

Peptide & Oligonucleotide Impurities

Assess the impurity profile of a synthetic peptide or oligonucleotide. ICH Q3A does not apply, so the tool uses the peptide or oligonucleotide thresholds and, for a generic peptide, the FDA ANDA rules against the reference listed drug.

WRITES

3.2.S.3.2

3.2.S.4.5

PRODUCT TYPE

Synthetic peptides
and
oligonucleotides

GUIDANCE IT FOLLOWS

FDA ANDAs for
Certain Highly
Purified Synthetic
Peptide Drug
Products That Refer
to Listed Drugs of
rDNA Origin (2021);
Ph. Eur. 2034
Substances for
pharmaceutical
use; EMA Guideline
on the
development and
manufacture of
synthetic peptides
(2025) and of
oligonucleotides
(draft, 2024); ICH
Q6A, Q11, M7(R2)

TIME TO LEARN

About 20 minutes
with the example

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

1. What this module does

You choose the modality and whether the product is a new drug or a generic referring to an rDNA-origin listed drug, then enter each impurity with its level and, for a generic, its level in the RLD.

The tool checks the identification and qualification thresholds, impurities above the RLD, new impurities above 0.5%, and new impurities between 0.1% and 0.5% that need an immunogenicity assessment.

What you get

- A Word or PDF section: 3.2.S.3.2 Impurities (synthetic peptide or oligonucleotide).

2. Before you start

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

- Impurity levels from LC-MS with their identity and type.
- RLD impurity levels (for a generic).
- Counter-ion, residual TFA, residual solvents and aggregation results.

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/peptide-oligonucleotide.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 Describe the substance

Choose the modality and the application type, and confirm the sequence and higher-order structure work.

CMCfy | Peptide & Oligonucleotide Impurities | 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.

3.2.5.3.2 3.2.5.4.5

[Save project](#) [Open project](#) [Start blank](#) [Load example](#)

Assess the impurity profile of a synthetic peptide or oligonucleotide drug substance. ICH Q3A does not apply, so the tool uses the peptide (Ph. Eur.) or oligonucleotide thresholds, and for generic peptides the FDA ANDA rules against the reference listed drug, including immunogenicity assessment of new impurities.

Guidance: FDA ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin (2021); Ph. Eur. 2034 Substances for pharmaceutical use; EMA Guideline on the development and manufacture of synthetic peptides (2025) and of oligonucleotides (draft, 2024); ICH Q6A, Q11, M7(R2)

1 · DRUG SUBSTANCE

Drug substance
Liraglutide (synthetic, Fmoc solid-phase synthesis)

Regulations: Both US and EU
Modality: Synthetic peptide

Application: Generic referring to an rI
Report number: IMP-PEP-004

☒ Sequence or structure confirmed (MS/MS, amino acid analysis or sequencing)
☒ Higher-order structure and aggregation compared (CD, SEC, oligomerisation)

RESULT

6 impurities · profile acceptable

Peptide thresholds: report 0.1%, identify 0.5%, qualify 1%. Total 1.06%. 1 new impurity between 0.1% and 0.5%.

IMPURITIES	TOTAL	NEW (VS RLD)
6	1.06%	1

MODALITY
Peptide

IMPURITIES

IMPURITY	TYPE	LEVEL (%)	RLD (%)	IDENTIFIED	QUALIFIED	OUTCOME
...	...	...	...	...	...	...

2

Enter the impurities

One row per impurity. Leave the RLD level empty for an impurity not found in the RLD (a new impurity).

3

Read the result

The headline gives the outcome: "6 impurities · profile acceptable".

IMPURITIES

IMPURITY	TYPE	LEVEL (%)	RLD (%)	IDENTIFIED	QUALIFIED	OUTCOME
[Asp9] - liraglutide	racemisation (D - Asp)	0.32	0.4	yes	yes	acceptable
Des - Gly4 liraglutide	deletion	0.18	0.25	yes	yes	acceptable
[+Gly] liraglutide	insertion	0.12	new	yes	yes	new, assessed
Trp - oxidised liraglutide	oxidation	0.21	0.3	yes	yes	acceptable
Unknown RRT 1.12	unknown	0.08	0.09	no	no	acceptable
Truncated (1 - 30)	truncation	0.15	0.22	yes	yes	acceptable

Impurities against the thresholds.

