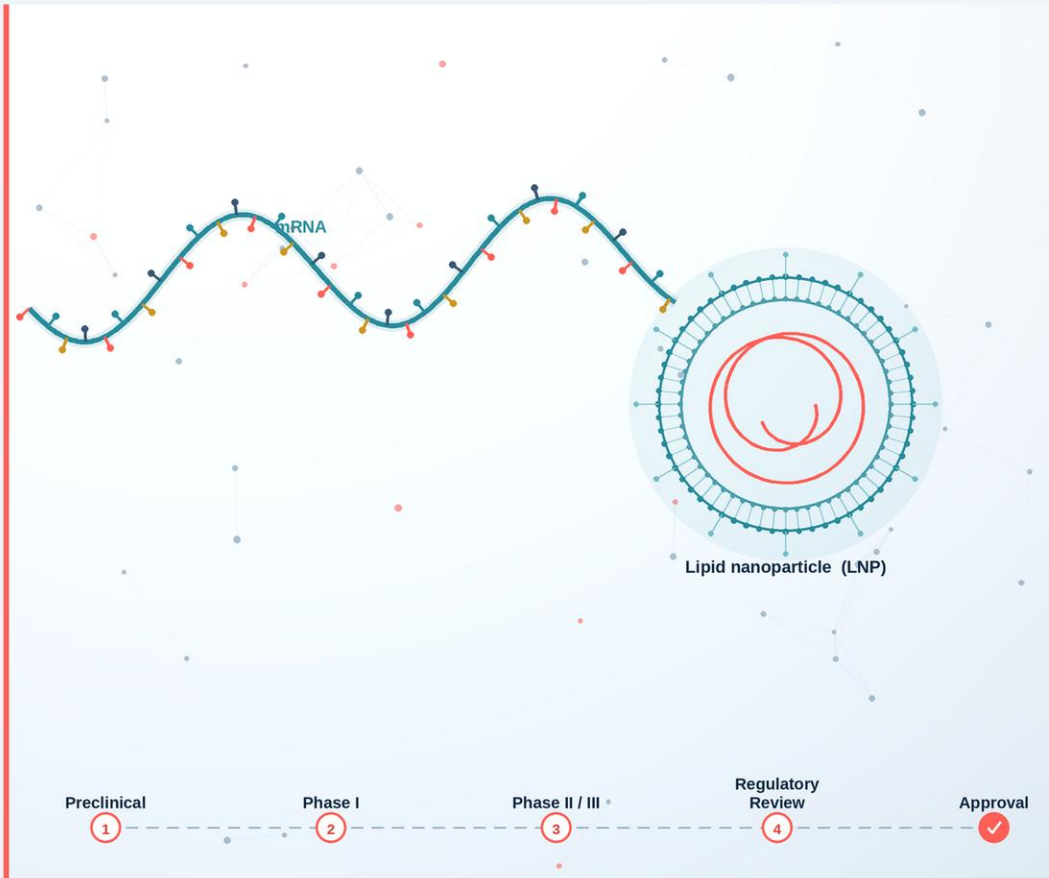
CEPI

WORKSHOP

Regulatory Pathways in the Development of RNA Vaccines

mRNA vaccine development • CEPI



WORKSHOP REPORT · DAYS 1 – 2

Regulatory Pathways in the Development of RNA Vaccines

A CEPI-led workshop for NRA regulators of the Americas

Complete report · Sessions 1 & 2 (Days 1–2) · 28–29 July 2026

Overview

This volume is the complete Workshop Report for both days of *Regulatory Pathways in the Development of RNA Vaccines*, a CEPI-led workshop for national regulatory authorities (NRAs) across the Americas. It was delivered online over two standalone two-hour sessions on 28–29 July 2026, with simultaneous English, Spanish, and Portuguese interpretation. The aim was to build reviewer fluency in RNA-vaccine science and to promote regulatory convergence — from the technical basis of the platform through emergency development, reliance, and RNA-specific GMP inspection.

Participation. The workshop drew national regulatory authorities from across Latin America and the Caribbean — COFEPRIS (Mexico), SRS (El Salvador), ISP (Chile), INVIMA (Colombia), ANVISA (Brazil), ANMAT (Argentina), and authorities from Costa Rica, Honduras, Peru, Cuba, Panama, Paraguay, Uruguay, Ecuador, Venezuela, Guatemala, and the Dominican Republic. The map that follows shows the participating authorities across the region. Overall, roughly 130 participants from these authorities took part — a large and engaged turnout that reflects strong regional interest.

