

European Directorate for the Quality of Medicines & HealthCare

Council of Europe

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COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

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cMEP
certified review of microbiological methods per the European Pharmacopoeia

Solène Le Maux, EDQM, Council of Europe

CASSS CGTP Europe Symposium, Lisbon, 20 October 2026

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European Pharmacopoeia (Ph. Eur.) and its structure



* EU: European Union; TFDA: Taiwan Food and Drug Administration; WHO: World Health Organization

- ★ 40 Members, 33 Observers
- ★ Protecting public health – one common compulsory standard
- ★ Legally binding quality standards; at the same date for all Members
- ★ Issue 12.3: ~2600 monographs, ~400 general chapters, ~3000 reagents

General chapters & general texts

- provide standard analytical procedures; guidance
- **become mandatory** when referred to in a monograph

Individual monographs

- Specific but not a stand-alone text
- Based on approved specifications backed up by batch data



General notices

- **Essential reading**
- Apply to all texts, address general topics
- Include rules to understand texts

General monographs

Dosage form monographs

- **Mandatory** for all substances/products within scope of their definition
- Not cross-referenced in individual monographs (exceptions)



Ph. Eur. Reference standards / preparations & reagents

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Cell and gene therapy – Ph. Eur. PORTFOLIO



General overarching texts

- ★ 3186 Gene therapy medicinal products for human use
- ★ 5.34 Additional information on gene therapy medicinal products for human use (including mRNA-based GTMPs)
- ★ 5.2.12 Raw materials of biological origin for the production of cell-based and gene therapy medicinal products
- ★ 5.32 Cell-based preparations for human use (+ Keratinocytes-based and T-cell-based preparations sections)
- ★ 5.47 Gene edited cells for human use

General methods: numeration & viability

- ★ 2.7.23 Numeration of CD34+/CD45+ cells in haematopoietic products
- ★ 2.7.24 Flow cytometry
- ★ 2.7.28 Colony-forming cell assay for human haematopoietic progenitor cells
- ★ 2.7.29 Nucleated cell count and viability
- ★ 2.6.35 Quantification and characterisation of host-cell DNA

General chapters: Microbiology aspects & viral safety

- ★ 2.6.1 Sterility
- ★ 5.1.6 Alternative methods for control of microbiological quality
- ★ 2.6.27 Microbiological examination of cell-based preparations
- ★ 2.6.39 Microbiological examination of human tissue
- ★ 5.1.13 Pyrogenicity - 2.6.30 MAT - 2.6.14 BET - ~~2.6~~
- ★ 2.6.7 Mycoplasmas
- ★ 5.1.7 Viral safety
- ★ 5.2.8 TSE



Under elaboration
Under revision
Recently adopted/published/revised
Planned suppression
Other published

Non exhaustive list

Individual monographs

- ★ Bovine serum (2262)
- ★ Human haematopoietic stem cells (2323)

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Cell and gene therapy – Ph. Eur.

PORTFOLIO



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Gene… Microbiology a…

- ★ 2.6. …
- ★ 5.1.6 …y
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- ★ 5.1.13 Pyroge… …6.30 … …2.6.14 BET - ~~2.6.32 rFC~~
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Important class of safety tests

Und… …ation
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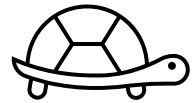
Let’s talk about microbiological testing

Conventional methods

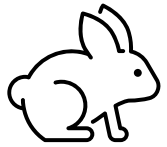


- ★ Incubation step to allow for growth of potential contaminants, e.g. *2.6.1 Sterility*: at least 14 days
- ★ In some cases, cannot be performed for technical reasons or due to characteristics of preparation
  - ★ Need for short analytical lead time - “wait time” critical for patient or products with short shelf-life
  - ★ Not for small batch size - limited sample volume

Alternative microbiological methods (AMM)

Depending on the methods:

- ★ Faster results (e.g. 5 days, 4h, 10 min)
- ★ Possibility of earlier corrective action
- ★ Lower sample volume requirements
- ★ Matrix compatibility
- ★ Broader detection
- ★ Greater automation potential





