European Directorate for the Quality of Medicines & HealthCare

Council of Europe

European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

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Use of a CEP

Nimet FILIZ, Certification of Substances Department

2025 EDQM virtual training program:

Module 5: Fundamentals of the CEP Procedure

8th December 2025

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Overview

- ★ Aim and scope of EDQM document “How to read a CEP”
- ★ How to interpret the information laid down on CEPs
- ★ Highlight of the most important changes following the implementation of “CEP 2.0”
- ★ How to use the CEP in marketing authorisation applications

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Policy document « How to read a CEP »

- EDQM policy document PA/PH/CEP (15) 31 “How to read a CEP”, revised in May 2025 to cover CEP 2.0 and hybrid CEP in addition to old ones: **Link**
- It does not contain new information or new instructions, but it describes in detail the information conveyed on a CEP and clarifies how this information should be interpreted by both industry and competent authorities.
- It should be read in conjunction with other applicable EDQM Certification policy documents and guidelines.
- It does not cover the use of a CEP in the context of a Marketing Authorisation Application (MAA). QWP Q&A How to use a CEP in the MAA and MAV: **Link**

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What is a CEP?

- A chemical or a herbal CEP **certifies** that the quality of the substance is suitably controlled by the Ph. Eur. monograph and any supplementary tests deemed necessary in line with (V)ICH and EMA guidelines.
- A TSE CEP **certifies** that the substance complies with the Ph. Eur. General Chapter 5.2.8 on minimising the TSE risk. It **does not** certify that the quality of the substance is suitably controlled by a specific Ph. Eur. Monograph.

- A CEP **does not** replace a certificate of analysis.
- A CEP **does not** replace the QP declaration.
- A CEP **is not** a GMP certificate.

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Formats of CEPs (all types of CEP)

In September 2023, major changes were introduced to the CEP document, which resulted in 3 different formats: “CEP 2.0”, “hybrid CEP” and “old CEP” :

	CEP 2.0	Hybrid	Old CEP
Format	Electronic document with electronic signature		Paper document with wet signature
Numbering	2-block code CEP 20XX-XXX-Rev 00		3-block code R0-CEP 20XX-XXX-Rev 00
Information on companies	Name and address of the holder and production sites completed by SPOR OMS LOC &ORG ID		Name and address of holder and production sites
Technical information (Chemical and herbal CEP)	Inclusion of the approved specification and description of additional methods required to control the substance	Limits for additional impurities and inclusion of tests used in addition to the Ph. Eur. monograph tests, required to control the substance	
Expiry date	No reference to a validity date of 5 years (renewal due date, available on public database)		Yes reference to expiry date (before renewal)
Box/Letter of access	Letter of access (template on EDQM website)		Box of access on CEP
Issue date	After 1 September 2023		Until 31 August 2023

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Communication CEP holder / MAH

Communication between CEP holder and drug product manufacturer/ MAH is key:

- ★MAHs are ultimately responsible for the quality of APIs used in their finished product(s) and are legally obliged to get information they need to take this responsibility.
- ★API manufacturers should be supportive to their customers and share information.
- ★EDQM Policy document PA/PH/CEP (21) 57 "CEP holders' responsibilities towards their customer" (January 2022)
- ★EDQM continues working with stakeholders to promote better sharing of information.

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On-line Certification database

- New features were introduced in 2023
  - EMA SPOR OMS ORG_ID and LOC_ID for holders
  - **Renewal date for the CEP (where not yet renewed)**
  - Access to short history of finalised procedures (which can be downloaded as pdf) with:
    - ✓ type of procedure (e.g. minor revision, notification, major revision, renewal, monograph revision)
    - ✓ closure date of the last procedure, outcome (i.e. CEP revised, CEP remains valid etc)
    - ✓ corresponding CEP number if any

History available only for procedures opened as of 1 January 2020 (due to change of IT tools).

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How to interpret the information laid down on each type of CEP?

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Sites

Sites (name + address) are mentioned with their roles:

- ★ CEP holder
- ★ Intermediate(s) manufacturer(s)
- ★ Substance manufacturer(s)

4	*Name of holder:*
5	**EDQM, COUNCIL OF EUROPE**
6	7 allée kastner
7	France-67081 Strasbourg
8	*Site(s) of production:*
9	**SEE ANNEX 1**

starting material manufacturers are NOT mentioned on a CEP

Additional sites, when applicable (subtitle):

- ★ Site(s) of physical treatment
- ★ Site(s) of micronisation
- ★ Site(s) of sterilisation

SPOR/OMS Loc and Org IDs are mandatory for all sites in all CEP applications

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Sites

- ★ Production sites are mentioned in **Annex 1** of the CEP
- ★ Name of the intermediate(s) is not specified on the annex
- ★ The CEP does not distinguish which manufacturer produces which intermediate (if more than one intermediate is involved)

Annex 1 : Site(s) of production for R0-CEP 2007-001-Rev 06

Production of intermediate(s):
LABORATORIES XXX Co. Ltd.
Survey No XX and YY
XX Mandal, XX District
India - 123 456 City C, Telangana