The arc of the two days

- **Day 1 — Technical & Regulatory Basis.** The mRNA molecule and cell-free manufacture; a novel one-component IAJD delivery platform (Penn); the platform-boundary question; and the six-domain readiness self-assessment, product classification, and the two NRA roles.
- **Day 2 — Regulatory Basis.** An industry view of the mRNA “revolution” and platform economics; a regional developer's manufacturing and regulatory journey (Fiocruz – ANVISA); PAHO's evidence on emergency-authorization practice; RNA-specific GMP inspection; and a way-forward for the region.

The recurring thread

Is your regulatory agency, whether a manufacturing or importing country, ready for review of RNA vaccine dossiers? Is your NRA a **manufacturing-country** authority — owning the full dossier, GMP inspection, and release at source — or an **importing-country** authority that relies on the work of others and focuses effort on local decisions? Reliance is the bridge between these two roles, and the practical answer for most NRAs in the region.

How this report is organized

A map of participating authorities and a single **Glossary of Key Terms** follow this overview and serve both parts. **Part One** is the full Day 1 report and **Part Two** the full Day 2 report, each with its own modules, illustrations, and reference list. Some datasets in the Day 1 IAJD module, and some ImmunoScript and Fiocruz material in Day 2, were marked confidential or proprietary in the original presentations and are reproduced here as presented, with the presenters’ permission; all IAJD results are preclinical.

CEPI · RNA VACCINE REGULATORY WORKSHOP

Participating Regulatory Authorities across the Americas

Countries with attendees, shown with their national regulatory agency

Authorities represented

17 national regulatory authorities

ANMAT	Argentina
ANVISA	Brazil
ISP	Chile
INVIMA	Colombia
Min. Salud	Costa Rica
CECMED	Cuba
DIGEMAPS	Dominican Republic
ARCSA	Ecuador
SRS	El Salvador
MSPAS	Guatemala
ARSA	Honduras
COFEPRIS	Mexico
MINSA	Panama
DINAVISA	Paraguay
DIGEMID	Peru
MSP	Uruguay
INHRR	Venezuela

Badges mark each country's national regulatory agency (acronym). Placeholder badges — official agency logos can be substituted.

Source: RNA Workshop RSVP Tracker (participating authorities). Map is a simplified schematic for illustration.

Participating regulatory authorities across the Americas, shown with each country's national regulatory agency. Source: RNA Workshop RSVP Tracker; agency badges are placeholders for official logos.

Glossary of Key Terms

A consolidated glossary for both parts of the report.

Term	Meaning
CEPI	Coalition for Epidemic Preparedness Innovations — public-private partnership founded 2017.
NRA	National Regulatory Authority — the body that reviews and authorizes medical products in a country.
Reliance	Using another authority's assessment, decision, or inspection to inform one's own review.
Reference NRA	A well-resourced authority (e.g., FDA, EMA, Health Canada, AEMPS), increasingly designated WHO Listed Authorities (WLAs), whose decisions others may rely on.
EUA / EUL	Emergency Use Authorization (national) / Emergency Use Listing (WHO) — use ahead of full licensure.
CRP	WHO Collaborative Registration Procedure — a reliance pathway for PQ/EUL products.
PAHO NRAr	PAHO's regional network of national regulatory authorities for work-sharing.
PAHO-RRF	PAHO Revolving Fund — a regional pooled-procurement mechanism for vaccines.
Variation pathway	A streamlined change procedure (e.g., a strain update) rather than a fresh dossier.
Pharmacovigilance	Ongoing monitoring of a product's real-world safety after authorization.
IVT	In-vitro transcription — the cell-free enzymatic reaction that makes mRNA from a DNA template.
ORF / UTR	Open reading frame (the antigen-coding region) / untranslated regions (5′ and 3′).
LNP	Lipid nanoparticle — the delivery vehicle that encapsulates the mRNA.
IAJD	Ionizable Amphiphilic Janus Dendrimer — a one-component mRNA delivery molecule (Day 1, Module 3).
mRNA / saRNA / circRNA	Messenger / self-amplifying / circular RNA — formats of one diversifying RNA platform.
CQA / CPP	Critical quality attribute / critical process parameter (e.g., encapsulation efficiency; mixing shear).
PDI / EE%	Polydispersity index (size uniformity) / encapsulation efficiency (fraction of mRNA packaged).
DLS / NTA	Dynamic light scattering / nanoparticle tracking analysis — LNP size, distribution, and zeta potential.

