# Regional Submissions Atlas

An overview of regional submissions requirements

ASPHALION
Knowledge from experience

EXTEDO
eRegulatory Affairs

A year ago Asphalion, an international Scientific & Regulatory Affairs Consultancy, together with EXTEDO©, Regulatory Software Solutions for Life Sciences, started a collaboration to identify and **understand regional requirements at an electronic submissions level in certain countries.**

From this collaboration a series of infographics were born. Each month we have focused on a different non-european country. So far, this journey has taken us to: **Canada, US, Taiwan, South Africa, GCC, China, Australia and Switzerland.**

eSubmissions can be a major challenge; that is why we have compiled the **main country guidelines** in form of infographics as a compass to regional electronic submissions for everyone who might be interested.

**Vicente Tur**
Regulatory Affairs Director
Asphalion

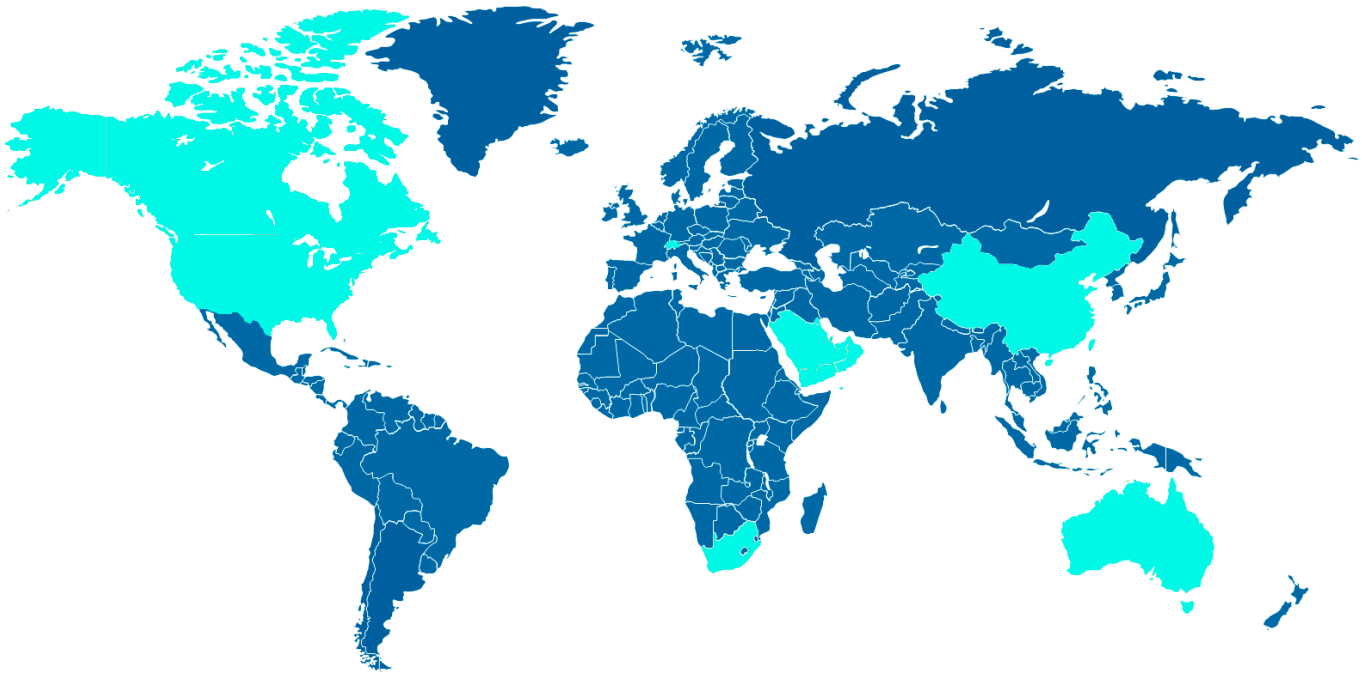
"At Asphalion, we have been at the forefront of electronic submission of regulatory information since the introduction of eCTD. As a result of our flexible support and dedicated project management, we can produce high quality submissions within critical timelines at any regional area.