LABORATORIES YYY Co. Ltd.
Survey No XX and YY
YY Mandal, YY District
India – 789 548, City D, Andra Pradesh

Production of Zinc undecylenate:
EDQM, COUNCIL OF EUROPE
7 Allée Kastner
France-67081 Strasbourg

CEP user should communicate with CEP holder to obtain more details on intermediates and manufacturers

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Subtitle (optional)

- A CEP can cover specific physico-chemical characteristics of a substance (e.g. specific polymorphic form or particle size distribution) or its sterility. These are indicated as “grades” and mentioned on the CEP as subtitle.
- A subtitle can also be used to differentiate CEP applications for the same substance from the same holder (e.g. “process B” or “produced in site X”).
- A subtitle is also used to reflect on the CEP, the requirements of the “labelling” section of the monograph, where applicable (e.g. presence of antioxidant for an API-mix).

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Subtitle

★ A grade (e.g. micronised, polymorphic form) is mentioned on the CEP as subtitle, **only if**:

1. requested by the CEP holder (application form)
2. accepted during the CEP evaluation procedure

★ The corresponding quality attribute(s) is included in the specification appended to CEP (CEP 2.0) or mentioned on the CEP (old and hybrid CEP) + analytical procedure(s) are annexed to the CEP.

★ A CEP may mention more than one grade provided they correspond to the same impurity profile of the substance; otherwise, separate CEPs will be issued.

What does it mean if a CEP has NO subtitle ?

★ Data relative to a particular grade are not included in the CEP dossier OR the CEP holder has not applied for a subtitle (even if data are provided in the dossier).

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Subtitle

Examples:

★ **Micronised, non-micronised**: data related to determination of particle size (e.g. laser diffraction spectroscopy) are assessed by EDQM

Name of the substance:
ESOMEPRAZOLE MAGNESIUM DIHYDRATE
Micronised, non-micronised

★ New: For non-micronised grade, when included together with micronised grade, the related specification parameter is not mandatory.

★ **Polymorphic form:** data concerning elucidation of the polymorphic form (e.g. XRPD) are assessed by EDQM

Name of the substance:
ATOVAQUONE
Form A

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Specification (CEP 2.0)

The specification of the substance is appended to the CEP

- ★ The specification should be based on the corresponding Ph. Eur. individual monograph as well as European regional requirements from Ph. Eur. general monographs and (V)ICH and EMA guidelines. Compliance with these texts is evaluated and approved during the assessment performed by EDQM
- ★ Quality attributes, acceptance criteria and reference to analytical procedures (e.g. Ph. Eur. or in-house) are included in the specification table
- ★ Parameters for compliance with pharmacopoeias other than the Ph. Eur. or other non-EU regional requirements → **should be** separate and clearly identified as such in the specification.

Quality attributes	Acceptance criteria	Reference of analytical procedures
Characters	White or almost white, crystalline powder	Substance monograph from Ph. Eur. current Ed.
Solubility	Practically insoluble in water, slightly soluble in anhydrous ethanol and in methylene chloride.	Substance monograph from Ph. Eur. current Ed.
Identification Test A (IR)	Complies with reference spectrum	Substance monograph from Ph. Eur. current Ed.
Specific optical rotation	+158° to + 167°	Substance monograph from Ph. Eur. current Ed.
Sulfated ash	Not more than 0.1%	Substance monograph from Ph. Eur. current Ed.
Loss on drying	Not more than 0.5%	Substance monograph from Ph. Eur. current Ed.
Related substances (by HPLC)		Substance monograph from Ph. Eur. current Ed.
Impurity A	Not more than 0.5%	
Impurity B	Not more than 0.3%	
Impurity C	Not more than 0.15%	
Impurity D	Not more than 0.15%	
Unspecified impurities	Not more than 0.10%	
Total	Not more than 1.5%	
Assay (by titration)	From not less than 99.0% to not more than 101.0%	Substance monograph from Ph. Eur. current Ed.
Residual solvents (by GC)		Ph. Eur. 2.4.24, system B, sample preparation 2
Ethanol	Not more than 5000 ppm	
N,*N*-dimethylformamide	Not more than 880 ppm	
N-Nitrosodimethylamine (NDMA) (by GC-MS)*	Not more than 3.0 ppm	In-house
Particle size distribution (by laser light diffraction)	D(0.9) not more than 15 µm D(0.5) between 2 µm and 8 µm D(0.1) not more than 2 µm	In-house

* tested in one batch out of ten

Specification parameters not necessary to satisfy European regional requirements		
Assay (by titration)	99.0% to 101.0%	USP
Heavy metals	≤ 10 ppm	Ph. Eur. 2.4.8
Water content (by KF)	≤ 0.5%	JP

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Specification (CEP 2.0)

★ Only specification parameters corresponding to the **quality claimed:**

	Specification parameter relating to grades (examples)		
Grade: micronised	Particle size dimension	X_{10} not less than 0.8 µm X_{50} not less than 3.5 µm X_{90} not less than 15 µm	In-house
Grade: Form-I	Polymorphism	Presents characteristic peaks corresponding to Form-I occurring at 2Θ values of 10.55, 15.99, 16.55, 17.93, 20.45 ± 0.2°	In-house

★ Specification may include information on skip testing.