4

Resolve alerts and download

A new impurity above 0.5% is critical. Impurities above the RLD, unidentified impurities above the threshold and missing immunogenicity assessments are flagged. Then preview and download.

Preview and review before download

Close

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 review 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

3.2.5.3.2 Impurities (synthetic peptide or oligonucleotide)
 Liraglutide (synthetic, Fmoc solid-phase synthesis) · IMP-PEP-004 · US (FDA) and EU (EMA)

Drug substance	Liraglutide (synthetic, Fmoc solid-phase synthesis)
Modality	Synthetic peptide
Application	ANDA (rDNA-origin RLD)
Regulations	US (FDA) and EU (EMA)

Thresholds
 Reporting 0.1%, identification 0.5%, qualification 1% (Ph. Eur. 2034). Each impurity at or below the RLD; new impurities not above 0.5%, with immunogenicity assessment above 0.1%.

Impurity profile

Impurity	Type	Level (%)	RLD (%)	Identified	Qualified
[Asp9]-liraglutide	racemisation (D-Asp)	0.32	0.4	Yes	Yes
Des-Gly4 liraglutide	deletion	0.18	0.25	Yes	Yes
[+Gly] liraglutide	insertion	0.12	New	Yes	Yes
Trp-oxidised liraglutide	oxidation	0.21	0.3	Yes	Yes
Unknown RRT 1.12	unknown	0.08	0.09	No	No
Truncated (1-30)	truncation	0.15	0.22	Yes	Yes

Discussion
 Liraglutide (synthetic, Fmoc solid-phase synthesis) is a synthetic peptide; ICH Q3A does not apply. Impurities are evaluated against the Ph. Eur. 2034 thresholds (reporting 0.1%, identification 0.5%, qualification 1%) and, as a generic referring to an rDNA-origin listed drug, against the RLD according to the FDA ANDA synthetic peptide guidance (2021).

Download Word (.docx)

Download PDF

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 · Drug substance

FIELD	WHAT TO ENTER
Drug substance	Type it in.
Regulations	Choose one: US: FDA; EU: EMA, Ph. Eur.; Both US and EU.
Modality	Choose one: Synthetic peptide; Oligonucleotide.
Application	Choose one: New drug (NDA / MAA); Generic referring to an rDNA-origin RLD (FDA ANDA).
Report number	Type it in.
Sequence or structure confirmed (MS/MS, amino acid analysis or sequencing)	Tick the box if it applies.

CMCfy training guide · Peptide & Oligonucleotide Impurities

Page 5 of 9

FIELD	WHAT TO ENTER
Higher-order structure and aggregation compared (CD, SEC, oligomerisation)	Tick the box if it applies.

2 · Impurities

Levels in % (area). For a generic, give the highest level in the RLD lots tested; leave empty for an impurity not found in the RLD.

FIELD	WHAT TO ENTER
Impurities	Write "yes" in the last column when the impurity is qualified or its immunogenicity has been assessed. A table. Columns: Impurity Type Level (%) RLD level (%) Identified (yes/no) Qualified or immunogenicity assessed (yes/no). Paste rows from Excel, type comma-separated rows, or press Load file (Excel, CSV, Word, PDF or a scan).
High molecular weight species (%)	Type a number.
RLD high molecular weight species (%)	Type a number.

3 · Other impurities

FIELD	WHAT TO ENTER
Counter-ion and residual TFA	Type it in.
Residual solvents and reagents	Type it in.
Immunogenicity risk assessment of new impurities (in silico and in vitro)	Type or paste text.

5. Checks and alerts

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

- Reporting, identification and qualification thresholds.
- ANDA: each impurity at or below the RLD; new impurities $\leq 0.5\%$.
- Immunogenicity assessment, aggregation and higher-order structure.

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: Impurity discussion. 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
3.2.S.3.2	Impurities

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 generics follow the FDA ANDA synthetic peptide guidance (2021). EU follows Ph. Eur. 2034 and the EMA synthetic peptide and oligonucleotide guidelines.

8. Working with other modules

- Mutagenic and nitrosamine impurities are assessed in the Impurity & Risk Studio and the Nitrosamine Risk Assessment.

9. Common pitfalls

- Applying ICH Q3A thresholds to a peptide.
- A new impurity with no immunogenicity assessment.

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 a new impurity**

Change [+Gly] liraglutide from 0.12% to 0.62%.

EXPECTED RESULT

The headline shows one new impurity above 0.5%.

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.