We are an international Scientific and Regulatory Affairs consultancy that offers strategic advice, expert consulting, operational support, and full outsourcing services for all types of products in every therapeutic area."

**Gerhard Neurauter**
Head of Regulatory Competence Center
EXTEDO

“EXTEDO is a trusted source of regulatory knowledge around the world. Over the past 25 years, EXTEDO has supported many organizations and over 35 regulatory authorities with their eCTD processes – from development to implementation and operation.

Our experience and expertise in regulatory affairs have allowed us to provide support to a great variety of organizations in different regions to help them master their challenges efficiently.”



# What you need to know for **Submissions in Switzerland**

## Updates

Switzerland's regulatory authority **Swissmedic** started with submissions for pharmaceuticals in **eCTD format in 2009**. Since 2010 Swissmedic is using eCTD M1 version 1.5. Additionally, Swissmedic is also accepting **eDok format and paper submissions**.

A Swiss specialty in eCTD is the "galenic form", an old term for the pharmaceutical form of the pharmaceutical product. In Switzerland, there needs to be a M1 folder for each "galenic form". Product life cycles with more than one galenic form contain a common folder in Module 1.

An **overview of the documents that need to be submitted** for different regulatory activities is **available.**

Paper submissions are still possible, also Paper submission with eDok copy (Swissmedic's application submission format), paper version + electronic version (see Swissmedic website), but eCTD is encouraged. Other electronic submissions, **e. g. NeeS, will be rejected.**

Submissions can be uploaded via **Swissmedic's eGov portal or submitted on CD/DVD.**

### Drug Master File

- The **eCTD DMF dossier is a stand-alone dossier** and is independent of the marketing authorization eCTD dossier. Therefore, the DMF (DMF Holder, substance name) and the Drug Product (Authorisation Holder, tradename) consists of two individual eCTD life cycles.
- It is possible to **submit the marketing authorization application as eCTD and the DMF/ASMF** dossier as a paper dossier and vice versa.
- The **DMF/ASMF can be a hybrid submission**, which means that the restricted part is submitted in paper, whereas the open part is submitted in eCTD format as part of Module 3.
- **M1 Galenic Form is "common"**.
- **Envelope Elements:**
  - Swissmedic DMF number (if known)
  - DMF Holder
  - Galenic form name is common
  - Marketing Authorisation Number is n/a
- **Submission description:** the corresponding version of the DMF should be described in the element, e.g.: AP & RP Version 3.00 / description.

### Clinical Trial Application

- **Sponsor needs location/agency in Switzerland.**
- Submission on **CD/DVD and Paper,** including cover letter and application form.
- **eDoc Folder Structure on CD/DVD** since 01.01.2022 to reduce paper usage:
  - **Submit CD/DVD and form «Confirmation electronic submission»** to allow Swissmedic to review the submission from CD/DVD.
  - Form **«Confirmation electronic submission» needs to be submitted each time** with follow-up submissions on CD/DVD.

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**EXTEDO's Regulatory Solutions for Switzerland:**

- eCTDmanager: eCTD compilation and publishing for Swiss submissions.
- eSUBmanager: Viewing and reviewing of archived and in-progress electronic submissions.
- eDOCSmanager: Manage all your regulatory documents in a secure document management system.

ASPHALION Knowledge from experience

**Asphalion can give you support in the following areas:**

- eCTD compilation and publishing for Swiss submissions
- Document formatting
- Non-eCTD compilation and publishing
- Transition from non-eCTD to the mandatory eCTD format
- Submission to the agency according to the latest version of Swiss validation rules

**For further information, please contact:** ectd@asphalion.com | info@extedo.com

# What you need to know for **eCTD submissions in Australia**

## Updates

The Therapeutic Goods Administration (TGA) has started a staged transition to Electronic Common Technical Document-only (eCTD-only) for all regulatory submissions in Australia.