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Analytical procedures (CEP 2.0, old and hybrid CEP)

Alternative analytical procedures to those described in Ph. Eur. monograph (e.g. developed in-house or taken from another pharmacopoeia) may be used provided these are at least equivalent to those of Ph. Eur. monograph

- ★The in-house method should be cross-validated against the Ph. Eur. method
- ★This is assessed by EDQM

In the event of doubt or dispute, the texts of the Ph. Eur. are authoritative

- ★When Ph. Eur. monograph is demonstrated to be suitable to control the quality attribute, the in-house analytical procedures <u>are not appended</u> to the CEP
- ★For quality attributes not covered by Ph. Eur. monograph but which are needed to control the quality of the substance, company's in-house analytical procedures ("additional") <u>are appended to the CEP</u> (e.g. GC for residual solvents, ICP-MS for elemental impurities, etc).

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Impurities statements (old and hybrid CEPs)

★Specification is not appended to the CEP

★In case limits for **“additional related substances”** to those already listed in the Ph. Eur. monograph are needed, **following statements** on the CEP are possible:

The following impurities are detected by the test for related substances of the monograph and their limits are set at:
Impurity at RRT 1.3 — not more than 0.15%
Any unspecified impurity — not more than 0.10%

This impurity is present in the substance above Identification threshold (as per Ph. Eur. 2034) and impurity can be controlled by Ph. Eur. test for related substances, no analytical procedure is appended to the CEP

- Ph. Eur. method is NOT suitable to control this impurity
- The monograph should be supplemented with an **“additional method”** (in-house analytical procedure)
- In-house method (developed and validated) is appended to CEP to control this impurity

– Test for related substances by liquid chromatography		(Annex 2)
Impurity X	not more than 0.15%	
Any unspecified impurity	not more than 0.10%	

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Mutagenic impurities on the CEP

- A mutagenic impurity is limited on the CEP or included in the specification appended to the CEP when it is (potentially) present in the substance

- The limit proposed by the applicant is assessed and accepted by EDQM in line with the ICH M7 requirements

- If the Ph. Eur. method is not suitable to control this impurity, the in-house analytical procedure is appended to the CEP.

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Mutagenic impurities on the CEP

What does it mean if no mutagenic impurities are limited on the CEP?

★There are **NO** potential mutagenic impurities formed/introduced in the route of synthesis proposed by the API manufacturer.

OR

★There are potential mutagenic impurities, and the control strategy put in place by the manufacturer allows **omission** of a limit in the substance specification (in line with ICH M7).

OR

★They are controlled by the monograph.

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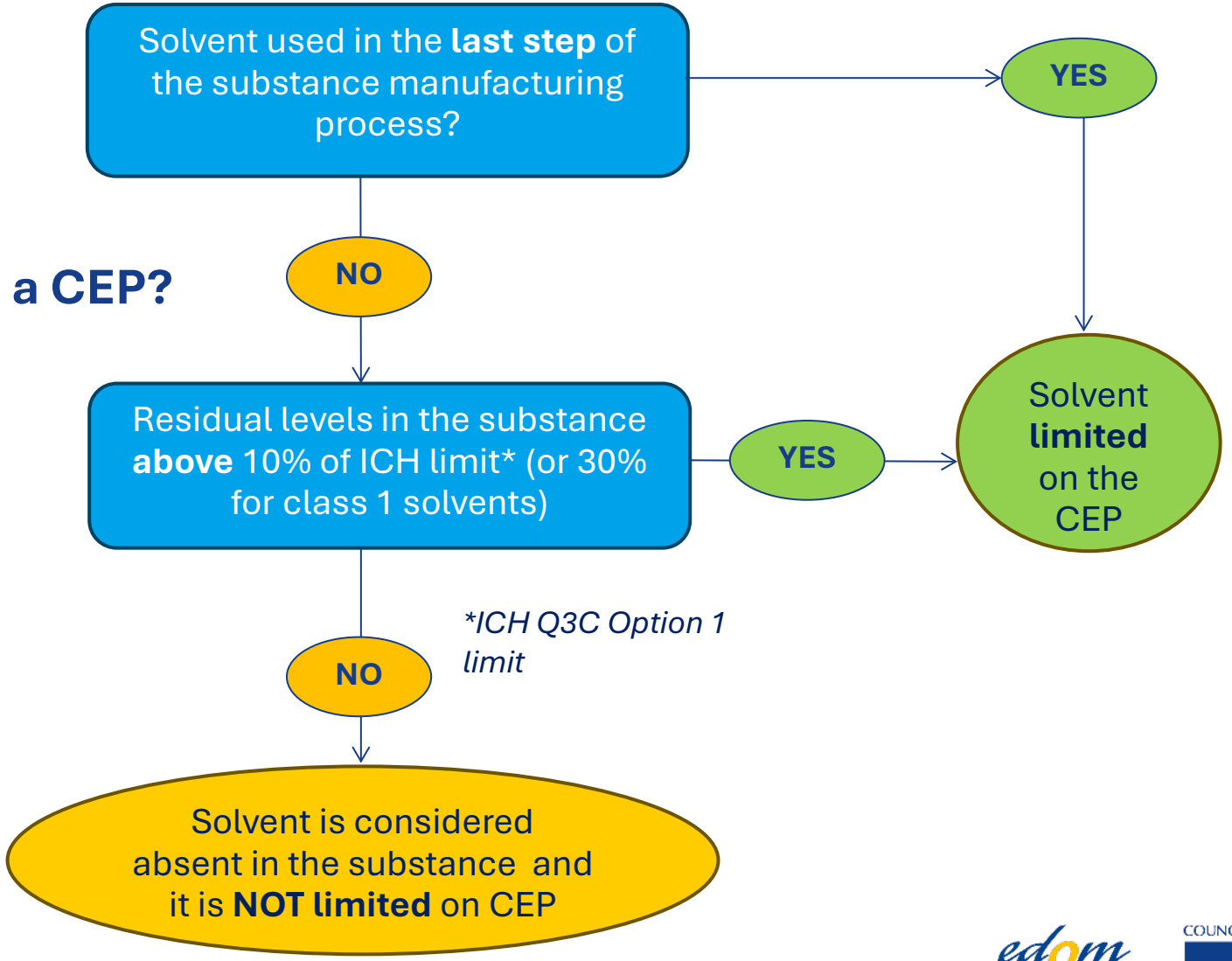
Residual solvents (old and hybrid CEPs)

