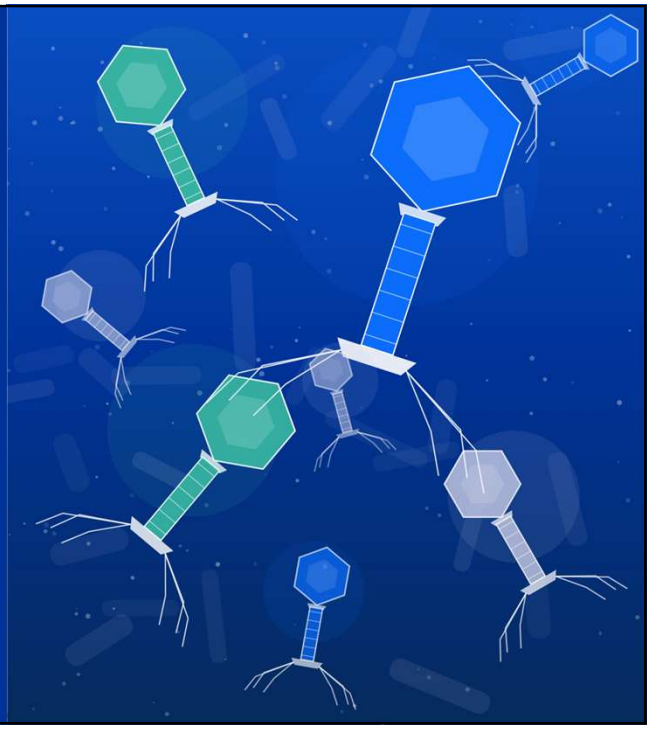
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Licensing something built to vary

A regulatory perspective on phage therapy in the EU

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Session: Phage therapy as a narrow-spectrum antimicrobial strategy



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> How much standardisation must phage accept to be licensable, dosable and trial-ready — without losing the personalisation that makes it work?

The session's organising question — this talk answers it from the regulator's perspective

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Where the morning has brought us

Programme design

The unit of development is the programme, not the molecule.

Reproducibility is the binding constraint.

PK–PD and dose

No antibiotic-style exposure curve for a replicating agent.

"Dose" = a validated regimen plus a delivered-potency specification.

Manufacturing platform

Phage bank + validated process + release specifications.

Consistency = within justified limits every time, not identical batches.

The regulator's question: how do you license something that is built to vary?

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Licensing something built to vary

What the marketing-authorisation framework assumes

- A defined product of fixed composition
- Reproducible from batch to batch
- One product ↔ one authorisation ↔ one dossier
- Quality, safety and efficacy shown once, for that product

≠

What personalised phage therapy is

- Variable by design — matched to the patient's isolate
- Composition may differ from patient to patient
- A living, co-evolving biological agent
- …yet the same quality, safety and efficacy standards apply

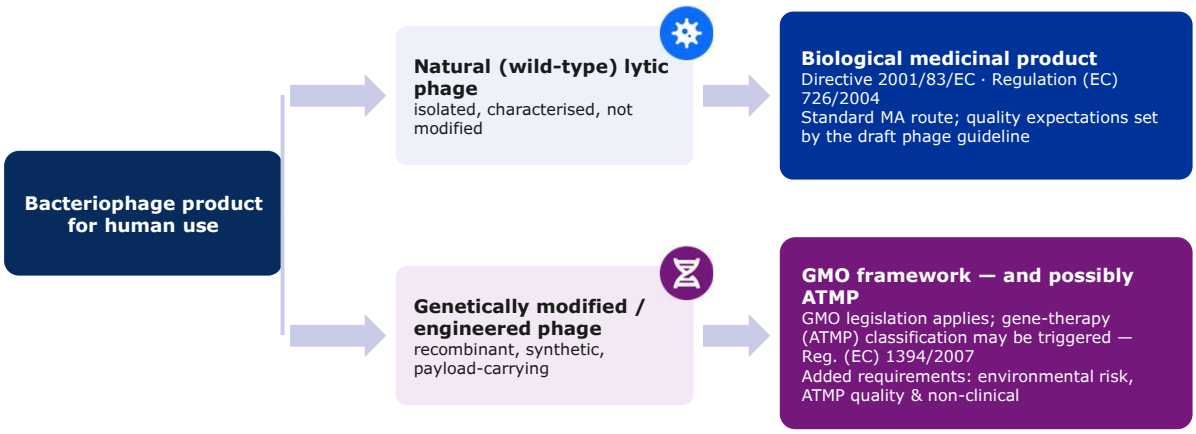
The task is not to lower the bar — it is to find routes that fit the product.