**1 November 2021 - eCTD-Only Stage 1:**

- New Chemical Entity Medicine (Type A)
- New Biological Entity Medicine (Type A)
- New Biosimilar Medicine (Type A)
- New Combination Medicine (Type B)

**1 June 2022 - eCTD-Only Stage 2:**

- Extension of Indications Medicine (Type C)
- Major Variation Medicine (Type F)
- New Generic Product (Type D)

**1 November 2022 - eCTD-Only Stage 3:**

- All remaining prescription medicine data including master files

eCTD format is now the accepted format for all prescription medicine applications.

TGA highly recommends to use a baseline when converting to eCTD from another format. However, you can choose to not baseline and submit a new application without resubmitting any previous documents.

The submissions of the sequences are via email, post or via TBS portal.

ASPHALION
Knowledge from experience

Asphalion can give you support in the following areas:

- eCTD compilation and publishing for TGA submissions
- Document formatting
- Non-eCTD compilation and publishing
- Transition from non-eCTD to the mandatory eCTD format
- Submission to the agency according to the latest version of TGA validation rules

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EXTEDO's Regulatory Solutions for Australia:

- eCTDmanager: eCTD compilation and publishing for Australian submissions.
- eSUBmanager: Viewing and reviewing of archived and in-progress electronic submissions.
- eDOCSmanager: Manage all your regulatory documents in a secure document management system.

**For further information, please contact:** ectd@asphalion.com | info@extedo.com

# What you need to know for **eCTD submissions in China (NMPA)**

## Updates

The final version of the specification v.1.0 was released at the end of September. Along with the release, it was announced that starting December 29, 2021, eCTD submissions for some submission types would be accepted.

### eCTD Submission Types

- Initial NDA for Type 1 and Type 5.1 Chemical drugs.
- Initial BLA for Type 1 of Therapeutical and Preventive Biological drugs.
- At this time, no lifecycle or variations or other types of dossiers, such as INDs can be submitted in eCTD format.

### eCTD Specifics in China

- A paper copy will need to be submitted as well within 5 working days of the eCTD submission acceptance.
- The paper cover letter should confirm that the paper and eCTD content is the same.
- M2 to M5 are defined according the ICH and M1 is unique for China.
- In M4 and M5, studies are expected to use study tagging files using the current ICH STF v2.2 DTD and valid values 5.0.
- The underscore is allowed to be used with file names.
- Bookmarks and hyperlinks are required for Chinese documents and are allowed for documents in English.
- Two documents are required for all submissions: cover letter and application form. Other files will be required as well depending on the application type.
- The validation criteria has both errors and warnings. If you send a submission with warnings, you will need to update your cover letter to explain why there are warnings and these have not been corrected.
- There is no gateway at this time and eCTD submissions will need to be submitted using labeled CDs/DVDs (single side only). Password protection is not allowed.
- Discs should be virus checked and an explanation letter will need to be provided with the details in a statement, together with the disc(s).

ASPHALION
Knowledge from experience

Asphalion can give you support in the following areas:

- Non-clinical and clinical development
- CMC
- Dossier writing
- Regulatory procedures
- Vigilance
- eSubmissions
- Data management

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EXTEDO's Regulatory Solutions for China:

- eCTDmanager: eCTD compilation and publishing for Chinese submissions.
- eSUBmanager: Viewing and reviewing of archived and in-progress electronic submissions.
- eDOCSmanager: Manage all your regulatory documents in a secure document management system.

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# What you need to know about **Taiwan (TFDA) submissions**

## Updates

As of January 1st, 2020, the use of the eCTD format is mandatory for NDA submissions and voluntary for all other submission types for pharmaceutical, biologic and radiopharmaceutical drugs for human use. We can guide you with the transition to eCTD to be filed for each submission after that.