Which solvents are mentioned on a CEP?

Those present in the substance

AND / OR

Those used in the last step



Annexes to:
CPMP/ICH/283/95 Impurities: Guideline for residual solvents &
CVMP/VICH/502/99 Guideline on impurities: residual solvents

Annex I: specifications for class 1 and class 2 residual solvents in active substances

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Residual solvents (old and hybrid CEPs)

What are the limits mentioned on the CEP for solvents?

Limits proposed by the manufacturer, as assessed and accepted by the EDQM

a) Limits on a CEP are mostly those of ICH Q3C Option 1:

– Tests for residual solvents by gas chromatography		
Dichloromethane	not more than 600 ppm	(Annex 2)
Ethyl acetate	not more than 5000 ppm	
Pyridine	not more than 200 ppm	
n-Pentanol	not more than 5000 ppm	(Annex 3)

b) Sometimes limits are tighter than ICH Q3C Option 1:

– Test for residual solvents by gas chromatography		(Annex 1)
Ethanol	not more than 2000 ppm	
Chloroform	not more than 50 ppm	
Toluene	not more than 200 ppm	
Methanol	not more than 1000 ppm	
Benzene	not more than 2 ppm	

c) Exceptionally, higher limits than ICH Q3C Option 1 are acceptable if suitably justified (e.g. Option 2, this is made transparent on CEP).

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Residual solvents (old and hybrid CEPs)

Applicant's specification:

Loss on drying (at 105°C for 3 hours)	Not more than 0.50% w/w

Residual solvents by GC-HS **Method-1**	
a) Toluene	Not more than 890 ppm
b) *o*-Xylene	Not more than 2170 ppm
c) Dichloromethane	Not more than 600 ppm
d) Ethyl acetate	Not more than 5000 ppm
e) Tetrahydrofuran	Not more than 720 ppm
f) Acetone	Not more than 5000 ppm
g) Methanol	Not more than 3000 ppm
h) Ethanol	Not more than 5000 ppm

However, the CEP mentions only this:

– Test for residual solvents by gas chromatography (Annex 2)
Methanol not more than 3000 ppm

In the last steps of the synthesis acetone is used as solvent. Its residual content is limited by the test for loss on drying described in the monograph, with a limit of not more than 0.5%.

Why? Acetone and methanol are used in the last purification step. All other solvents are used earlier in the process and found < 10% of ICH Q3C Option 1 limit in the substance. In addition acetone is a class 3 solvent and there is a test for LOD in the Ph. Eur. monograph.

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Residual solvents (old and hybrid CEPs)

When is a loss on drying (LOD) test mentioned on the CEP?

- When class 3 solvents are used in the last steps of the process and are controlled by LOD test
  - Either with the loss on drying test of the specific Ph. Eur. monograph

> In the last steps of the synthesis isopropanol is used as solvent. The residual content is limited by the test for loss on drying described in the monograph, with a limit of not more than 0.5%.

  - Or with the LOD test of Ph. Eur. general chapter 2.2.32 (if LOD test is NOT included the Ph. Eur. monograph of the substance)

> In the last steps of the synthesis water and acetone are used as solvents. Their residual content is limited by the test for loss on drying (2.2.32) of the European Pharmacopoeia, with a limit of not more than 0.5%.

