alone clinical stage - the regulatory clock has already been running for years. The non-clinical tox studies completed last year, the API batches manufactured for those studies, the SOPs your CRO followed, the stability samples sitting in a freezer - all of it will be scrutinized. And if the underlying systems and data were not GxP-compliant when those activities happened, no amount of retroactive effort can fully fix that.

For European development, the same logic now applies with even more operational visibility. Since CTIS (Clinical Trials Information System) became the EU entry point for clinical trial applications, sponsors need controlled, complete and traceable documentation for Clinical Trial Application (CTA) submission, assessment, substantial modifications and ongoing trial supervision. The EU process does not replace the US IND logic; it adds another reason to build the foundation early.

This document outlines the concrete regulatory requirements that apply at the pre-clinical stage, why a GxP system is the only practical way to meet them, and what happens to companies that try to catch up later.

1. Non-Clinical Data: SEND[1] Compliance Is Not an NDA[2] Problem - It's an IND[3] Problem

What SEND Is

The Standard for Exchange of Nonclinical Data (SEND) is the FDA's mandatory data format for non-clinical study submissions. It is part of the CDISC standards family, alongside SDTM (Study Data Tabulation Model) and ADaM (Analysis Data Model) for clinical data, and governs how toxicology and pharmacology study data must be structured and submitted.

SEND is a US FDA submission data standard; it is not an EMA/CTIS requirement in the same form. But the underlying principle is shared across regulatory pathways: non-clinical evidence must be complete, traceable, reviewable and usable when the first clinical trial application is prepared.

[1] Standard for Exchange of Nonclinical Data
[2] New Drug Application
[3] Investigational New Drug

The Critical Rule That Most Biotechs Miss

The SEND requirement is triggered by the study start date, not by the submission date.

SEND datasets are required for single-dose, repeat-dose, carcinogenicity, cardiovascular safety pharmacology, respiratory safety pharmacology, and embryo-fetal development (EFD) studies whose start dates fall after the thresholds in the FDA Data Standards Catalog. For most companies operating today, those thresholds have long passed:

- SEND v3.1 is required for IND-supporting studies started after March 2020.
- Since September 2021, CBER and CDER may reject electronic submissions that do not meet the specified data criteria - not issue a warning, reject.

This means: a company that ran its pivotal GLP tox studies in 2022 or 2023 using Excel outputs and PDF reports from a CRO, without planning SEND deliverables at the time of the study, cannot assume that late-stage reformatting will be straightforward. If the raw data, metadata and study structure were not captured appropriately, the options are expensive: a remediation exercise with the CRO, complex data reconstruction, or in the worst case, repeating the study.

For an EU CTA, the issue is different, but the business risk is similar. CTIS assessment relies on a coherent dossier, including the evidence supporting the risk-benefit assessment and the IMPD quality package. If the non-clinical rationale, study reports, source-data traceability and vendor oversight are fragmented, the sponsor may struggle to answer questions during assessment or later inspection.

What a GxP System Enables

An eTMF and non-clinical data management module within your GxP system ensures:

- SEND-compatible data capture and deliverable planning are built into the study setup workflow from day one, where applicable.
- Study datasets, define files, reviewer guides, final reports and key correspondence are managed as controlled deliverables, not as disconnected files.
- Data provenance and traceability are maintained throughout, satisfying the ALCOA+ standard (Attributable, Legible, Contemporaneous, Original, Accurate - plus Complete, Consistent, Enduring, Available).
- Non-clinical evidence remains usable for US IND activities, EU CTA preparation through CTIS and later marketing application work.
- The submission package is audit-ready at filing, not assembled under deadline pressure.

The Practical Implication for Your IND Timeline

FDA will review the technical conformance and usability of your SEND datasets before the scientific narrative can carry the argument. A submission with non-conformant or missing SEND data can trigger a technical rejection or, at minimum, a data quality review that adds weeks or months to your IND clock. For a small biotech, a 30, 60, or 90-day delay at IND filing is not a bureaucratic inconvenience - it is a burn rate event.

