Leveraging Novel Vaccine Platforms to Accelerate HIV Vaccine Development

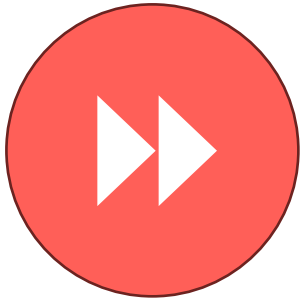
Cathy Hoath

Global Regulatory Affairs Strategy Lead, CEPI

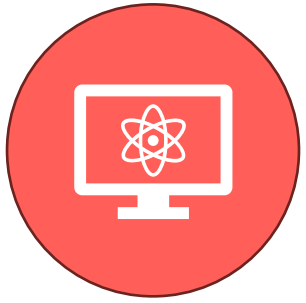
19-May-2026

HIV requires a novel approach

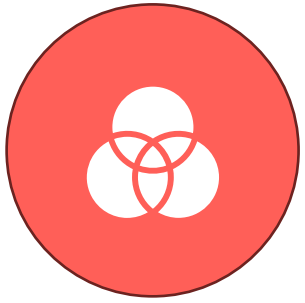
- HIV remains one of the most scientifically complex vaccine challenges of our time. Its extraordinary genetic diversity, ability to evade immune responses, and need for durable protection mean that traditional, single-product vaccine development approaches are unlikely to succeed alone.
- To meet this challenge, the global community is increasingly turning to novel vaccine platforms – technologies designed to be adaptable, iterative, and fast, enabling rapid hypothesis testing, learning, and optimization.
- Rather than starting from scratch for each new candidate, platforms allow developers to build on prior knowledge, accelerating progress while maintaining high standards of quality and safety, enabling:



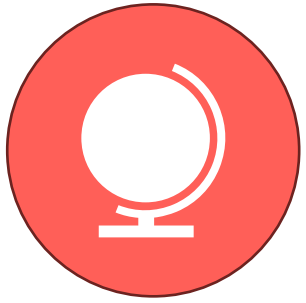
Speed and adaptability



Learning across candidates



Consistency and comparability



Global scalability

CEPI

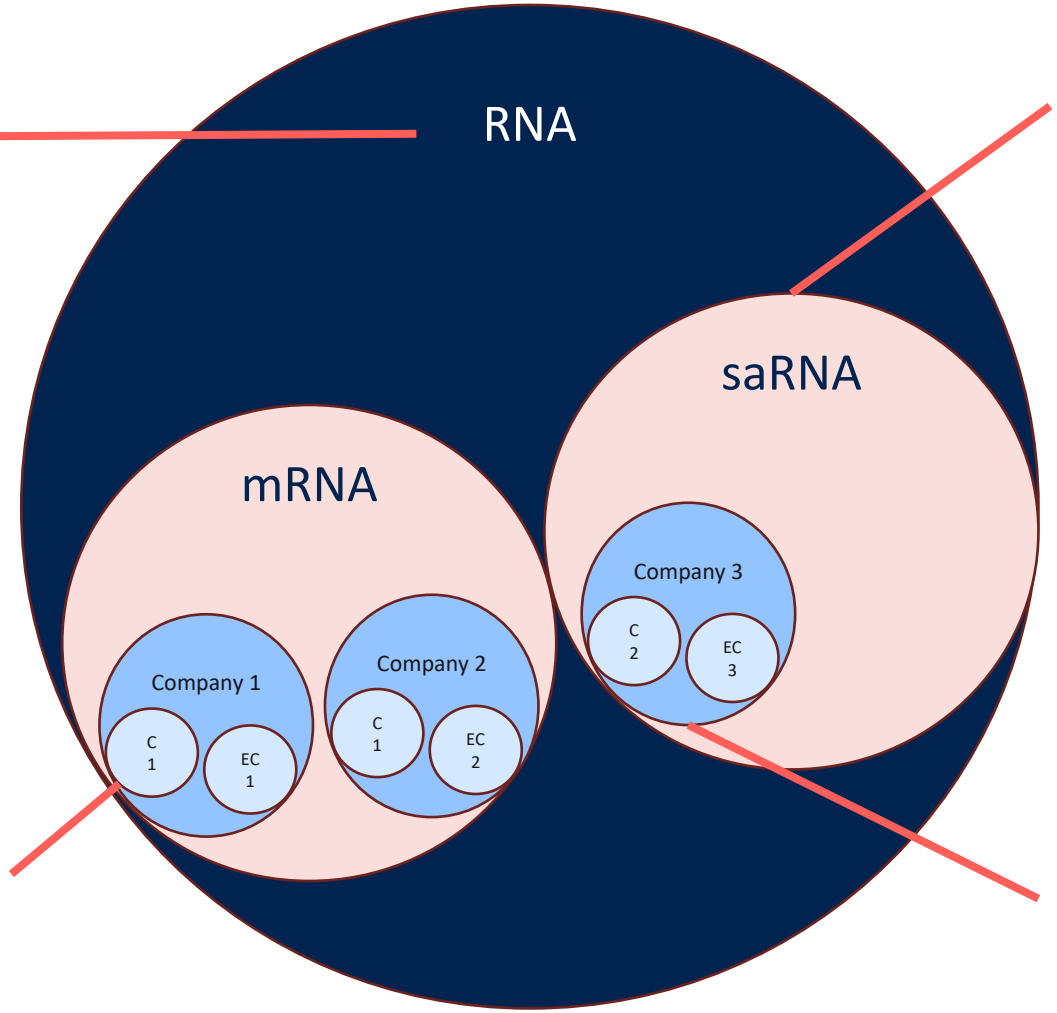
Definitions are important to understand regulatory pathways