Term	Meaning
Zeta potential	The net surface electrical charge of the lipid nanoparticles (LNPs) carrying the mRNA — a controlled quality attribute.
Capillary electrophoresis	An assay for RNA integrity, fragment sizing, and percent-intact transcript.
IP-RP-HPLC	Ion-pair reversed-phase HPLC — with mass spectrometry, detects dsRNA, residual DNA, and RNA-lipid adducts.
RNase control	Measures to keep the environment free of RNA-degrading enzymes — the organizing principle of an RNA facility.
IVIS	In-vivo imaging system — measures luciferase expression and biodistribution in animals.
GMP	Good Manufacturing Practice — the quality standard inspected at manufacturing sites.
Form 483 / EIR	FDA inspector's observations / the Establishment Inspection Report — observations, not a final GMP verdict.
VAI	“Voluntary Action Indicated” — an FDA inspection classification for minor, non-critical findings.
CAPA	Corrective and Preventive Action — the plan a site commits to after inspection findings.
PIC/S	Pharmaceutical Inspection Co-operation Scheme — international GMP-inspection cooperation.
OMCL	Official Medicines Control Laboratory — performs independent product testing / lot release.
TRS 1039	WHO Technical Report Series No. 1039, Annex 3 (2022) — regulatory considerations for mRNA vaccines.
PTMF / vPTMF	(Veterinary) Platform Technology Master File — a certification approach for platform data.
TRL	Technology Readiness Level (1–9) — a scale from discovery to clinical readiness.
Thermostability	The ability to store a vaccine at 2–8 °C (or warmer) rather than an ultra-cold chain.
RAG / TTX	CEPI Regulatory Advisory Group / tabletop exercise for readiness stress-testing.
RWE	Real-world evidence used to support benefit-risk assessment.
DCGI / AEMPS / ANVISA / COFEPRIS	National medicines authorities of India / Spain / Brazil / Mexico.

Session 1 — Workshop Report

A CEPI-led workshop for National Regulatory Authority (NRA) regulators of the Americas. Day 1 of a two-day workshop, delivered online on 28 July 2026 · two hours · five modules. Simultaneous interpretation was provided in English, Spanish, and Portuguese.

How to use this report. This report consolidates all Session 1 presentations into one reference document. It follows the running order of the day: an orientation to CEPI and the regional context, the technical foundation of RNA vaccines, a spotlight on a novel one-component delivery platform, and the regulatory considerations that frame how NRAs review these products. A glossary and reference list are provided at the end.

Session 1 Agenda at a Glance

Session 1 lays the technical and regulatory groundwork for the workshop. It is designed for NRA reviewers, and is primarily closed to regulators, with a small number of academic and industry participants joining to add context; presenters use live polling to capture where each agency stands. The five modules are:

Time	Module	Presenter
10:00–10:15 (15 min)	Opening & Context	April Hernandez (CEPI)
10:15–10:45 (30 min)	Introduction to RNA Vaccines	Hassan Askary (CEPI)
10:45–11:15 (30 min)	New Horizons in RNA Technology: Novel One-Component IAJD Delivery Platform for mRNA Vaccines & Therapeutics	Elena N. Atochina-Vasserman, M.D., Ph.D. (Penn Institute for RNA Innovation, University of Pennsylvania)
11:15–11:50 (35 min)	Regulatory Considerations	April Hernandez (CEPI)
11:50–12:00 (10 min)	Wrap-Up, Discussion & Bridge to Session 2	April Hernandez (CEPI)

Learning objectives

By the end of both sessions, participants should be able to:

- **1.** Describe the technical basis of RNA vaccines — the molecule, in-vitro transcription (IVT), and why the platform is more straightforward than conventional manufacturing.
- **2.** Discuss the platform question — is it the RNA, the LNP, or both? — and its consequences for platform designation, shared vs. product-specific data, and change management.
- **3.** Apply WHO TRS 1039 and the EMA draft guideline, and recognize how they extend to (and fall short for) self-amplifying and other RNA-based products.

- **4.** Discuss regulatory considerations for developing an RNA vaccine during a public-health emergency.
- **5.** Identify how regional resources can be leveraged and where capacity gaps remain.
- **6.** Understand product-specific GMP and inspection considerations for RNA facilities.

Module 1 — Opening & Context

Presenter: April Hernandez, CEPI Regulatory Affairs (Americas)
This module sets the stage: who CEPI is, why regulatory systems sit at the heart of its mission, and how the workshop connects to the priorities of funders and regulators in the Latin America and Caribbean (LAC) region.