The European implication is not a copy of SEND. It is that CTIS submissions and requests for information run on defined timelines. If the sponsor needs to reconstruct non-clinical evidence while the clock is running, the problem is no longer just document management - it becomes a development timeline risk.

2. GLP Compliance (21 CFR Part 58): The Quality System Behind Every Tox Study

Good Laboratory Practice is not an aspiration. It is a legal requirement codified in 21 CFR Part 58 for US submissions, and equivalent GLP expectations apply internationally through OECD GLP principles and EU Member State GLP compliance frameworks. The rule applies to every non-clinical safety study intended to support a regulatory submission - regardless of whether you run that study in-house or outsource it to a CRO.

What GLP Actually Requires - Right Now

A formal Quality Assurance unit. GLP mandates an independent QA function that:

- Maintains a master schedule of all non-clinical studies.
- Inspects each study at defined intervals to ensure integrity.
- Reviews final study reports for accuracy against methods and SOPs.
- Issues written status reports documenting problems and corrective actions taken.

Standard Operating Procedures - in controlled, auditable form. GLP requires written SOPs for receipt, identification, storage, handling, mixing, and sampling of test and control articles; animal care, transfer, placement, and identification; equipment calibration and maintenance; data recording, storage, and retrieval. These SOPs must be version-controlled, approval-tracked, and accessible to study personnel at the point of use.

Study protocols reviewed and approved before study initiation. Every study must have a written protocol reviewed by the Study Director that defines purpose, experimental design, bias controls, and other essential elements. Protocol deviations must be documented, justified, and approved - not quietly corrected.

Complete, traceable raw data. Every result must be traceable to the analyst, instrument, and sample that generated it, recorded in real time, and preserved without alteration. Amendments must be logged and justified. A printout from an unvalidated system is not raw data under GLP; if the underlying electronic record was never captured, the printout cannot serve as a substitute.

Training records for all study personnel. Every person involved in or supervising a GLP study must have documented training records demonstrating competency for their role.

Why "We Use a CRO" Is Not a GxP Strategy

Many early-stage biotechs assume that outsourcing tox studies to a GLP-certified CRO transfers all compliance responsibility. It does not.

As the sponsor, you are responsible for the integrity of your IND package and for the credibility of your EU CTA dossier. Regulators expect you to have:

- A supplier qualification process documenting how you selected and audited the CRO.
- Oversight records demonstrating your QA function reviewed the study conduct.
- A copy of all study protocols, deviations, amendments and final reports in your own controlled archive.
- Confidence that the data you received is in the right structure, format and metadata context for your submission pathway.
- A clear handover process for data, reports and source documentation from CRO to sponsor-controlled systems.

A CRO operating under its own GLP system generates data that is compliant for its archives. Getting that data into your eTMF in submission-ready format, with the right metadata, traceability and, where applicable, SEND structure, is your responsibility. A GxP system makes that handoff systematic rather than ad hoc.

3. CMC (Chemistry, Manufacturing and Controls) Documentation: The IND Clock Starts Earlier Than You Think

What the IND Requires in CMC

The Chemistry, Manufacturing and Controls section of an IND is not a formality - it is the FDA's primary assurance that the investigational drug is safe to administer to humans. Even for a Phase 1 IND, FDA requires:

Drug Substance (Module 3.2.S equivalent):

- Manufacturing process description with in-process controls.
- Characterisation data: structure, physicochemical properties, biological activity, purity, impurity profile.
- Analytical method descriptions and validation data, or a development-stage justification for the current level of method qualification.
- Batch release data from representative batches - the actual material to be used in clinical studies.

- Stability data under defined storage conditions, with a stability commitment for ongoing testing.
- Reference standard documentation.

Drug Product (Module 3.2.P equivalent):

- Formulation development rationale.
- Manufacturing process and controls for the clinical trial material.
- Container-closure system characterisation.
- Batch records from clinical batch manufacturing.
- Analytical specifications and test results.
- Stability data for the finished product.

The key point: all of this documentation must exist, be controlled, and be traceable before the IND is submitted. It is not created at submission - it is the record of what already happened during pre-clinical development.