Modality

'Modality' refers to the structure of a product's active substance.

Technology

'Technology' refers to the particular type of antigen vehicle within a modality



C = Chromatography
EC = Enzyme Capping

Platform Technologies

'Platform Technologies' are antigen-agnostic technologies that can be used across multiple products

Regulatory Platform

A 'Regulatory Platform' follows a specific, well-defined process to make products with uniform specifications and highly predictable characteristics

CEPI

Types of RNA Vaccine Technologies

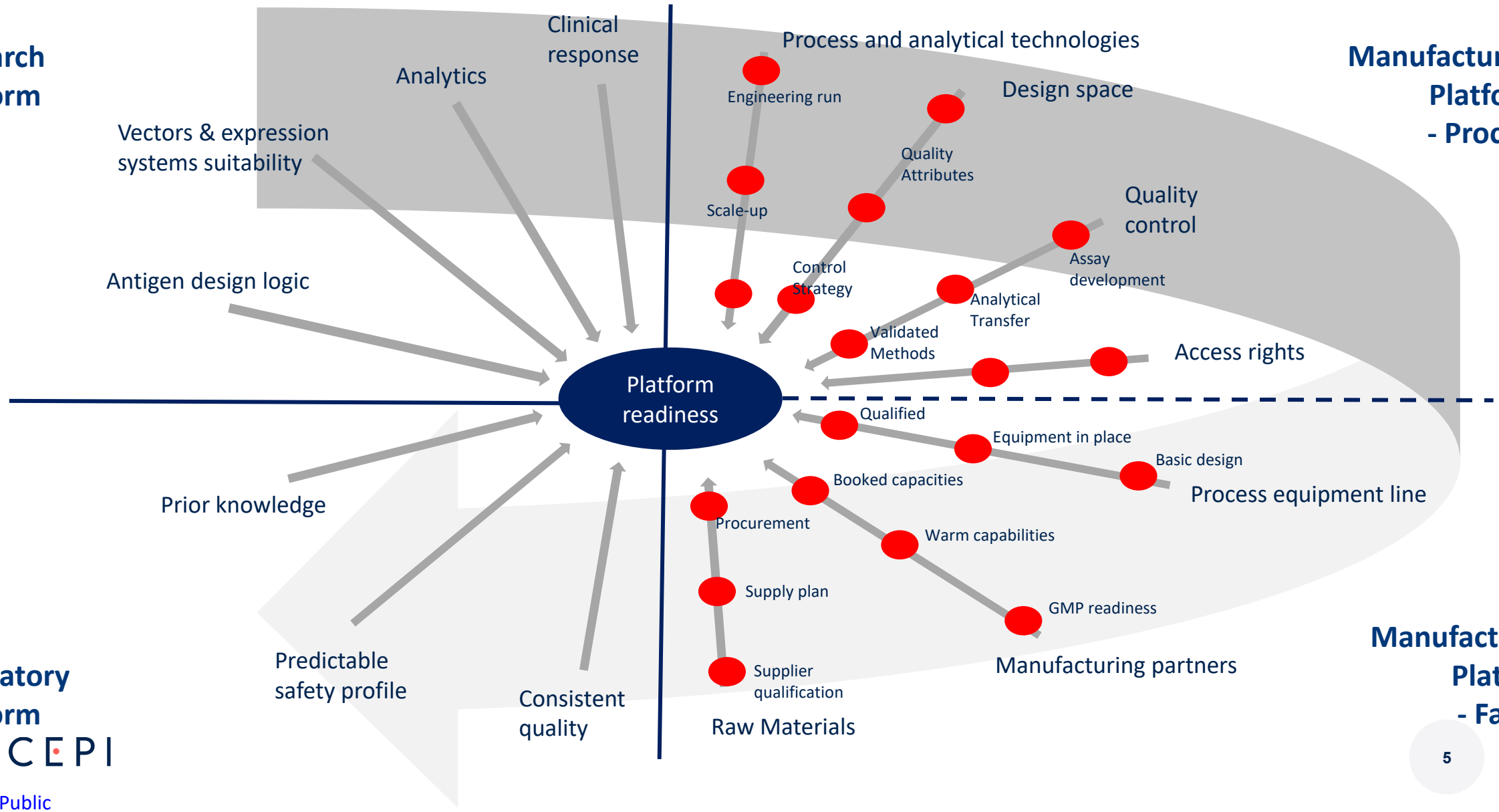
Non-replicating mRNA	Self-amplifying RNA	Trans-amplifying RNA	Circular RNA	RNA Replicon Particles
• Linear RNA • No replication • Approved	• Replicase-driven • Low dose • Advanced	• Split system • Modular • Emerging	• Closed loop • High stability • Early	• Viral Delivery • Immunogenic • Hybrid

