

Regional Information (3.2.R and Module 1)

Write the US and EU regional information (3.2.R) and the CMC items of Module 1: the manufacturing establishments, the environmental assessment or categorical exclusion, the EU environmental risk assessment, the manufacturers in the application form and the QP declaration.

WRITES

3.2.R Module 1

PRODUCT TYPE

Small molecule and biologics

GUIDANCE IT FOLLOWS

ICH M4Q(R1) 3.2.R; FDA M4Q guidance and Form FDA 356h; 21 CFR 25.15, 25.31 and FDA Environmental Assessment of Human Drug and Biologics Applications (1998); EU Notice to Applicants Volume 2B; EMA process validation guideline (EMA/CHMP/CVMP/QW Regulation (EU) 2017/745 Article 117; EU GMP Annex 16; EMEA/CHMP/SWP/444 Rev. 1 (ERA)

TIME TO LEARN

About 20 minutes with the example

Open the tool at <https://app.cmcfy.com/app/regional-information.html>. This guide is also online at <https://cmcfy.com/guides/regional-information.html>

1. What this module does

You list the manufacturing and testing sites with their role, country, FEI or DUNS number and EU manufacturing authorisation or GMP certificate, the CEPs and master files you reference, and the

regional items (executed batch records, method validation package, comparability protocols, process validation scheme, device).

The tool calculates the US expected introduction concentration (EIC) to see whether a categorical exclusion under 21 CFR 25.31 applies, and the EU predicted environmental concentration in surface water (PEC_{sw}) to see whether an ERA Phase II is needed. It checks that an EEA site releases batches, that every site has the identifiers each region needs, and that a letter of access exists for each master file.

What you get

- US: 3.2.R regional information, establishment list for Form 356h, and the 1.12.14 environmental analysis (categorical exclusion claim or EA).
- EU: 3.2.R regional information, manufacturers for the application form, QP declaration basis and the 1.6 environmental risk assessment.

2. Before you start

Have these ready. You can still start with the example data and replace it piece by piece.

- Each site's name and address, country, role, FEI or DUNS, MIA or GMP certificate and last inspection or audit.
- CEPs, DMFs and ASMFs referenced, with letters of access.
- Maximum daily dose, expected annual production in year five and log K_{ow} of the active substance.
- Executed batch records, method validation package and any comparability protocols (US); process validation scheme, device status and QP declaration basis (EU).

Your data stays on your computer. The bar under the title counts every network request the page makes; it stays at 0 because your data never leaves your computer. [Download offline](#)

[copy](#) saves a single file that opens from your own computer with all network access blocked, for air-gapped PCs.

3. Step by step with the example

Open the tool at app.cmcfy.com/app/regional-information.html. The example is loaded when the page opens, so every panel already has realistic data. Follow the steps to see how it works, then replace the example with your own data.

1 Choose the regions and the application

Pick US, EU or both, the application type (NDA, ANDA, BLA or MAA) and the product type. Fields for a region you did not choose are hidden.

CMCfy Regional Information Projects All modules Training Security Runs entirely on this device Training guide

PROJECTS Keep this work in a project, with version history and your company logo on every report. Choose projects folder Keep in this browser

- Network requests since load: 0**
Counted live by your browser. Your data never leaves this device.
- Works offline**
Everything the tool needs is inside this page.
- Locked offline copy**
Save a single file that opens from your own computer with all network access blocked.

3.2.R Module 1 Save project Open project Start blank Load example

Write the regional information for 3.2.R and the CMC items of Module 1: for the US, executed batch records, the method validation package, comparability protocols, the establishment list for Form FDA 356h and the environmental assessment or categorical exclusion; for the EU, the process validation scheme, CEP and ASMF references, the medical device opinion, the QP declaration, the manufacturers for the application form and the environmental risk assessment.