- ★ Validation (fit for purpose)
- ★ Comparability to official method

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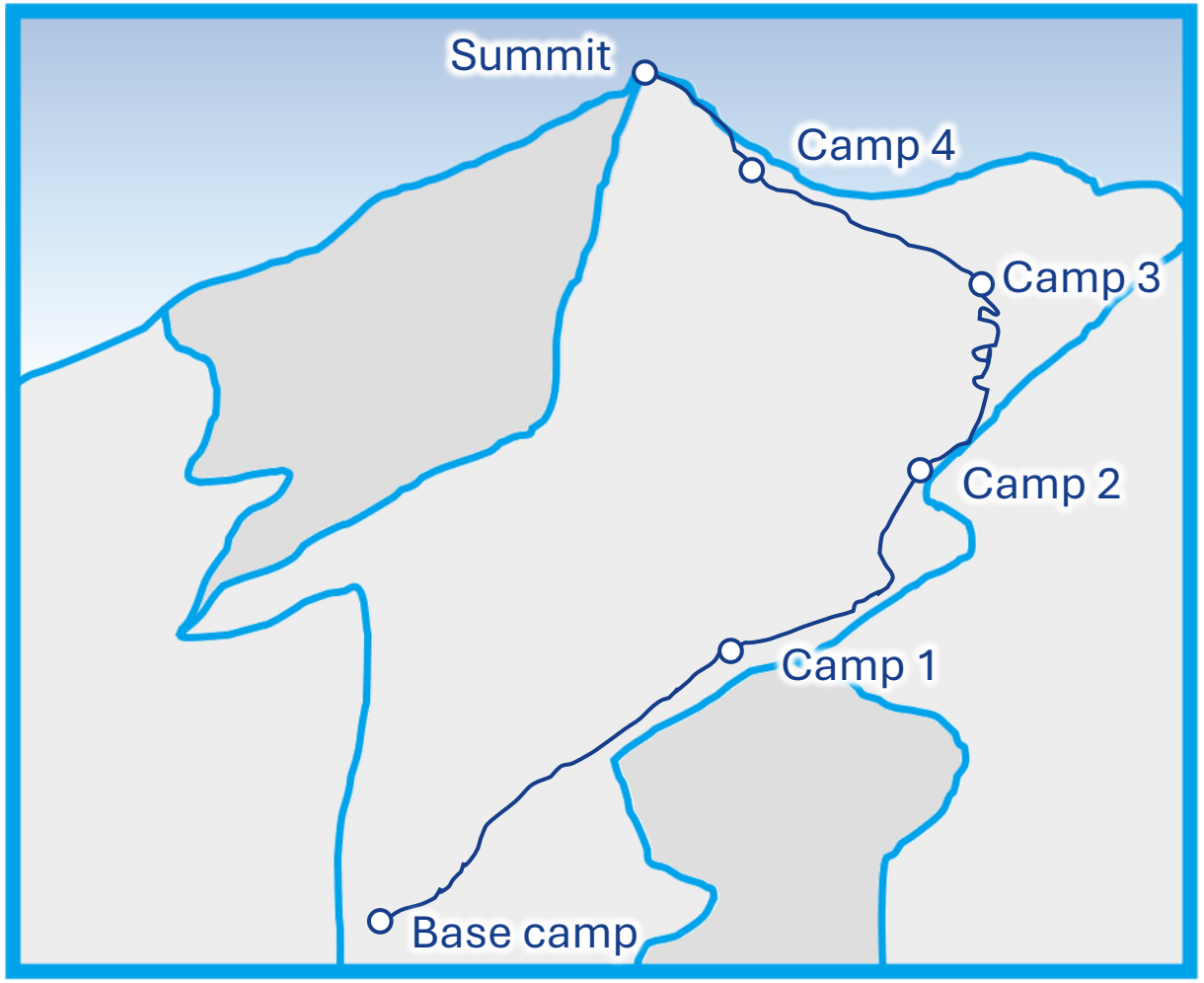
Before using AMM, you have to climb!



Ph. Eur.

- ★ Devoted significant efforts in facilitating use of AMM
- ★ Cannot provide detailed methods as they are equipment related
- ★ A milestone was the publication in 2006 of a new general chapter *5.1.6. Alternative methods for control of microbiological quality*

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5.1.6. Alternative methods for control of microbiological quality

***Objective**: Facilitate implementation and use of AMM through a flexible, risk-based, fit-for-purpose approach*

General principles of alternative microbiological methods

Basic principles of methods

- No recommendation of one method over another
- Not an exclusive or exhaustive list
- Other methods may be applicable

Implementation of alternative microbiological methods

- **Method selection**
- **Equipment qualification**
- **Primary validation**
- **Product-specific validation**
- **Comparability**
- **Application to routine use**

Update and clarification, incl.:

- Additional information to **optimise the implementation strategy** by capitalising on suitable tests previously performed and by evaluating different implementation activities simultaneously;
- **Clarification of the responsibilities of suppliers and users**, in particular for the primary validation and the comparability

Published in Ph. Eur. Issue 13.2
Implementation 1 Apr 2027



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Programme included :

- ★ Dedicated **training session** on the newly revised chapter *5.1.6* (free e-learning to be made available shortly)
- ★ 2 sessions focused on AMM
- ★ Symposium report currently in preparation for publication

https://www.edqm.eu/en/edqm-symposium-microbiology-on-the-move

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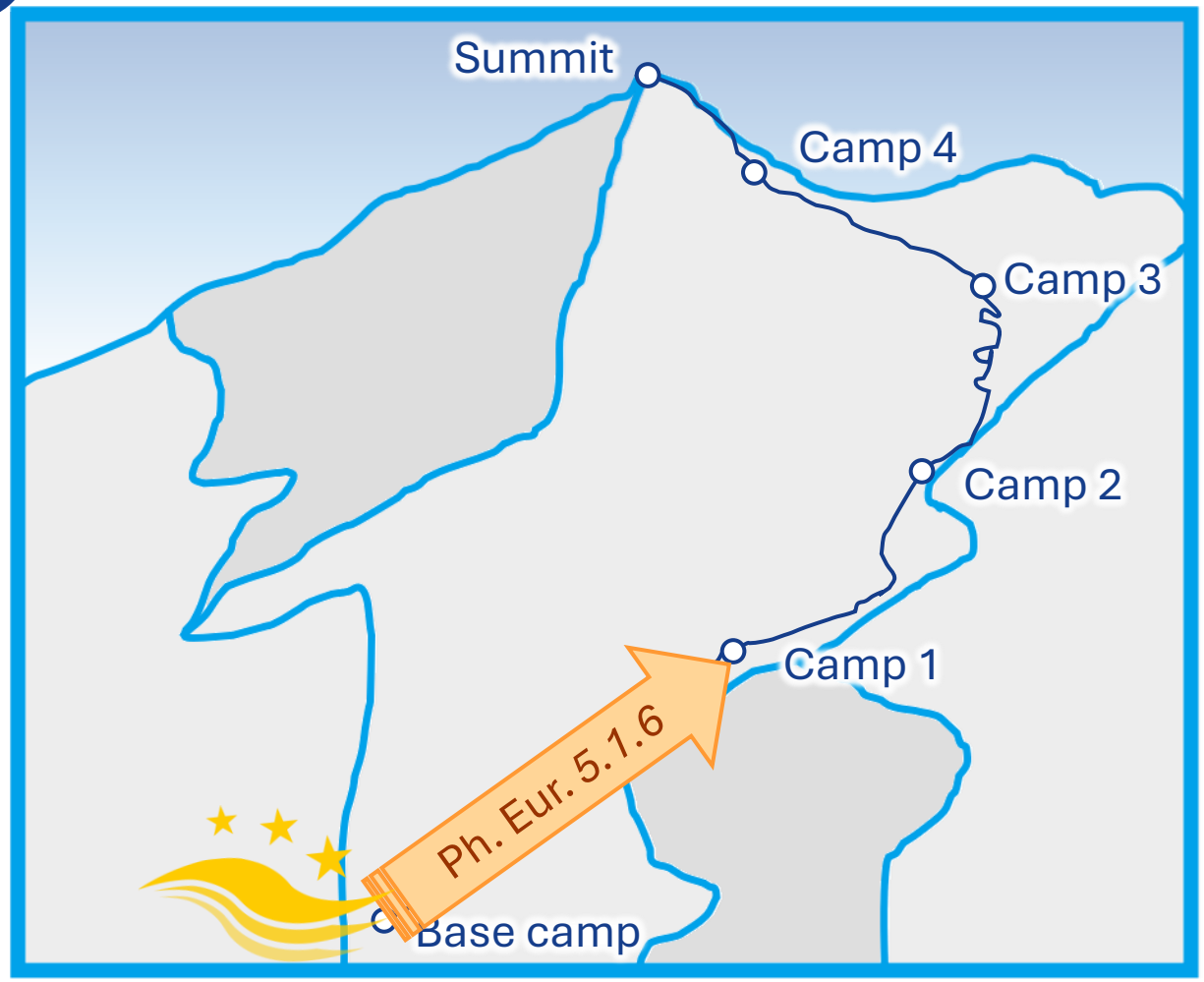