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How phage are classified in the EU

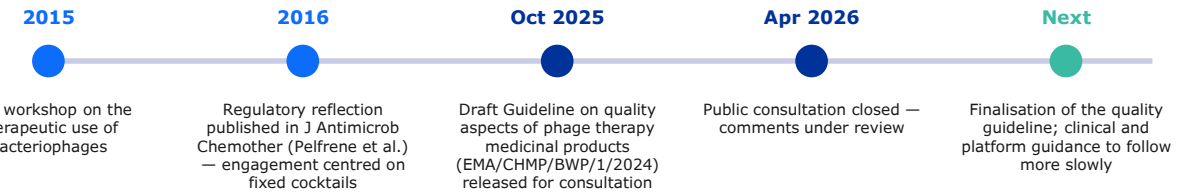


The structural problem: personalisation sits uneasily with the one-product, one-authorisation model — whichever box you land in.

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Where EMA is today



The draft guideline covers
CMC for active substance and finished product: manufacture, characterisation, specifications, reference standards, stability

It does not yet address
Clinical development, personalised preparations, or a platform/bank authorisation model — expectations must be calibrated accordingly

Partially adaptable today
Existing EMA guidance on PK–PD and clinical evaluation of antibacterials offers principles that can be adapted, not copied

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The platform approach

ONE QUALITY SYSTEM

Characterised phage bank
sequenced, curated, master/working banks

Validated process
controlled host, purification, release specifications

Control strategy
comparability & change management

Authorised once, as a system — then a family of defined preparations or cocktails is deployed under it, adding or swapping phage through comparability and change-control rather than starting from zero.

- **Preparation A**
- **Cocktail B**
- **Preparation C**
- **…and the next**

What it would require
A robust control strategy · comparability between components · change management across the family · a susceptibility test that links bank to patient

Status
A direction of travel — not yet an established route. Fixed cocktails remain the nearer-term MA path.

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The magistral formula pathway

Art. 3(1) Dir 2001/83/EC — a medicine prepared in a pharmacy for an individual patient, outside the MA system. The Belgian model:

Phage active substance
GMP-grade, against a national monograph; centrally quality-controlled

Hospital pharmacy
magistral compounding of a patient-specific preparation

Individual patient
phage matched to the isolate by phagogram; often with antibiotics

Strengths
- Access for patients now
- True personalisation
- Centralised quality control of the active substance

Limits
- No MA-level evidence generated
- National fragmentation, variable oversight
- Weak commercial incentive

Does it work in practice?
100 consecutive personalised cases

77%
clinical improvement

61%
target-pathogen eradication

Pirnay et al., Nat Microbiol 2024. Observational; eradication ~70% less likely without concomitant antibiotics.

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Other access routes — and their limits

Route	Legal anchor	What it gives	What it does not give
Magistral formula	Art. 3 Dir 2001/83/EC	Access now; genuine personalisation	MA-level evidence; EU-wide consistency
Hospital exemption	Art. 28 Reg (EC) 1394/2007 — ATMP-classified engineered phage only	National, small-scale, non-routine use in a hospital	Routine supply or a route to a licence
Compassionate use / named-patient supply	Art. 83 Reg (EC) 726/2004 · Art. 5 Dir 2001/83/EC	Case-by-case access for patients without options	A development pathway
Unlicensed 'specials'	National provisions	Supply where no licensed product exists	The evidence generation that advances the field

Several routes give patients access — **none of them, alone, generates the controlled evidence that supports a licence and broad availability.**

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The evidence-generation gap

Access routes deliver…

- Treatment for individual patients
- Case series and observational outcomes
- Heterogeneous products, doses and comparators

magistral · named-patient · hospital exemption

THE GAP

Bridging tools

- Structured registries and observational networks — e.g. the Belgian consortium, Phage Australia (STAMP)
- Adaptive and novel trial designs that accept matched, variable products
- Common data elements: product identity, titre, phagogram, antibiotics

What an MA needs…

- Comparative, controlled evidence
- A defined product with a defined regimen
- Reproducible benefit–risk across patients

centralised procedure · CHMP opinion

The personalised-vs-RCT paradox is, at root, an evidence-architecture problem — not proof that phage do not work, and not something a single trial design will resolve.