Guidance: ICH M4Q(R1) 3.2.R; FDA M4Q guidance and Form FDA 356h; 21 CFR 25.15, 25.31 and FDA Environmental Assessment of Human Drug and Biologics Applications (1998); EU Notice to Applicants Volume 2B; EMA process validation guideline (EMA/CHMP/CVMP/QWP/BWP/70278/2012); Regulation (EU) 2017/745 Article 117; EU GMP Annex 16; EMEA/CHMP/SWP/4447/00 Rev. 1 (ERA)

1 - APPLICATION

Product
CMX-101 Tablets, 50 mg (cmxitinib)

Submission region
Both US and EU

Application type
NDA (505(b)(1) or (b)(2))

Product type
Small molecule

Maximum daily dose of the active substance (mg)
100

RESULT

4 sites · US: categorical exclusion 25.31(b) · EU: ERA Phase II needed

EIC 0.019 ppb (limit 1 ppb). PECsw 0.50 µg/L (action limit 0.01 µg/L).

SITES	US EIC	EU PECsw
4	0.019 ppb	0.50 µg/L
EEA RELEASE SITE	MASTER FILES	
yes	2	

MANUFACTURERS AND ESTABLISHMENTS

2 List the sites and master files

One row per site with its role (drug substance, drug product, packaging, testing, batch release). Put names that contain commas in quotes. List each CEP, DMF or ASMF with the holder and whether you have a letter of access.

3 Read the environmental result

The headline sums it up: "4 sites · US: categorical exclusion 25.31(b) · EU: ERA Phase II needed". The note gives the EIC against the 1 ppb limit and the PECsw against the 0.01 µg/L action limit.

MANUFACTURERS AND ESTABLISHMENTS

SITE	COUNTRY	ACTIVITY	FEI / DUNS	MIA / GMP CERTIFICATE
Chem API Ltd., Plot 12, Hyderabad 500078	India	Drug substance manufacture	3004567890	EudraGMDP certificate IN/GMP/2025/0123
CMX Pharma Inc., 4 Research Way, Raleigh NC 27601	USA	Drug product manufacture	3009876543	EudraGMDP certificate (MRA)
CMX Pharma Inc., 4 Research Way, Raleigh NC 27601	USA	Quality control testing	3009876543	EudraGMDP certificate (MRA)
CMX Europe GmbH, Hafenstrasse 8, 60327 Frankfurt	Germany	Batch release (EU) / release testing	missing	MIA DE_HE_01_MIA_2024_0042

Sites and environmental calculation.

4

Resolve alerts and download

Missing FEI numbers, a missing EEA batch release site, master files without a letter of access, an EIC at or above 1 ppb and a log Kow above 4.5 are flagged. Then preview and download each document.

Close

Preview and review before download

Review

Checked on this device: gaps in the data, gaps in the report against ICH and regional expectations, and differences from the protocol.

No open gaps

No open gaps: the data, the report and the protocol (if given) match every rule checked, or you accepted the rest. Read the preview before you sign.

Compare with the protocol

Load or paste the approved protocol. Every requirement and acceptance criterion in it is looked for in the report.

Paste the protocol text here, or load the file.

Load protocol file

Compare

AI review against guidance

AI reads the report, the protocol and the data against the ICH, FDA or EMA requirements for these sections, and lists gaps with the guideline it applies, protocol and data mismatches, and how to fix them. You see exactly what is sent before anything leaves this device. Results and pass/fail are not changed.

Run AI review

3.2.R Regional information (US)

CMX-101 Tablets, 50 mg (cmxitinib) - US (FDA) and EU (EMA)

Executed batch records

Executed batch records for exhibit batches LOT-2401 (drug product, 150 000 tablets) and DS-2311 (drug substance) are in 3.2.R; master batch record MBR-101 v7 for the commercial batch size (500 000 tablets).

Method validation package

Analytical procedures and validation reports for the non-compendial methods (assay and related substances HPLC-101, dissolution DIS-101, residual solvents GC-101) and a list of samples available for FDA laboratory testing.

Comparability protocols

None submitted.