In Europe, the equivalent operational pressure appears in the Investigational Medicinal Product Dossier (IMPD), including the quality information that supports the CTA submitted via CTIS. The terminology differs; the need for controlled, traceable CMC evidence does not.

When CMC Documentation Starts

CMC-relevant activities begin at the very first synthesis or expression of drug substance:

- Discovery / early research: Method development notebooks, reagent records, cell line characterisation documents.
- Process development: Batch records for development batches, process parameter studies, scale-up reports, deviation records.
- Analytical development: Method development reports, qualification/validation protocols and results, reference standard COAs.
- Stability: Stability protocols placed on stability at the first formal batch, time-point data captured systematically.
- Supplier management: Certificate of Analysis for all raw materials, excipients, and biologics; supplier qualification records.

If any of these are captured in lab notebooks, shared drives, or email threads without version control or audit trails, they are not reliably usable in a submission. FDA reviewers and EU assessors may ask for primary documentation or clarification. "We have the data somewhere" is not an adequate answer during IND review, CTA assessment, due diligence or inspection.

The Change Control Problem

One of the most common CMC-related IND deficiencies is inadequate documentation of manufacturing changes. Drug substance processes evolve substantially between early development batches and clinical material batches. FDA expects a comparability trail demonstrating that the material used in tox studies is representative of - or demonstrably comparable to - the material proposed for clinical use.

The same comparability logic matters for the IMPD quality section in a European CTA. Under CTIS, requests for information may come within structured assessment timelines. Without a formal change control system running from the beginning of process development, that comparability trail is nearly impossible to reconstruct. A GxP system with integrated change management makes comparability documentation a routine output of the development process rather than a retroactive burden.

GMP for Clinical Trial Material

The API and drug product used in tox studies, and certainly the material used in Phase 1, must be manufactured under GMP. This means:

- Batch records executed against approved master batch records.
- In-process and release testing against approved specifications.
- Deviation and out-of-specification (OOS) investigation records.

- Environmental monitoring data for sterile products.
- Stability programme records.
- Quality agreements and supplier oversight records, especially when manufacturing is outsourced.

All of these are eQMS functions. Running them through a validated, audit-trailed system from the first GMP batch is the baseline - not an upgrade.

4. Pre-IND and INTERACT Meetings: You Need Documentation to Walk In the Door

The Meeting Landscape

Before submitting an IND, FDA offers structured interaction opportunities. The most relevant for early-stage biotechs are:

- INTERACT meetings - available very early in development, covering CMC, non-clinical, and clinical strategy for innovative products still in the discovery or early pre-clinical phase.
- Pre-IND (Type B) meetings - typically held 6–12 months before a planned IND submission, covering non-clinical study design, CMC, and initial clinical protocol.

These meetings are not mandatory, but for a small biotech navigating a novel mechanism or complex modality, they are effectively essential. FDA's feedback at a pre-IND meeting can validate your tox study design before you run it - saving months and millions if the agency's requirements differ from your assumptions.

For European development, the comparable early-engagement route is EMA scientific advice or, depending on the question and development strategy, national scientific advice. EMA scientific advice is prospective: it helps developers discuss how to generate robust evidence for a medicine before major development decisions become locked in. For some products, protocol assistance or other specialised routes may also be relevant.

What You Need to Bring

To request a pre-IND meeting, you must submit a formal briefing package 30 days before the meeting date, containing: a product description and development rationale; a summary of CMC development to date; a summary of non-clinical data already generated; specific, well-formed questions for the agency.

For EMA scientific advice, the same operational principle applies: the value of the interaction depends on the quality of the development evidence and the clarity of the questions. A sponsor cannot ask for meaningful regulatory advice if it cannot retrieve, explain and defend the documentation behind its assumptions.

If your CMC documentation is sitting in an uncontrolled state across multiple CRO reports, spreadsheets, and email attachments, assembling a coherent, credible briefing package is a significant exercise. If your non-clinical data has not been captured in submission-ready formats or linked to controlled study documentation, your data summaries cannot reference a reliable evidence base.

A GxP system transforms this from a scramble into a structured output. The documents and data already exist in controlled, retrievable form. The briefing package, EU scientific advice package, CTA dossier or CTIS response is a subset of what you can already pull from the system.