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Residual solvents (CEP 2.0)

- Limits for residual solvents stated in the specification and the corresponding analytical procedures appended to the CEP are those proposed by the CEP holder (as accepted by the EDQM)

  Note: If all solvents used in the process are limited in the specification, these controls are appended to the CEP as part of the specification.

- If class 3 solvents used in the last steps of the process are controlled by LOD test of Ph. Eur. monograph or by Ph. Eur. General chapter 2.2.32, a corresponding statement is mentioned on the CEP.

  Note: If class 3 solvents are controlled by a specific analytical procedure with other class 2 solvents (e.g. GC), these are not mentioned on the CEP as used in the last steps.

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Residual solvents

When is water mentioned on the CEP?

★ Water is mentioned on the CEP if used in the last process step(s) → likely to be present in the substance.

★ **For old and hybrid CEP:**

> In the last steps of the synthesis water is used as solvent.

★ **For CEP 2.0:** The **quality** of water (in line with the EMA "Guideline on the quality of water for pharmaceutical use" EMA/CHMP/CVMP/QWP/496873/2018, i.e. potable water, purified water, water for injections) is specified.

> In the last steps of the process, purified water is used as solvent.

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Elemental impurities

- ICH Q3D on elemental impurities has been applied to medicinal products for human use from September 2016
- Since January 2021 risk assessments regarding elemental impurities in veterinary medicinal products are also performed
- EDQM policy document **PA/PH/CEP (16) 23, 2R "Implementation of policy on elemental impurities in the Certification Procedure"** was published in April 2021
- EDQM does not make a decision on compliance with ICH Q3D
- The CEP provides transparency and information to be considered by the manufacturer of medicinal product in the context of a MAA.

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Elemental impurities

★ **When a risk management summary (RMS) is provided** by the CEP holder, its summary is annexed to the CEP with the necessary information on the level of elemental impurities of the substance (presence/absence).

★ **For old and hybrid CEP:**

A risk management summary for elemental impurities has been provided.	(Annex 2)

★ **For CEP 2.0:**

The section miscellaneous information includes a risk management summary for elemental impurities.

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Intentional introduction

Route of administration

Example of Risk Management Summary to be prepared:

Route of administration considered in the risk assessment:

Element	Class	Intentionally added?	Considered in risk management?	Conclusion
Cd	1	*	Yes	**
Pb	1	*	Yes	**
As	1	*	Yes	**
Hg	1	*	Yes	**
Co	2A	*	Yes	**
V	2A	*	Yes	**
Ni	2A	*	Yes	**
Tl	2B	*	*	**
Au	2B	*	*	**
Pd	2B	*	*	**
Ir	2B	*	*	**
Os	2B	*	*	**
Rh	2B	*	*	**
Ru	2B	*	*	**
Se	2B	*	*	**
Ag	2B	*	*	**
Pt	2B	*	*	**
Li	3	*	*	**
Sb	3	*	*	**
Ba	3	*	*	**
Mo	3	*	*	**
Cu	3	*	*	**
Sn	3	*	*	**
Cr	3	*	*	**

*** Yes / No**

**** The control strategy followed should be clear and mentioned on the RMS:**

- **"Absent"** should be defined (e.g. "less than 30% of ICH Q3D option 1 limit")
- **or "NMT limit in ppm"**calculated based on option 1 (or alternatively and if justified, based on option 2a)
- **or "No risk identified"**

All 24 elemental impurities as mentioned in ICH Q3D

See EDQM policy document **"Implementation of policy on elemental impurities in the Certification Procedure"** (PA/PH/CEP (16) 23, 2R)

Should mention the basis on which "absence" of elemental impurities has been determined

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Elemental impurities

★**When an RMS is <u>not</u> provided**, the CEP is transparent on the introduction of elemental impurities, not on their absence/presence.

> No elemental impurity classified in ICH Q3D is intentionally introduced in the production of the substance.

OR

> The following elemental impurities classified in ICH Q3D are intentionally introduced in the production of the substance: Lead and Palladium.

*Note: The applicant might have set a **limit** in the specification → in this case, analytical procedure is appended to the CEP and the limit is either mentioned on the CEP itself (old and hybrid CEP) or part of the appended specification (CEP 2.0).*

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Omission of Ph. Eur. tests

- When it is demonstrated that a test specified in the Ph. Eur. monograph is not necessary for a named compound because the impurity/solvent/compound cannot be present with the applied route of synthesis or is not used, the absence of control may be accepted (when justified).

Note: Omission is acceptable for specific tests to control one or few impurities; however, it does not apply to the test for related substances.

- **For old and hybrid CEP**: a specific sentence on the omitted test in mentioned on the CEP.
- **For CEP 2.0**: the omission is transparent from the specification appended to the CEP.

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Microbiological quality

- ★ Microbiological control should generally not be part of the specification proposed in a CEP dossier
- ★ Generally, this aspect is NOT addressed in the CEP (even if limits are proposed by the manufacturer), unless the Ph. Eur. monograph indicates specific requirements related to microbial quality.

