FDA eSubmission Services

ASPHALION
Knowledge from experience

25 years

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FDA eSubmission Services

Our eSubmission department can support you across a full range of activities for the **U.S. Food and Drug Administration (FDA).**

- **Consultancy** support for Regulatory Operations activities.
- Dossier document **templates** creation.
- Documents **formatting** to agreed ICH and FDA standards.
- Administrative **Module 1** issuance.
- **eCTD** Publishing.
- Portals **Submission**.
- Creation of **Structure-Data Files (SDF).**
- Creation and maintenance of **Structured Product Labeling (SPL)**.
- Creation of **Datasets (DS)**.
- **FDA Adverse Events Reporting** through eCTD and ICH E2B(R3).
- **US Agents** Support through our network of resident agents.
- **DMF Representatives**.

Don't miss the chance to download our **FDA brochures** and connect with our regulatory operations expert.

IND PROCEDURES
Regulatory Assistance

The US law requires that a drug be the subject of an approved marketing application before it is transported across state lines, e.g. to clinical investigators. The IND is the way for the sponsor to get this exemption from the FDA. So, before a new drug in a preclinical development status can be used for clinical studies, an IND has to be submitted.

IND Lifecycle summary

Steps	Regulatory Activity		Description	Regulatory timings
IND Application	1. PRE-IND MEETING		This is an opportunity for sponsors/ investigators to **gain valuable feedback on the data necessary** to warrant IND submission.	Scheduled Meeting Date: 1 - 4 months from receipt of request
	2. IND SUBMISSION		The **FDA** has an opportunity to **review the IND for safety** to assure that research subjects will not be subjected to unreasonable risk. FDA reviewers may request information during the review period and the Sponsor is expected to respond quickly with answers.	30 days FDA review
	3. REVIEW OUTCOMES	ACTIVE	**Some review divisions** may issue a "safe to proceed letter". Otherwise, "no news is good news".	0 days
		CLINICAL HOLD	- **Full Clinical Hold:** A delay or suspension of all clinical studies under an IND. - **Partial Clinical Hold:** A delay or suspension of only part of the clinical studies under an IND.	30 days FDA revision after receipt of the response letter addressing the clinical hold deficiencies.
Once the IND is active:				
IND Maintenance Activities	AMENDMENTS		- **Protocol Amendments:** new protocols, changes in protocol or new investigators. - **Information Amendments:** new toxicology, chemistry (CMC) or other technical information or discontinuance of a clinical investigation	Submission within 30 days
	SAFETY REPORTING		Serious and unexpected **adverse reactions must be reported**.	Submission no later than 7-15 daysed.
	ANNUAL REPORTING		Report of the **progress of the investigation.** The annual report can be satisfied by submission of a DSUR	Submission within 60 days of the 1-year anniversary of IND effective date

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We can support you throughout the whole lifecycle of the IND procedure in a variety of activities:

- eCTD publishing of initial submissions
- eCTD publishing of maintenance activities:
  - Protocol Amendments
  - Information Amendments
  - Annual Reports
  - IND Safety reports
- Document formatting following FDA specifications
- Personalized templates
- eCTD Submission trough FDA Electronic Submissions Gateway (ESG)

EXTEDO
eRegulatory Affairs

Regulatory Solutions for US FDA INDs

- eCTDmanager: eCTD compilation and publishing for all US FDA submissions, including INDs.
- eSUBmanager: Viewing and reviewing of archived and in-progress electronic submissions.
- eDOCSmanager: Manage all your regulatory documents in a secure document management system.
- SafetyEasy: It handles the reporting and management of all serious and non-serious adverse events, including DSUR documentation.

FDA – FAERS (FDA Adverse Event Reporting System)

What is FAERS?

The FDA Adverse Event Reporting System (FAERS) is a database that contains adverse event reports, medication error reports and product quality complaints resulting in adverse events that were submitted to FDA.

FAERS Electronic Submissions Update

Currently, Premarketing and Postmarketing Safety Reporting can be done through eCTD format or E2B(R2) xml format, respectively.

Effective from April 1st, 2026, all submissions to FAERS must be submitted in **E2B(R3) XML format**.

	CURRENT	FUTURE
Pre-marketing (IND)	eCTD	ICH E2B (R3)
Post-marketing (NDA, BLA, ANDA)	ICH E2B (R2)	ICH E2B (R3)

Companies may choose to submit in ICH E2B (R3) format before the 2026 deadline. However please note that once a company submits in E2B(R3) format, it is not allowed to revert to previous formats or standards.

Submission Portals for FAERS

FAERS with E2B(R3) XML format can be submitted through the **FDA Electronic Submission Gateway (ESG)** or through the **Safety Reporting System (SRP)**.

More information regarding this process can be found at: https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions

FDA SPL (Structured Product Labeling)

The Structured Product Labeling (SPL) is a document markup standard developed by Health Level Seven (HL7). Adopted by FDA as a mechanism for exchanging product and facility information, using extensible markup language (XML).