5. 21 CFR Part 11: Your "Fit-for-Purpose" System Is Probably Non-Compliant Today

21 CFR Part 11 governs electronic records and electronic signatures in FDA-regulated activities. It applies to any company - at any stage of development - that chooses to maintain GxP records in electronic form. There is no exemption for early-stage companies.

In Europe, the equivalent conversation typically includes EU GMP Annex 11 for computerized systems, Annex 13 expectations for investigational medicinal products where applicable, and broader data integrity expectations across GxP records. The detailed legal framework differs, but the practical question is the same: can you prove that electronic records are controlled, complete, attributable, protected from unauthorised change and retrievable?

The requirements include: validated electronic systems; complete, time-stamped audit trails; access controls with unique user identities; electronic signatures that meet specific legal standards.

What this means in practice:

- Excel files used to capture stability data: not compliant if they lack controlled access, audit trail, version control and approved review.
- Shared drive folders used to store batch records: not compliant if there is no reliable access control, version control or change history.
- Email threads used to manage SOP review and approval: not compliant if there is no controlled workflow, signature record or durable approval trail.
- Google Docs used for protocol development: not compliant if collaborative editing history is treated as a regulatory audit trail without defined GxP controls.
- CRO/CDMO deliverables received only as PDFs: not sufficient if metadata, source traceability, transfer responsibilities and controlled archival are not defined.

If your current "fit-for-purpose" system consists of these tools - and for most early-stage biotechs it does - you are generating GxP records in a form that may not support inspection, IND review, CTA assessment or partner due diligence. When regulators or partners ask about your electronic systems, the answer "we used shared drives and Excel" will prompt follow-up questions. The answer "we operate a validated electronic QMS and eTMF with controlled workflows, audit trails and role-based access" changes the conversation.

6. Investor and Partner Diligence: GxP Readiness Is a Valuation Signal

Beyond direct regulatory risk, there is a commercial dimension to early GxP adoption that increasingly matters to sophisticated life sciences investors and potential partners.

Series A / B Diligence

Technical diligence for a biotech fundraise now routinely includes assessment of:

- Data integrity of pre-clinical datasets supporting the investment thesis.
- Compliance status of CMC documentation and IMPD/IND readiness.
- Whether the company's systems would survive a regulatory inspection at the proposed clinical stage.
- Organisational maturity indicators - quality culture, SOP coverage, training records, vendor oversight.
- Clarity on whether development evidence can support both US IND and EU CTA/CTIS pathways.

A company that can demonstrate a functioning, validated GxP system at Series A sends a signal that the scientific team understands the regulatory environment and has built compliance into the development process rather than treating it as a future problem.

Partnership and Licensing

If the commercial strategy includes out-licensing or partnering with a larger pharmaceutical company, that partner will conduct technical due diligence on your data package. Large pharma technical teams are experienced at identifying data integrity gaps. Undocumented deviations, missing audit trails, non-SEND-compliant tox datasets, unclear IMPD quality documentation and uncontrolled CMC records will surface. These gaps depress valuations and can kill deals.

CRO and CDMO Qualification

As you engage larger, more sophisticated CROs and CDMOs, they will ask about your quality system. A contract manufacturing organisation supplying clinical trial material under GMP will require you, as the sponsor, to have a quality agreement and demonstrate oversight capability. Without a functioning QMS, you are not a credible counterparty.

7. The Retroactive Remediation Problem: Why "We'll Fix It Later" Fails

The most compelling argument for early GxP adoption is the cost and, more importantly, the limits of retroactive remediation.