Microbiological quality is to be addressed considering the final use of the substance in the finished medicinal product, and this aspect should be assessed by the national competent authorities which receives the CEP in a MAA.

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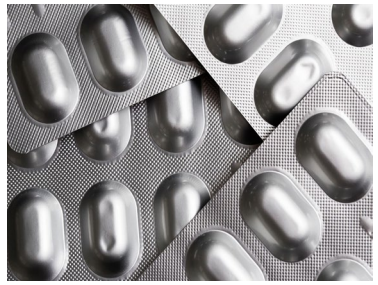
Container closure system

★The full packaging material (immediate and outer) is described on the CEP even when no re-test period is requested by the CEP holder.

Examples:



The substance is packed in double polyethylene bags (outer black), in a triple laminated aluminium foil bag, placed in a polyethylene drum.

The substance is packed under nitrogen in double polyethylene bags (outer black), with silica gel bags in between, in a triple laminated aluminium bag, placed in a polyethylene container.

The substance is packed in a glass flask closed with either a glass stopper or with a polypropylene screw cap, in a polyethylene bag, placed in a paper drum.

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Re-test period (optional but highly recommended)

The CEP statement reflects the fact that the substance **is stable**

- ★ during XX months mentioned on the CEP
- ★ in the packaging material mentioned on the CEP
- ★ in long-term conditions (e.g. 25°C ± 2°C/40% RH ± 5% RH or 30°C ± 2°C/35% RH ± 5% RH, short term excursions are covered by additional testing at accelerated test conditions)

- ★ Different re-test periods and storage conditions can be proposed within one CEP application (e.g. different re-test period depending on the container closure system or climatic zone or grade claimed).

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Re-test period

- **What does it mean if a CEP does NOT indicate a re-test period?**
  - Not requested by the CEP applicant (thus stability data not assessed).

  OR

  - Requested by the CEP applicant, however stability data presented did not allow granting a re-test period (e.g. insufficient data, invalid data obtained under non-regulatory storage conditions, OOS observed, etc).

Stability data should be evaluated during the assessment of the MA dossier; alternatively, the finished product manufacturer should demonstrate that the substance complies with the Ph. Eur. monograph (any additional tests in the specification) immediately before its use.

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Storage conditions

- The absence of any specific storage conditions (e.g. temperature) on the CEP means that the substance is stable under climatic conditions for zone I/II (combination of long-term and accelerated conditions).

- **Why do some CEPs indicate specific storage conditions?**
  - either that they are needed to ensure the stability of the substance in the described container closure system.
  - or that the CEP holder/applicant is applying stricter storage conditions than those recommended by EU/ICH guidelines.

Example:

> The re-test period of the substance is 36 months if stored at a temperature between 2°C and 8°C in double polyethylene bags (outer black) with desiccant bags in between, placed in a polyethylene drum.

  - In any case, the re-test period is supported by stability data obtained in the appropriate conditions.

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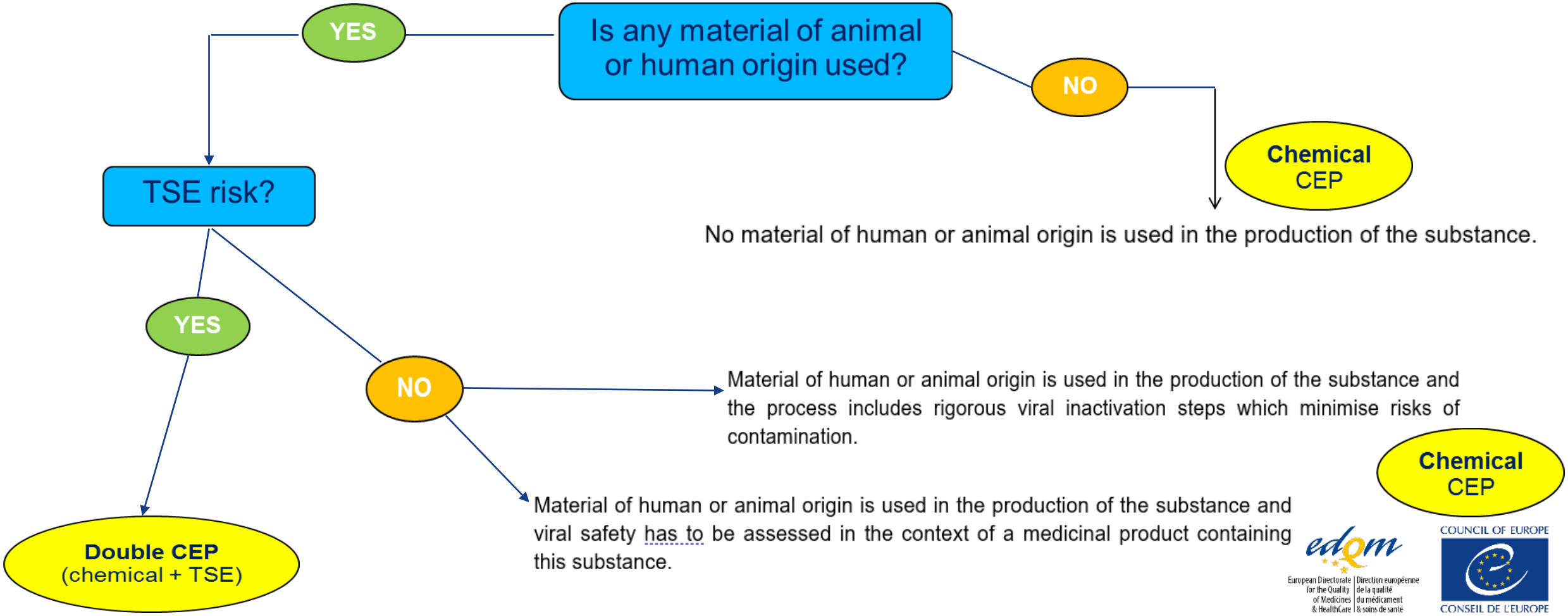
Material of human/animal origin