Drug master files

Material	Holder	Reference	Letter of authorisation
Cmxitinib (drug substance)	Chem API Ltd.	US DMF 038812; EU ASMF EMEA/ASMF/00123	Provided in Module 1
Hypromellose 2910	Excipient Co.	CEP R1-CEP 2017-055 (not required; compendial)	Not applicable

Draft prepared with CMCfy Regional Information on 2026-10-29. Guidance applied: ICH M4Q(R1) 3.2.R; FDA M4Q guidance and Form FDA 356h; 21 CFR 25.15, 25.31 and FDA Environmental Assessment of Human Drug and Biologics Applications (1998); EU Notice to Applicants Volume 2B; EMA process validation guideline (EMA/CHMP/CVMP/QWP/BWP/70278/2012); Regulation (EU) 2017/745 Article 117; EU GMP Annex 16; EMEA/CHMP/SWP/4447/00 Rev. 1 (ERA). To be reviewed and approved by a qualified person before submission.

4. Field reference

Every input in the tool, panel by panel. Tables accept rows pasted straight from Excel, comma-separated text, or a loaded file; check the columns after loading a file. Fields marked “when it applies” appear only for the choices that need them.

1 - Application

FIELD	WHAT TO ENTER
Product	Type it in.
Submission region	Choose one: US: FDA (NDA, ANDA, BLA, IND); EU: EMA and national agencies (MAA); Both US and EU.
Application type	Choose one: NDA (505(b)(1) or (b)(2)); ANDA; BLA; EU MAA (centralised or DCP).
Product type	Choose one: Small molecule; Biological.
Maximum daily dose of the active substance (mg)	Type a number.

2 · Manufacturers and establishments

One row per site and activity. US: give the FEI or DUNS number. EU: give the manufacturing authorisation or GMP certificate. Role: drug substance, drug product, testing, packaging or batch release.

FIELD	WHAT TO ENTER
Sites	Role words the tool recognises: release, substance, product, fill, pack, test, manufacture. A table. Columns: Name and address Country Role FEI or DUNS (US) MIA or GMP certificate (EU) Last inspection or audit. Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).
CEPs and master files referenced	A table. Columns: Material Holder CEP / DMF / ASMF number Letter of access (yes/no). Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).

3 · US regional information (3.2.R) and environmental assessment shown when it applies

FIELD	WHAT TO ENTER
Executed batch records provided	Type or paste text.
Method validation package	Type or paste text.
Comparability protocols	Type or paste text.
Maximum expected annual production of the active (kg/year, fifth year)	Use the fifth-year estimate from your forecast, in kg of active per year. Type a number.
Naturally occurring substance (25.31(c))	Tick the box if it applies.
Extraordinary circumstances known (for example toxicity to aquatic life at expected levels)	Tick the box if it applies.

4 · EU regional information (3.2.R) and Module 1 shown when it applies

FIELD	WHAT TO ENTER
Manufacturing process	Choose one: Standard process: validation data at submission or a validation scheme; Non-standard process: full-scale validation data at submission; Biological: process validation data at submission.
Process validation scheme or data	Type or paste text.
Medical device	Choose one: No device; Separate CE-marked device (co-packaged); Integral drug-device combination (MDR Article 117).
Notified body opinion or EU declaration of conformity when it applies	Type it in.
QP declaration basis	Type or paste text.
Market penetration factor Fpen (default 0.01)	Leave 0.01 unless you have prevalence data to refine it. Type a number.
ERA Phase II summary (if needed)	Type or paste text.
log Kow of the active substance	Above 4.5 the EU guideline requires a PBT screening. Type a number.

5. Checks and alerts

Calculations and pass/fail outcomes always come from fixed rules, never from AI. The tool checks:

- US: FEI or DUNS for every site; EIC = annual production / $(1.214 \times 10^{11} \text{ L/day} \times 365)$ against 1 ppb for 25.31(b); 25.31(a) and (c) where they apply; extraordinary circumstances.
- EU: an EEA site for batch release; MIA or GMP certificate for each site; $\text{PEC}_{\text{sw}} = \text{dose} \times \text{Fpen} / (200 \text{ L} \times 10)$ against $0.01 \mu\text{g/L}$; PBT screening when log Kow is above 4.5; device opinion for an integral device.
- Letters of access for each CEP, DMF or ASMF referenced.