Current leading technology for HIV

RNA platforms differ by replication, structure, and delivery – shaping dose, stability, and regulatory pathways

CEPI

Progression toward Platform Readiness



CEPI

Rethinking Regulatory Pathways for Platform-Based HIV Vaccines

Traditional regulatory pathways were built for stand-alone products, reviewed independently and sequentially. While this model has served public health well, it can slow progress when applied to platform-based innovation.

A modern approach recognizes that:

- Some data are platform-level and reusable
- Other data are specific to the HIV immunogen or regimen
- Regulatory review can be risk-proportionate and science-based

This enables regulators and developers to focus scrutiny where it matters most – on what is new and uncertain – while relying on accumulated platform knowledge where appropriate.

We see examples of reusable data in applications for flu vaccines based on platforms used for multiple variants. That concept can be expanded to include multiple viruses.

CEPI

Many options exist for conducting clinical trials

1. Marketing Authorization using standard, separate Phase 1, 2 and 3 trials (longest timeline) — Low risk
2. Marketing Authorization using seamless, adaptive Phase 2/3 trials (shorter) — Low-Med risk
3. Emergency Use Authorization based on non-clinical efficacy, Phase 2 safety, immunogenicity and early efficacy data, with RWE (shorter) — Med-High risk
4. Emergency Use Authorization based on non-clinical efficacy, Phase 2 safety, and immunogenicity data, with RWE (shortest) — High risk

The fastest options have the highest risk of not being effective. However, the **benefit may outweigh the risk** if data exist that show that the vaccines are safe and the impact of the disease is significant. Safety data from other vaccines manufactured using the platform may help support benefit-risk assessments.