CEP applicants should declare whether any material of human or animal origin is introduced in the manufacture of the substance



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Production section in monographs

★ Instructions to manufacturers about particular aspects of the manufacturing process (e.g. source materials, in-process testing or testing to be carried out by the manufacturer on the product prior to release).

★ Not all statements of the Production Section can be verified during the CEP procedure:

★ If assessed: nothing mentioned on the CEP ⟶ No further action needed during the assessment of the MA dossier

★ If not assessed: statement on the CEP ⟶  Information in the Production section is to be addressed during the assessment of the MAA

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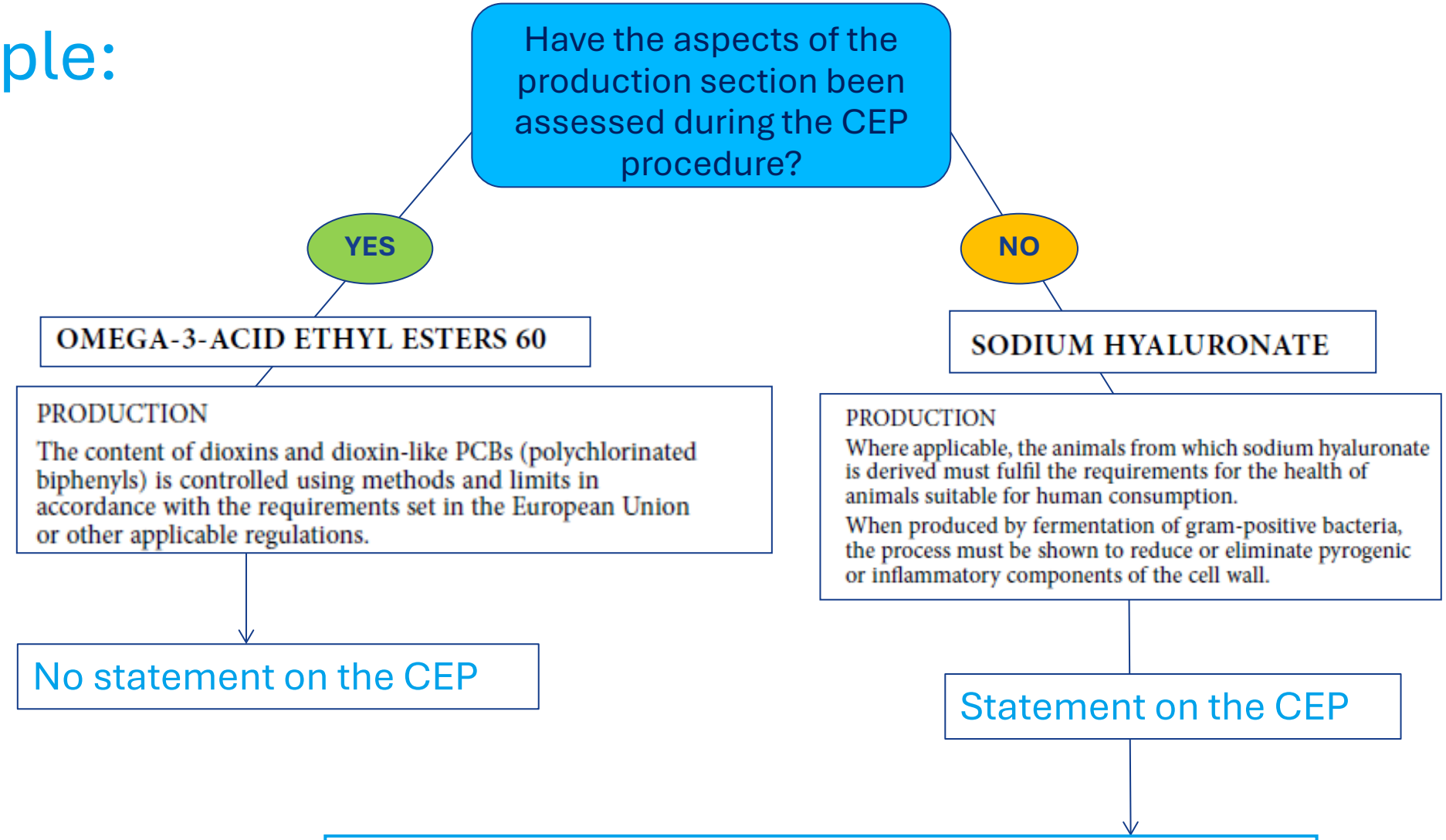
Example:



Compliance with the Production Section of the monograph should be assessed in the context of a medicinal product containing this substance.