What Remediation Looks Like

If a company reaches IND submission, EU CTA submission through CTIS - or worse, clinical stage - with a non-GxP data history, the remediation pathway includes:

- SEND conversion: If the raw CRO data still exists in structured form, SEND conversion is expensive and time-consuming. If it does not, the study may need to be repeated.
- CTIS dossier reconstruction: If CTA-relevant evidence, Part I/Part II documents, IMPD quality information and sponsor oversight records are scattered, answering requests for information becomes a time-critical reconstruction exercise.
- Data migration and validation: Historical data in legacy systems or unvalidated environments must go through a formal migration plan with validation and data verification before it can be cited in submissions.
- Access control remediation: Shared credentials across electronic systems must be eliminated and replaced with individually authenticated access - historically.
- Audit trail reconstruction: Where audit trails were not enabled, there is no retroactive fix. The record is incomplete by definition.
- Study repeat: In the most serious cases - where a pivotal GLP study is found to have undocumented deviations or non-compliant data capture - regulators can challenge the usability of the study. An expensive tox study conducted at a reputable CRO with clean safety findings can lose much of its value if the GLP documentation record is not compliant.

The Timeline Cost

A biotech that discovers GxP gaps at IND filing faces delays of weeks to months resolving FDA queries. A company that discovers gaps during EU CTA assessment may lose valuable time responding to requests for information, preparing substantial modifications or reconciling Member State questions. A company that discovers gaps before an NDA, Biologics License Application (BLA) or MAA inspection can face much longer delays, remediation commitments or refusal-to-file / non-approval risks.

The Arithmetic

The cost of implementing a validated GxP system at the pre-clinical stage - eQMS, eTMF, non-clinical module, CMC document management - is a small fraction of the cost of a single tox study repeat, a six-month IND delay, a delayed CTA, or an NDA/BLA/MAA remediation exercise. For a company spending $2–5M per year on pre-clinical activities, the compliance infrastructure is not a significant additional cost. The risk of not having it, measured in lost time, repeated studies, failed submissions and weakened fundraising rounds, is substantial.

Summary: What a GxP System Actually Manages at Pre-Clinical Stage

Regulatory Area	Specific Requirement	GxP Module
Non-Clinical / Tox	SEND-formatted datasets for all qualifying FDA studies (mandatory at IND when applicable)	eTMF / Non-Clinical module
Non-Clinical / Tox	GLP compliance: QA unit, SOPs, study protocols, deviation records	eQMS
Non-Clinical / Tox	Training records for all study personnel	eQMS
Non-Clinical / Tox	CRO / supplier qualification and audit records	eQMS
CMC	Batch records for API and drug product (GMP)	eQMS / CMC module
CMC	Analytical method development and validation records	eQMS / CMC module
CMC	Stability protocols and data - from first formal batch	CMC module
CMC	Change control for manufacturing process evolution and tox-to-clinical comparability	eQMS
CMC	Supplier COAs and raw material qualification records	eQMS
Regulatory	Pre-IND and INTERACT meeting briefing packages	eTMF

Regulatory	EMA scientific advice / national scientific advice packages	eTMF
Regulatory	CTA / CTIS dossier documents, including Part I / Part II evidence and IMPD support	eTMF + eQMS + CMC module
All	21 CFR Part 11 / EU Annex 11 controls: audit trails, e-signatures, access control	eQMS + eTMF
All	ALCOA+ data integrity across all GxP records	eQMS + eTMF

The Conversation to Have

When a pre-clinical biotech tells you they already have a fit-for-purpose system and will think about GxP at clinical stage, the questions to ask are:

1. "Your next repeat-dose tox study - is the data being captured in SEND format from study initiation where required? Because your US IND submission may face technical rejection if applicable SEND data are missing or non-conformant."
2. "When you file your IND, the CMC section will reference batch records for the API used in those tox studies. Are those batch records in a controlled, audit-trailed system that FDA can inspect?"
3. "When you submit your first EU CTA through CTIS, can you retrieve the IMPD quality evidence, non-clinical rationale, protocol history, vendor oversight records and Part I / Part II documents without reconstruction?"
4. "If an investor or potential partner runs technical due diligence on your pre-clinical data package next year, will the data integrity record hold up?"
5. "If FDA, an EU Member State authority or a partner asks about the electronic systems used to generate and store your pre-clinical and CMC data, what will your answer be?"

➔ The GxP system is not the story for when clinical trials start. It is the foundation on which the clinical programme stands.

This brief is intended as a strategic discussion document. Regulatory requirements vary by product type, modality, jurisdiction and development strategy. Companies should engage qualified regulatory affairs professionals to assess their specific compliance obligations.

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