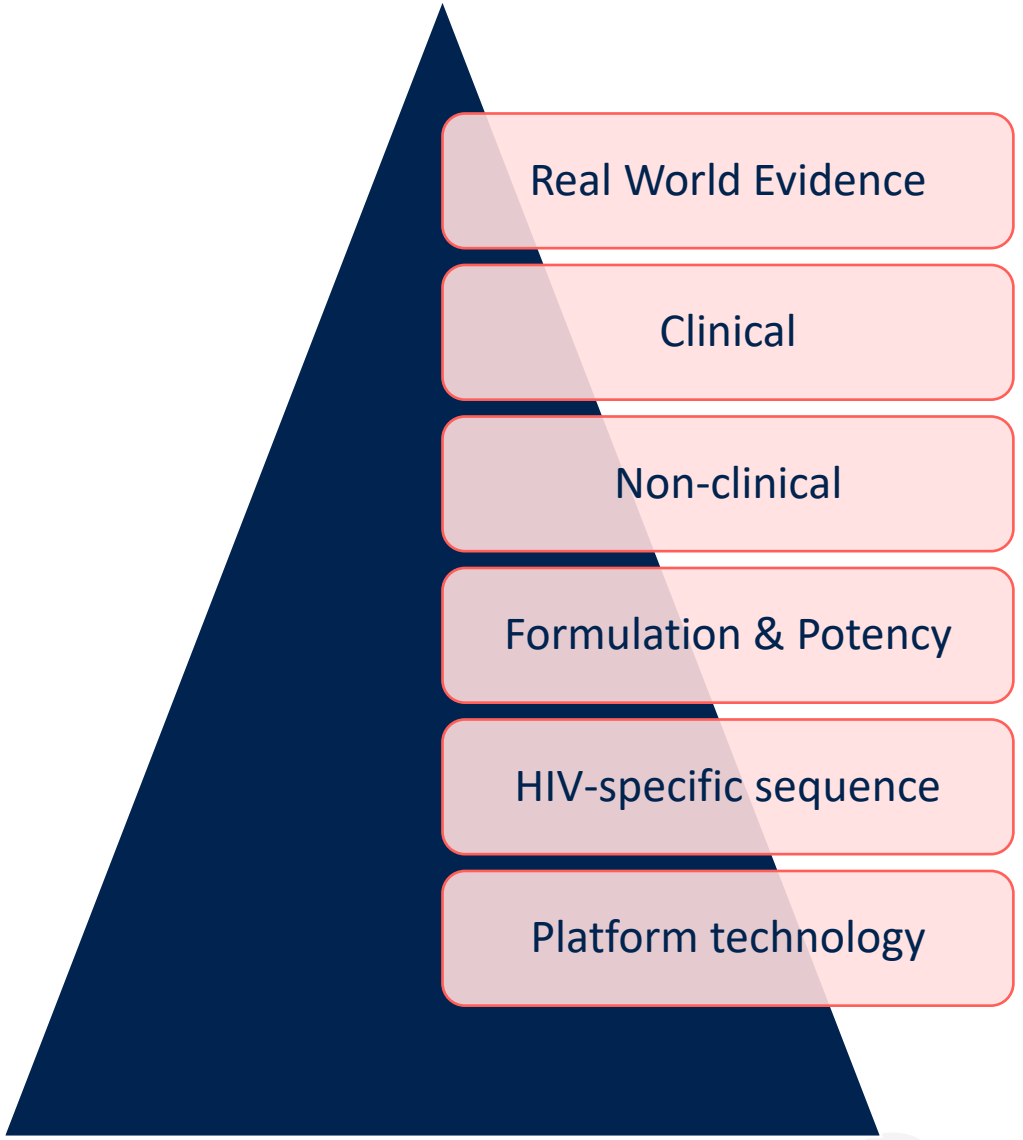
CEPI

Layered Evidence Framework

Platform-enabled HIV vaccine development increasingly follows a layered evidence model:

1. **Platform foundation**: Manufacturing quality, delivery mechanism, and prior safety experience
2. **HIV-specific sequence**: Antigen design, expression and immunogenicity
3. **Formulation & Potency:** Vaccine is developed for subsequent testing
4. **Non-clinical learning**: Test immune hypotheses in established models
5. **Clinical use**: Early-phase trials designed to test immune hypotheses in humans rapidly (including regimen)
6. **Real World Evidence**: Regional considerations, population diversity, and long-term monitoring