Since October 31, 2005, labeling submissions to the FDA's Center for Drug Evaluation and Research **(CDER) must be in SPL format**. It became mandatory for submission to **CBER** in **October 15, 2008**.

SPL Types:

Labeler Code	Code to identify the labeler, needed for the NDC (National Drug Code)
Prescribing Information	Draft labeling SPL (of the package insert) with the eCTD
Product Drug Listings	Initial electronic listing, Updates and Annual Drug Listing Certification (between October 1st and December 31st).
GDUFA Self-Identification	Operators of facilities involved in the development and manufacturing of generic drugs. Annual renewal between May 1st and June 1st.
Establishment Registration	Listing of Establishments related with the manufacturing of any product approved in FDA. Annual renewal between October 1st and December 31st (for expedited updates to be provided within 30 days of a change).
LDR (Lot Distribution Reports)	Licensed manufacturers of products distributed under a BLA must submit every 6 months about the quantity of the product distributed.
REMS (Risk Evaluation and Mitigation Strategies)	All REMS documents submitted to FDA on or after December 28, 2022 must be in SPL format.

Asphalion Regulatory Services

We can support you throughout the whole SPL procedure in a variety of activities:

- SPL creation with available software like SPL XForms.
- SPL validation and troubleshooting.
- SPL pre-population templates.
- FDA submission (ESG NextGen or CDER Direct) and communication.
- Tailored trainings.
- Wider regulatory consulting.

Are you planning to send a submission to the FDA? Will this submission contain study data? If the answer to these 2 questions has been yes, this brochure may be of your interest!

FDA STUDY DATA

(aka. DATASETS)

Since September 15th, 2021, FDA applies the Technical **Rejection Criteria (TRC) for Study Data submitted in eCTD to CDER and CBER FDA divisions**

What is the Technical Rejection Criteria?

The TRC consists in an automated validation that occurs upon receipt of a submission.
If the submission fails eCTD validations in TRC, CDER/CBER will reject it.
TRC has been created by the FDA to ensure study data compliance with the required
electronic standards specified in the FDA Data Standards Catalog.

What procedures does TRC apply to?

NDAs, ANDAs, certain BLAs and commercial INDs.

For regulatory assistance, you can contact us at:

What studies does TRC apply to?
What do I have to submit to comply with TRC?

Data Type	Modules & Submodules	Center	Application Type	Study Start Date	Requirement
Non-clinical	4.2.3.1, 4.2.3.2, 4.2.3.4	CDER	NDA, BLA, ANDA	On/Prior to December 17, 2016	Submit simplified ts.xpt*
				After December 17, 2016	Comply with CDISC standards
			Commercial IND	On/Prior to December 17, 2017	Submit simplified ts.xpt*
				After December 17, 2017	Comply with CDISC standards
		CBER	NDA, BLA, ANDA, Commercial IND	On/Prior to March 15, 2023	Submit simplified ts.xpt*
				After March 15, 2023	Comply with CDISC standards
Clinical	5.3.1.1, 5.3.1.2, 5.3.3.1, 5.3.3.2, 5.3.3.3, 5.3.3.4, 5.3.4, 5.3.5.1, 5.3.5.2	CDER & CBER	NDA, BLA, ANDA	On/Prior to December 17, 2016	Submit simplified ts.xpt if study contains xpt dataset (other than ts-xpt)
				After December 17, 2016	Comply with CDISC standards
			Commercial IND	Rejection criteria not applied	

*Rejection criteria will be applied if a study report with one of the three file tags, "pre-clinical-study-report", "legacy-clinical-study-report", or "study-report-body" is included, and/or an xpt file (other than the ts.xpt) is submitted.

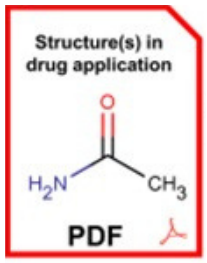
Are you holding a dossier in US?

If the answeris YES, this brochure may be of your interest!

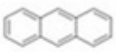
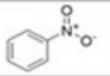
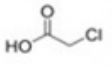
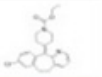
NEW US FDA Structure-Data File Format (SD)

Since 1st October 2022, applicants may now submit chemical structures as a single Structure-Data File

FDA dossier holders may now provide SD Files (.sdf) through eCTD across Module 3
New Method of Processing and Registering Chemicals



Sample SD File

Structure	ID	NAME	UNII	CAS	ROLE	APPLICATION_NUMBER
	Structure 1	anthracene	EH46A1TLD7	120-12-7	process impurity	MF-012345
	Structure 2	nitrobenzene	E57JCN6SSY	98-95-3	starting material	MF-012345
	Structure 3	2-chloroacetic acid	5GD84Y125G	79-11-8	starting material	MF-012345
	Structure 4	loratadine	7AJO3BO7QN	79794-75-5	active ingredient	MF-012345

The SD (Structure-Data) file is an extensible, portable text file encoding computer-readable chemical structures linked to associated data fields.

Asphalion can support your company creating the SD File using chemical software and publishing it in eCTD format within your FDA application dossier.