### Drug Master File

Dossier ID at first submission from Receive Table Person

CTD compilation and publishing (Disk or Paper)

Local (TW) API plant submit DMF to TFDA (DMF Team)

Foreign API plant needs local API import Agent to submit

### Pharmaceuticals and biologicals

Dossier ID via ExPRESS portal

eCTD compilation and publishing
Document formatting

Conversion to eCTD format
Validation TFDA Validation Rules
Submission via ExPRESS portal

### Clinical Trial Application

CTA Application ID via ExPRESS portal

Pre-Meeting possible but not mandatory (to consult submission information compliance or not).

CTA submit on ExPRESS portal by un-eCTD format

Submission via ExPRESS, no paper version to provide

Submission via disk, a paper version is still to provide

After approval by TFDA – Finish clinical study.

Submit clinical close report

ASPHALION
Knowledge from experience

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- Non-clinical and clinical development
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- Dossier writing
- Regulatory procedures
- Vigilance
- eSubmissions
- Data management

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eRegulatory Affairs

Regulatory Solutions for Taiwan

- eCTDmanager: eCTD compilation and publishing for all Taiwanese submissions.
- eSUBmanager: Viewing and reviewing of archived and in-progress electronic submissions.
- eDOCSmanager: Manage all your regulatory documents in a secure document management system.
- SafetyEasy: Reporting and management of all serious and non-serious adverse events.

**For further information, please contact:** ectd@asphalion.com | info@extedo.com

# What you need to know about **South African (SAHPRA) submissions**

## Updates

- In 2013, the South African authority SAHPRA started accepting submissions in eCTD format for pharmaceuticals. They included an enhanced granularity in Modul 3.2.R which should be technically built with node extensions and subfolders.
- In 2019, SAHPRA introduced the additional “eSubmission” format, which will be accepted for a limited time. Currently it is not communicated how long this additional format will be accepted since SAHPRA currently reconsiders its eCTD roadmap.
- In 2020, SAHPRA updated section 3.2.R with new titles, but no update of the specification and eCTD structure. The previous titles can still be used in eCTD submission. We can guide you with the transitions in South African eCTD submissions.

### Master File (APIMF)

APIMF number (Dossier ID) allocated after submission

Open and closed part

Request SAHPRA portal access for closed part

Document formatting

CTD compilation and publishing “eSubmission” format

Submission via e-mail
“eSubmission” validation and Submission

### Pharmaceuticals and biologicals

Application number request before submission to SAHPRA

Document formatting

eCTD compilation and publishing

Conversion to eCTD format

Validation ZA Validation rules Submission (DVD/CD/USB)

### Clinical Trial Application

Predetermined dates for submission and obtain proof of delivery

Contact CTU (Clinical Trials Unit) to inform about submission

Application form accompanied by the prescribed fee

Document formatting in PDF Communication via e-mail

CTC (Clinical Trials Committee) meeting to discuss reports

ASPHALION
Knowledge from experience

Asphalion can give you support in the following areas:

- Non-clinical and clinical development
- CMC
- Dossier writing
- Regulatory procedures
- Vigilance
- eSubmissions
- Data management

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eRegulatory Affairs

EXTEDO's Regulatory Solutions for South Africa:

- eCTDmanager: eCTD compilation and publishing for all South African submissions.
- eSUBmanager: Viewing and reviewing of archived and in-progress electronic submissions.
- eDOCSmanager: Manage all your regulatory documents in a secure document management system.
- SafetyEasy: Reporting and management of all serious and non-serious adverse events.

**For further information, please contact:** ectd@asphalion.com | info@extedo.com


# Gulf Cooperation Council (GCC)
## Regulatory Services

### Updates

Gulf Cooperation Council countries (Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and the United Arab Emirates) have implemented eCTD format for submissions as per the following schedule:

- Saudi Arabia (July 17th, 2016)
- United Arab Emirates (October 1st, 2017)
- Oman (January 1st, 2015)
- Bahrain (November 1st, 2016)
- Qatar (optional as of September 1st, 2019, and mandatory starting September 1st, 2020)

GCC countries follow the GCC eCTD specifications, common for the entire region. This includes a specific Module 1.