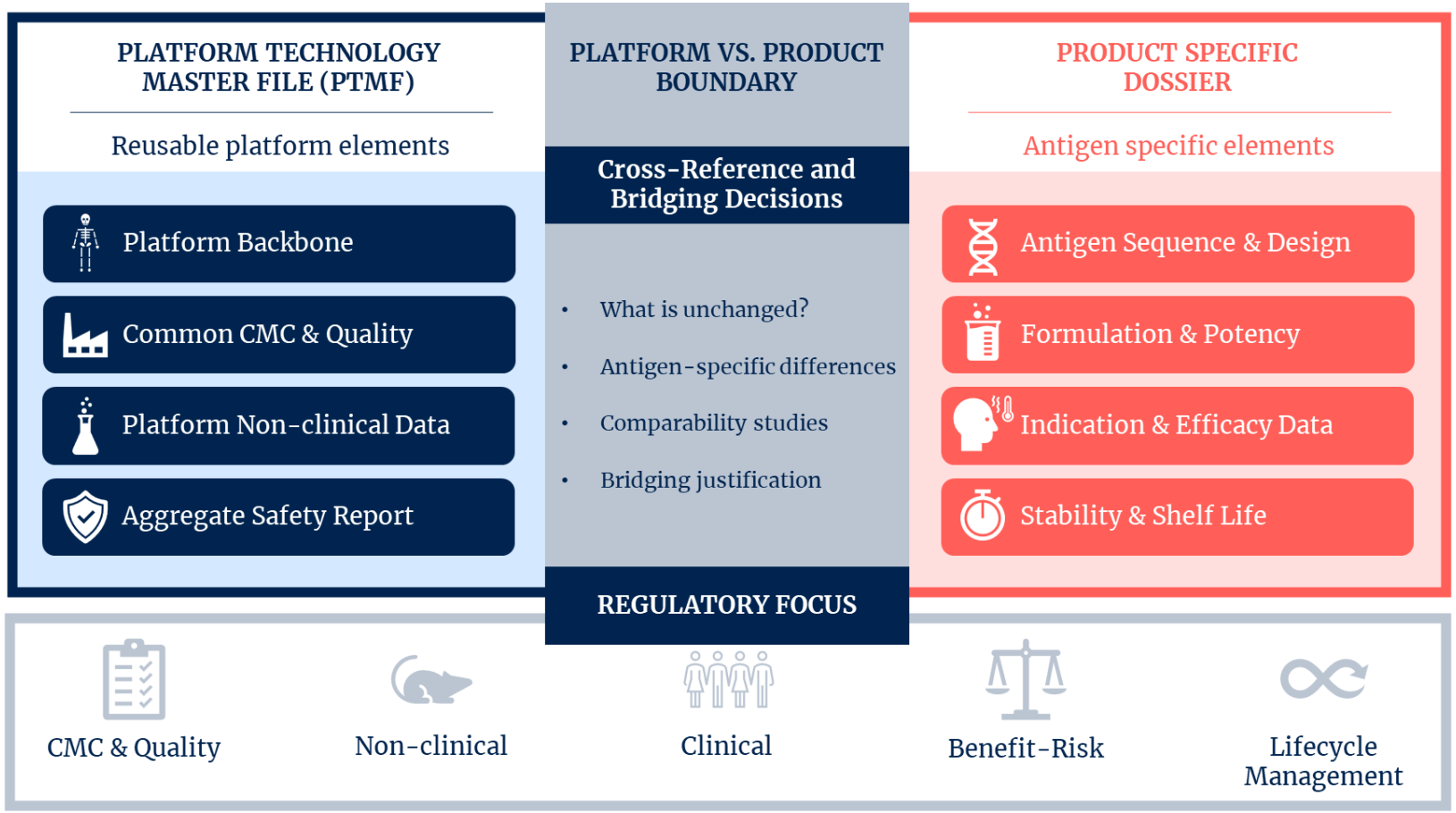
This approach supports faster learning while maintaining robust oversight.