How to resolve alerts

- **Critical** alerts block the download and must be fixed in the data. A failing result can instead be linked to an investigation: type the investigation reference and outcome and press **Record**.
- **Major** alerts block the download until you fix them or type a justification and press **Accept justification**.
- **Minor** alerts do not block anything. They are listed in the documents so the reviewer sees them.
- Some alerts have an **Apply fix** button that makes the change for you. **Reopen** undoes a justification.

Narratives

This module writes: Environmental statement. Each narrative is written by fixed rules from your data. You can edit it in the box. **Rewrite with AI** (where your plan includes AI) rewrites it in regulatory style; every number in the text is checked against your data, and a number that does not match is flagged under the box and blocks the download until you correct it. **Reset to rule-based text** brings back the original.

6. Preview, gap review and download

1. Press **Preview** next to a section, or **Preview and download all**. The document opens in a preview window, exactly as the Word file will read.
2. The left side lists the review, run on your device: **gaps in the data** (missing values, open alerts), **gaps in the report** (missing content the guidance expects, placeholders such as [site] or TBD left in the text) and, if you load the approved protocol under **Compare with the protocol**, **differences from the protocol** (requirements, criteria, batches or time points it plans that the report does not show).
3. Click a finding to jump to the place in the preview. Fix it in the tool, then preview again.
4. Optional **AI review**: a second read for contradictions, claims without data and vague wording. The report text is sent to Claude only when you press it, and only where your plan includes AI. Check every AI finding; AI can be wrong.
5. Press **Download Word (.docx)** or **Download PDF**. With several documents open, **All as Word (.zip)** and **All as PDF (.zip)** download the set. The download buttons stay disabled while a blocking alert is open; the preview still works.

Documents this module produces

SECTION	DOCUMENT
US 3.2.R	Regional information: executed batch records, method validation package, comparability protocols

SECTION	DOCUMENT
356h establishments	Sites with roles and identifiers
1.12.14	Categorical exclusion claim or environmental assessment
EU 3.2.R	Process validation scheme, device, TSE
Application form	Manufacturers and batch release
QP declaration	Basis for the declaration
1.6 ERA	Environmental risk assessment, Phase I and Phase II

Use **Save project** to keep your work as a file on your computer, and **Open project** to continue later. **Start blank** clears every field; **Load example** brings the example back. Nothing is stored on CMCfy servers.

7. US and EU submissions

US follows 21 CFR 25 and the FDA guidance on environmental assessment of human drug and biologics applications (1998); the 3.2.R content follows the FDA M4Q guidance. EU follows the EMA guideline on the environmental risk assessment of medicinal products (EMA/CHMP/SWP/4447/00 Rev. 1) and the notice to applicants for Module 1 and the application form.

8. Working with other modules

- Sites and master files also appear in the DMF & ASMF module and in 3.2.S.2.1 and 3.2.P.3.1.
- Assemble the sections in the QOS Composer & Dossier Assembler.

9. Common pitfalls

- Claiming a categorical exclusion without checking the fifth-year production estimate.
- Listing a non-EEA site as the batch release site.
- Forgetting the letter of access for a DMF or ASMF.

10. Practice exercises

Each exercise starts from the example (press **Load example** to reset). We run these on every update of this guide, so the result you see should match.

1. Raise the production estimate

Set **Maximum expected annual production** to 50000.

EXPECTED RESULT

The headline says the US needs an environmental assessment.

2. Enter a lipophilic substance

Set **log Kow of the active substance** to 5.

EXPECTED RESULT

The note asks for a PBT screening.

Guide updated 28 October 2026 for the current version of the tool. CMCfy drafts are for review by a qualified person before use in a submission.