Asphalion ensures that eCTD submission will always follow the most updated Module 1 specifications and validation rules (current Module 1 version for GCC Countries is v1.5).

When needed or required, Asphalion can give you support on preparing physical media to be exchanged with the Regulatory Authorities (CD/DVD or paper copies).

### Registration procedures

- National Procedure in one specific country
- Centralized Procedure in all GCC countries simultaneously through the Central Gulf Committee for Drug Registration

### Submission Types

Most relevant are:

- ASMF
- MAA (Biological, Generic,
- New chemical Entity or Radiopharmaceuticals)
- Reformatting from any format to eCTD (Baseline)
- Renewal
- Variation (Type 1 or Type 2)

ASPHALION
Knowledge from experience

Asphalion ensures that eCTD submission will always follow the most updated Module 1 specifications and validation rules (current Module 1 version for GCC Countries is v1.5).

When needed or required, Asphalion can give you support on preparing physical media to be exchanged with the Regulatory Authorities (CD/DVD or paper copies).

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EXTEDO's Regulatory Solutions for GCC:

- eCTDmanager: eCTD compilation and publishing for GCC submissions.
- eSUBmanager: Viewing and reviewing of archived and in-progress electronic submissions.
- eDOCSmanager: Manage all your regulatory documents in a secure document management system.
- SafetyEasy: Reporting and management of all serious and nonserious adverse events.

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# What you need to know about Health Canada

## Updates

As of October 1st, 2020, the use of the Regulatory Enrolment Process (REP) is mandatory for pharmaceutical, biologic and radiopharmaceutical drugs for human use. We can guide you with the transition to REP and with all the REP templates (RT, PI and CO) to be filed for each submission thereafter.

### Flowchart

**Master Files (types I-IV)**

- Dossier ID request
- **eCTD** compilation and publishing
- **non-eCTD** compilation and publishing
- Document **formatting**
- Conversion to eCTD format

**Pharmaceuticals and Biologics**

- Dossier ID request
- **eCTD** compilation and publishing
- Document **formatting**
- Conversion to eCTD format
- Implementation and lifecycle of **REP**

**Clinical Trial Applications**

- Dossier ID request
- **Pre**-Clinical Trial Application Consultation Meeting (Pre-CTA)
- Clinical Trial **Application** (CTA)
- Clinical Trial Applications – **Amendments**

**VALIDATION**
(HC validation rules)

**SUBMISSION**
(CESG)

ASPHALION
Knowledge from experience

### Regulatory Services for Health Canada

- eCTD compilation and publishing for all Health Canada submissions (Master Files, Pharmaceuticals/Biologics and Clinical Trial Applications).
- Transition from non-eCTD to the mandatory eCTD format.
- Submission package fulfills all the strict requirements of the agency and validation according to the latest version of Health Canada validation rules.
- Submit to Health Canada on your behalf via the Common Electronic Submissions Gateway (CESG).

EXTEDO
eRegulatory Affairs

### Regulatory Solutions for Health Canada

- eCTDmanager: eCTD compilation and publishing for all Health Canada submissions.
- eSUBmanager: Viewing and reviewing of archived and in-progress electronic submissions.
- eDOCSmanager: Manage all your regulatory documents in a secure document management system.

**For further information, please contact:** ectd@asphalion.com | info@extedo.com

# 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.<br>FDA reviewers may request information during the review period and the Sponsor is expected to respond quickly with answers. | 30 days<br>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.<br><br>- **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.<br>- **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.**<br>The annual report can be satisfied by submission of a DSUR | Submission within 60 days of the 1-year anniversary of IND effective date |

ASPHALION
Knowledge from experience

### Regulatory Services

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)

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### 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.

**For further information, please contact:** ectd@asphalion.com | info@extedo.com