CEPI

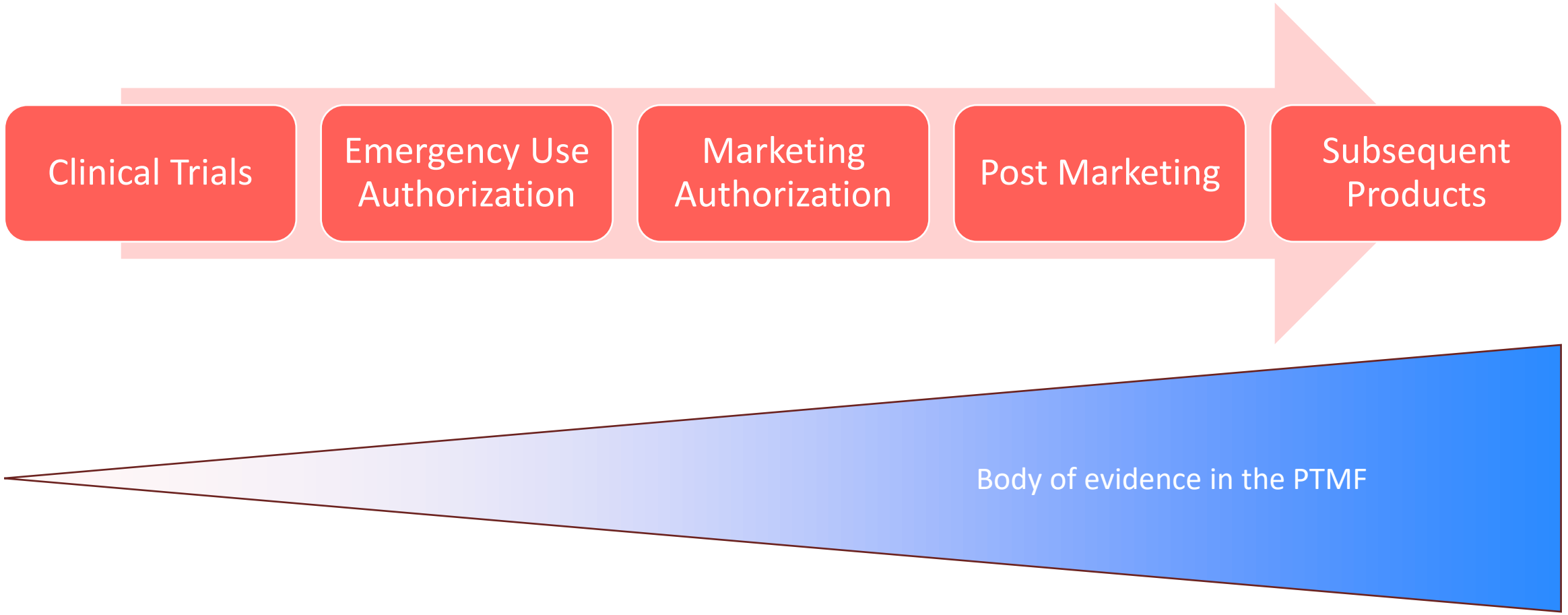
EMA Pharmaceutical Legislation Establishes the Context

- Revised EU pharmaceutical legislation recognizes platform technologies and introduces concepts enabling reliance on pre-evaluated data
- Reflects shift toward platform-based regulatory knowledge prepared in advance of public health emergencies



CEPI

Platform understanding will grow as long as the platform is used



CEPI

Regulatory strategies for managing changes to the platform needed

STEP 1

Within established conditions?

If changes fall within design space and analytical characterization confirms high similarity, a focused CMC comparability report suffices—reflecting ICH Q5E lifecycle management principles

STEP 2

CMC comparability?

Head-to-head analytical testing, CQA evaluation, impurity profiling, stability bridging, and process performance data. CMC evidence is always the first line of assessment before in vivo studies.

STEP 3

Targeted non-clinical studies?

When residual uncertainty exists (e.g., biodistribution, innate immune activation), hypothesis-driven non-clinical studies address specific questions—not full toxicology program replication.

STEP 4

Clinical bridging?

Only when uncertainty remains regarding human immunogenicity or safety does the framework escalate—typically immunobridging with focused safety data collection.

CEPI

What will other countries do?

1. Develop their own framework?
2. Rely on the EMA certification?
3. Work together to create a collaborative review process for PTMFs?
4. Operate as usual, re-reviewing platform data in each new application?
5. Come up with another approach?

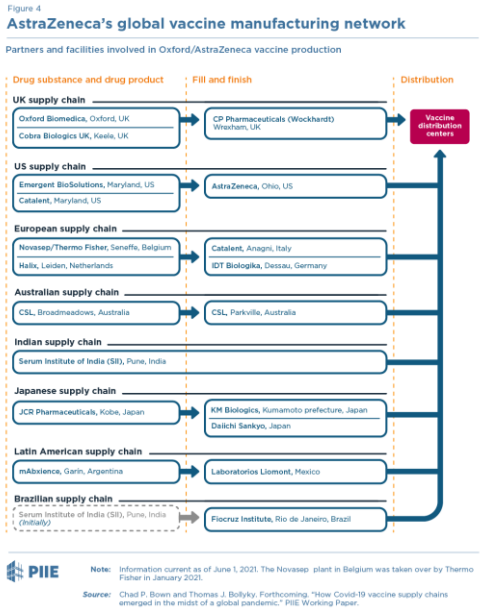
CEPI is exploring these options with regulators now to better understand what will work best to balance leveraging work already being done with each country's autonomy to support rapid global and equitable access.