Stakeholders FEEDBACK received over the years

- ★ Chapter *5.1.6* facilitates the use of these methods as alternative
- ★ But implementing AMM still challenging
- ★ Users are eager for the EDQM to play a bigger role in the facilitation of the use of these methods
- ★ A system of AMM certification has been suggested by a stakeholder

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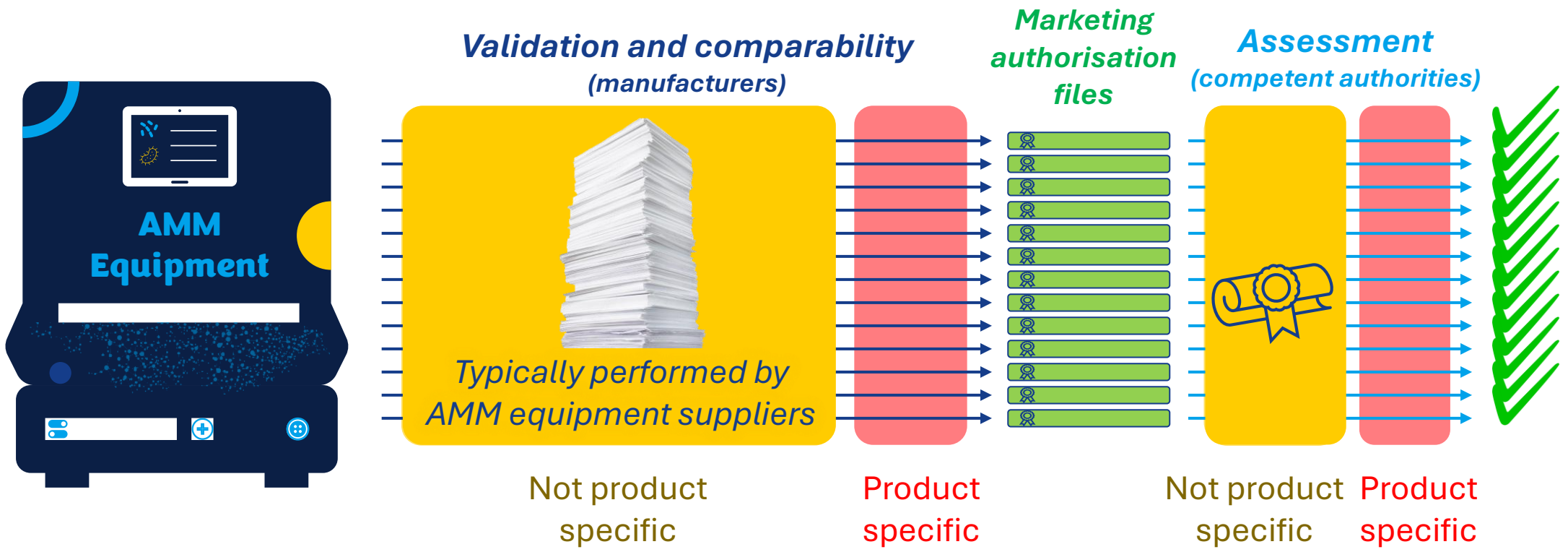
cMEP (*certified review of microbiological methods per the European Pharmacopoeia*)

Method-centric system that would facilitate the use of AMM by providing an independent review of their validation and comparability, with the Ph. Eur. as reference



- ★ *Facilitate method selection by users (providing confidence in method and data package)*
- ★ *Support regulatory assessment (providing an harmonised review to CA, avoiding re-evaluation of common AMM dossier elements)*
- ★ *Save time and promote wider use of AMM (reducing duplication of effort for both users and regulators)*