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Statements on CEP for sterile substances

★A “sterility CEP” does not exist on its own.

★Always combined with a Chemical CEP or with a Double CEP (chemical + TSE).

★The CEP includes the typical statements of each type of CEP (as applicable).

The European system requires that sterilisation data should be included in the MAA even if a CEP for a sterile substance is submitted

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Typical sterility related statements

★ Subtitle “Sterile”

Name of the substance:
CEFUROXIME SODIUM
Sterile

★ Statement regarding compliance with the test for sterility (2.6.1) of the Ph. Eur. (old CEP)

★ Statement that the sterilisation process has been assessed and accepted (old CEP)

★ Sterilisation(s) method (old, hybrid and CEP 2.0)

★ **For old CEP:**

The substance is sterile and shall comply with the test for sterility (2.6.1.) of the European Pharmacopoeia. The method used for sterilisation is a sterile filtration and the sterilisation process has been assessed and approved.

★ **For hybrid and CEP 2.0:**

The substance is sterile and is produced by sterile filtration.

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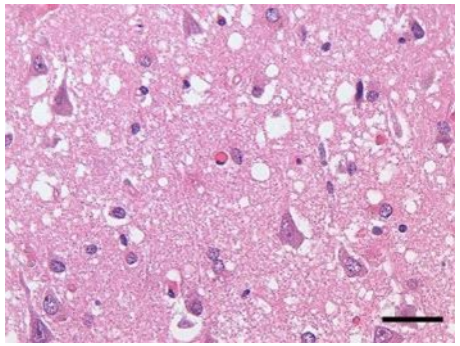
Statements on TSE CEP



Additional information, as applicable:

- ★Subtitle (e.g. manufacturing process for gelatin)
- ★Country(ies) of origin of source materials
- ★Nature of animal tissues used in manufacture
- ★Manufacturing process applied (if relevant for the safety of the product e.g. gelatin)

A TSE CEP does <u>not</u> certify that a particular source of a substance complies with the corresponding Ph. Eur. monograph for that substance.
A TSE CEP certifies that the substance is compliant with Ph. Eur. Monograph 1483 → it is **"TSE safe"**

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Statements on herbal CEPs

For extracts:

- ★Drug extract ratio (DER) calculated on genuine extract (without excipients)
- ★Extraction solvent(s) used
- ★Information on excipients used: name and percentage.

For all types of products:

- ★**For CEP 2.0**: the specification is appended
- ★**For old and hybrid CEP**: residual solvents if used in last steps or any other parameter such as aflatoxins and ochratoxins where applicable, are mentioned on the CEP with acceptance criteria and control methods

- ★Sentence on use of water in the last steps of the process (quality of water if CEP 2.0).
- ★Packaging material
- ★Re-test period if requested by the applicant
- ★Use/non-use of material of animal or human origin

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CEP in a Marketing Authorisation Application **in** the EU

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

3 January 2024
EMA/CHMP/CVMP/QWP/5/2024
Committee for Medicinal Products for Human Use (CHMP)
Committee for Medicinal Products for Veterinary use (CVMP)

QWP Questions and Answers (Q&A): how to use a CEP in the context of a Marketing Authorisation Application (MAA) or a Marketing Authorisation Variation (MAV)

→ **Q&As only applicable for MAAs/MAVs in EU/EEA**

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European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

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CEP in a Marketing Authorisation Application **in** the EU

- Collection of 18 Q&As
- General Cases
  - QP Declaration
  - Information to be included in S-Part of the MA
- Specific Cases
  - Intermediate covered by CEP
  - CEPs for sterile substances
  - API mix
  - TSE CEPs
- And others

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CEP in a Marketing Authorisation Application **outside** the EU

- ★CEPs are accepted in countries outside Europe
- ★At the discretion of the authorities of those countries
- ★These authorities decide on the scope of the acceptance of CEPs and the conditions that may apply, e.g. in addition to the CEP there may be a requirement for provision of a DMF (open part or full content) or other documents
- ★Applicants to verify the acceptability and conditions associated with the use of a CEP in such countries prior to submission.

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Final words

- Read available documents to understand the content of a CEP and use it in the best way
  - How to read a CEP (PA/PH/CEP (15) 31, 1R): **link**
  - Other applicable EDQM guidelines and policy documents: **link**
  - FAQs: **link**
- As CEP holder, communicate actively with your customers
- As drug product manufacturers, communicate actively with your suppliers

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Thank you for your attention

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