Trial design & funding: handed to the next session (10:30)

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Timing — and what not to wait for

Guidance will arrive in layers

Now → 2026/27
Quality guideline: consultation closed; finalisation

Following
Clinical expectations for phage products

Later
Platform / bank and personalised models

Use the tools that exist now

Scientific advice
CHMP/SAWP; qualification of novel methods (e.g. a phagogram)

PRIME eligibility
for products addressing unmet need with early clinical signal

Early, repeated engagement
Innovation Task Force; bring your control strategy to the table

Do not wait for perfect guidance — engage early, with your control strategy in hand.

EU Pharma Package — the evolving context

Political agreement reached in 2026; formal adoption pending; application expected from ~2028

Transferable data-exclusivity voucher for 'priority antimicrobials'

Regulatory sandboxes named for innovative antimicrobials — phage therapy already in annex VII, so no sandbox needed, just work on an adaptive framework

May shape the commercial case; not a substitute for a dossier

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Synthesis: a realistic near-term EU picture

Fixed cocktails
Marketing authorisation where feasible — defined, manufacturable, licensable

Platform / phage bank
The bridge — carried by quality systems, comparability and change control

Magistral preparation
Genuine personalisation and access — with registries to capture the evidence

◄ *a hybrid, not a single route* ►

Open questions for the field

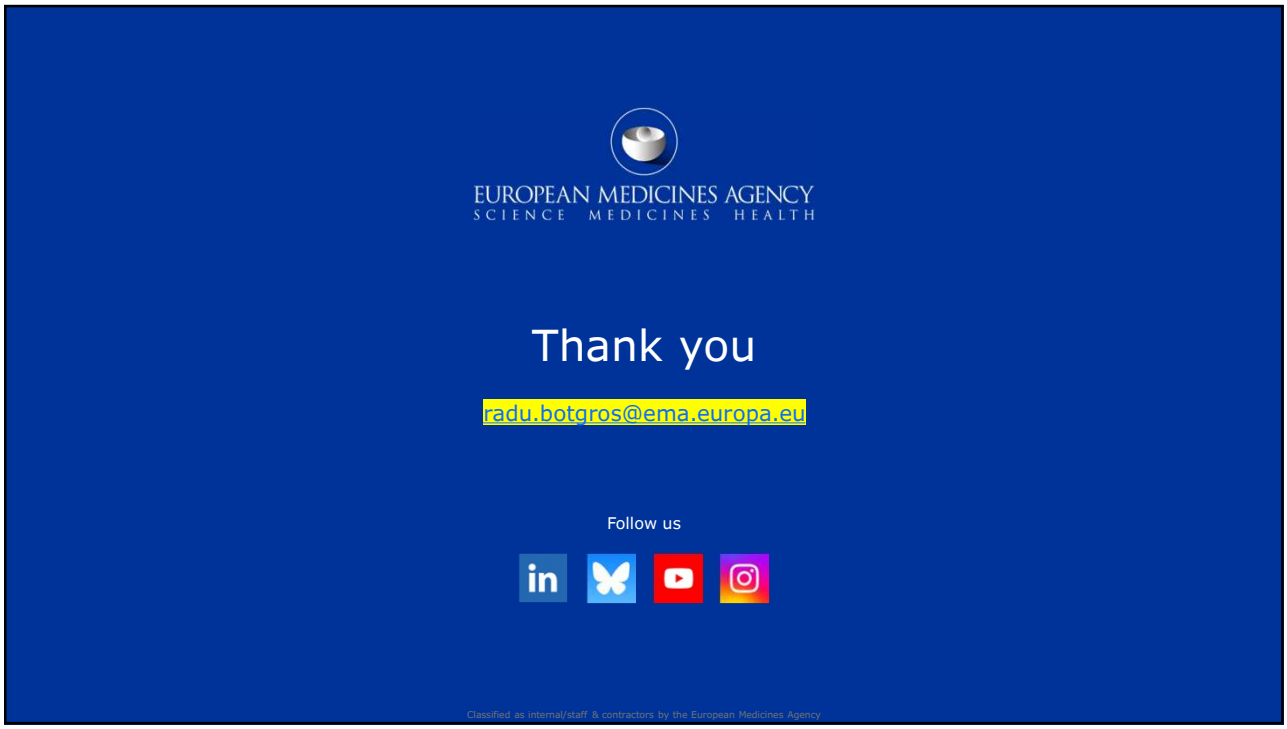
- Standardised susceptibility testing — the phagogram
- The unit of evidence: product, platform or programme?
- A sustainable incentive for narrow-spectrum, personalised medicines

Answering the organising question
Substantial standardisation is unavoidable — but a platform-plus-magistral hybrid can protect the personalisation that makes phage work.

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