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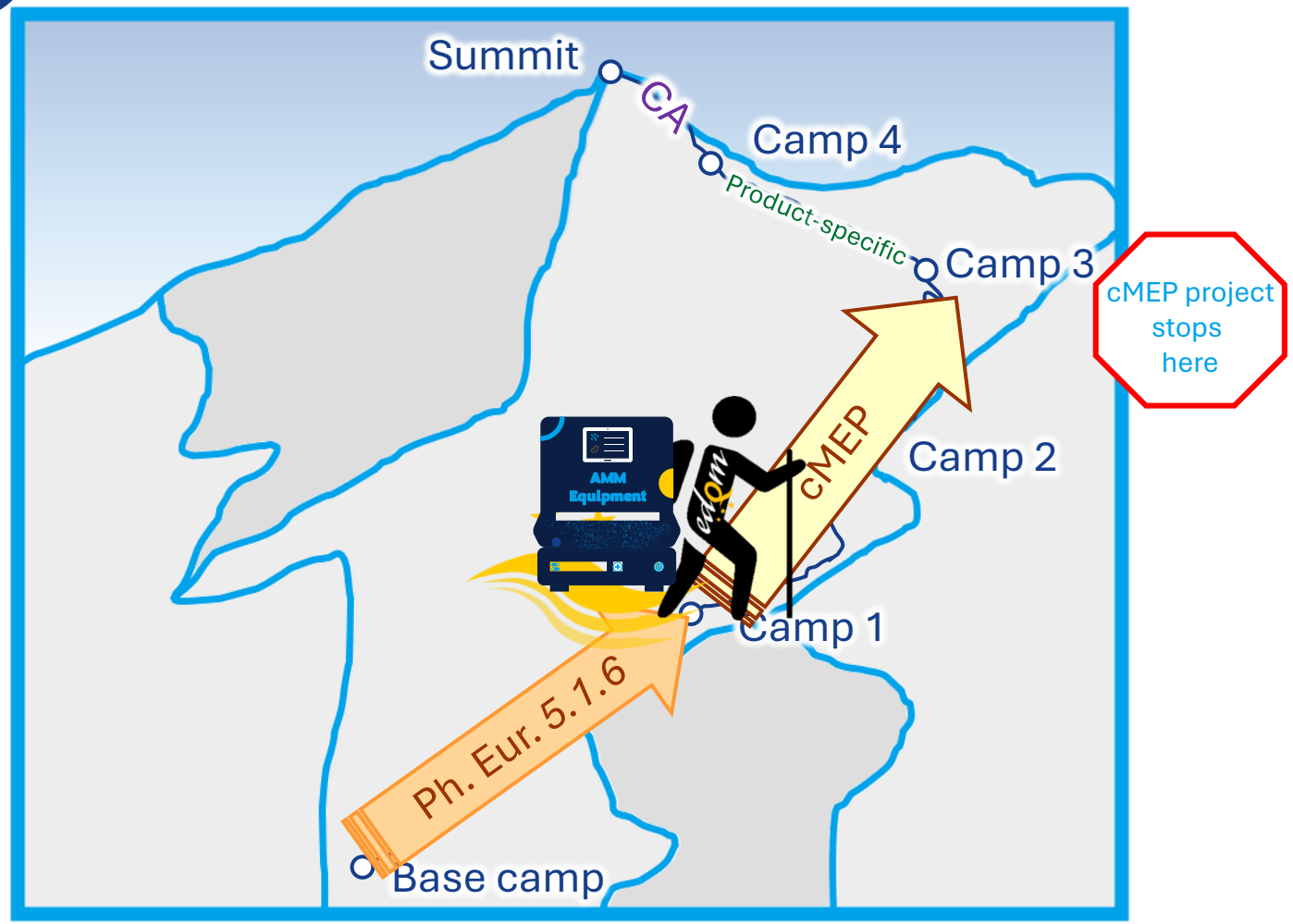
Before using AMM, you have to climb!



cMEP system

- Independent scientific review of non-product-specific validation and comparability data
- **NOT** a review of product-specific data
- **NOT** a replacement of the role of competent authorities (CA) in marketing authorisation

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The cMEP project

Exploration phase

Stakeholders support



- Ph. Eur. family
- Regulatory and public workshops (Apr & Oct 2024)

Conception phase



cMEP WP established in 2026

External expertise essential due to technical complexity and the importance for broad stakeholder acceptance

Pilot phase

Consultation
Communication

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Take home message

- The Ph. Eur. has a longstanding commitment to facilitating the use of AMM
  - Chapter 5.1.6 is a key text
  - Revised text published in Ph. Eur. Issue 13.2 (implementation 1 Apr 2027)
- With a pragmatic approach
  - Science- and risk-based approach allowing for fit-for-purpose and flexibility
  - Technology-neutral, with no preference for specific methods or platforms
  - Enables efficient implementation by leveraging existing data and prior studies, and by combining implementation activities, where appropriate
- Chapter 5.1.6 as a foundation for cMEP:
  - Support a method-centric approach to facilitate the use of AMM
  - Provide a harmonised scientific review of validation and comparability in accordance with the Ph. Eur.



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thank you







- Ph. Eur. experts groups, especially Group 1 (microbiology), cMEP WP, CTP WP, GTP WP
- EDQM colleagues
- All contributors to the Ph. Eur. CGTP and microbiology activities

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