CEPI

Enabling Global and Equitable Access

Novel platforms are not only about speed, they are also about equity. Platform approaches can help reduce duplication and delays that disproportionately affect low and middle-income regions through:

Technology transfer and decentralized manufacturing



[See Chad P. Bown and Chris Rogers, 2021, The US did not ban exports of vaccine supplies. But more help is needed, PIIE.]

Shared regulatory assessments across countries

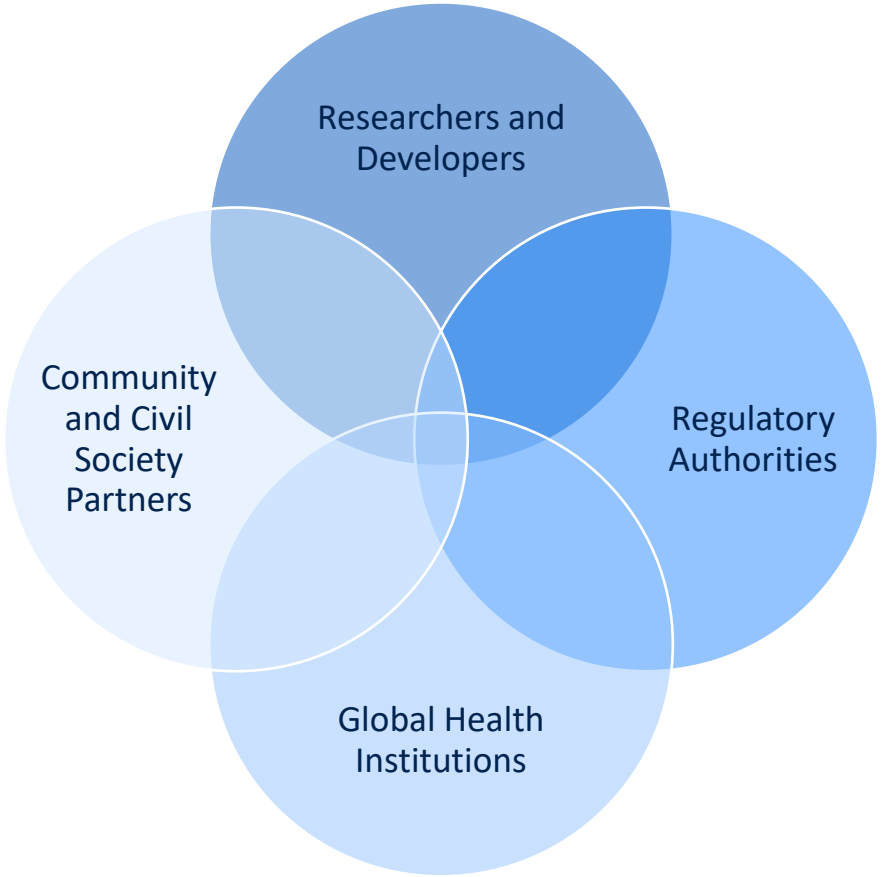
ONE WORLD, ONE DOSSIER

International Conference of Drug Regulatory Authorities (ICDRA) 2024

CEPI

Collaboration is Central

Early, transparent engagement around platform science helps build trust, align expectations, and ensure that innovation translates into real world impact.



CEPI

Looking Ahead

- Novel vaccine platforms will not, on their own, solve the HIV vaccine challenge. But they offer a powerful enabling framework – one that supports faster learning, more efficient development and a clearer path from scientific discovery to global access.
- By aligning innovation in science with innovation in regulatory and development pathways, the global community can increase the likelihood that effective HIV vaccines reach the people who need them – faster and more equitably than ever before.
- High performing platforms with the potential to be effective for HIV are being identified now.
- mRNA shows great promise while manufacturing capabilities are being created in many regions and countries that could be quickly adapted to a successful vaccine candidate.
- Each developer has their own unique mRNA process and most often facilities.
- Partnerships can be created now to facilitate implementation once it is known that a vaccine candidate is effective.