The CEPI Regulatory Affairs team. April Hernandez opened the session and led Modules 1, 4, and the wrap-up. She introduced the wider team: Danielle Craig (Regulatory Affairs Lead for the Americas), Gina Antaki, José Luis Di Fabio (Regulatory Affairs Consultant), and Syed Hassan Askary (Regulatory Affairs Lead), who delivered Module 2.

What is CEPI?

The Coalition for Epidemic Preparedness Innovations (CEPI) was founded in 2017 in Davos as a global public-private partnership between public, private, philanthropic, and civil-society institutions, operating from Oslo, London, and Washington, D.C.

- **Vision —** a world in which epidemics and pandemics are no longer a threat to humanity.
- **Mission —** accelerate the development of vaccines and other biological countermeasures against epidemic and pandemic threats so they can be accessible to all people in need.
- **Mandate —** epidemic preparedness and the 100 Days Mission.

A central point for regulators: CEPI works with funders, academia, industry, WHO, regulators, and national governments — not in parallel to them — because rapid access is only possible when those systems move together.

The 100 Days Mission

The organizing idea of CEPI 3.0 is to compress vaccine timelines to roughly 100 days. Recent outbreaks suggest this is achievable, not merely aspirational, when four capabilities advance together. Each is a system rather than a single product, and it is their joint progress that compresses the deadline:

- Early detection & initiation
- Accelerated vaccine development
- Resilient supply capabilities
- Regulatory & policy readiness

Impact: saving lives quickly, reducing risk, minimizing disruption, and making innovation accessible.

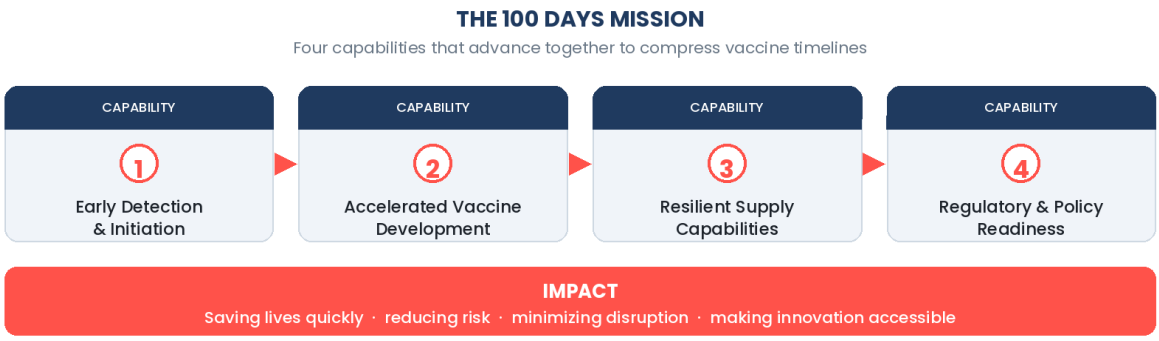


Figure 1. The 100 Days Mission — four capabilities that must advance together to compress vaccine timelines.

Trusted collaborations enable acceleration

Speed comes from trusted collaborations, not heroics. CEPI works along two tracks:

- **Incremental innovations —** pre-reviewed documentation, captured lessons learned, and cloud-based review, which remove friction from today's response.
- **Paradigm-shifting innovations —** maximal use of platform data, a framework for immune correlates of protection, and earlier benefit-risk assessment supported by real-world evidence (RWE).

Underneath sits an active global regulatory network — sustained through the Regulatory Advisory Group (RAG), disease-team meetings (e.g., Chikungunya, MERS, Rift Valley Fever), regulatory-readiness dashboards and tabletop exercises (TTX), and regional regulatory-innovation workshops across the Americas, EMEA, and Asia. In the region specifically, CEPI has already run regulatory-readiness tabletop exercises in Chile, Argentina, Brazil, Colombia, Honduras, El Salvador, and Guatemala. For LAC authorities, the message is that they are joining an ongoing global conversation, not stepping into an empty space.

The PAHO/WHO mRNA Hub in the Americas

The WHO mRNA technology-transfer program seeds local manufacturing capability across low- and middle-income regions, and Latin America hosts a designated hub building end-to-end RNA know-how. For NRAs this shifts the central question from importing a finished product to overseeing local development and manufacture — introducing the manufacturing-country vs. importing-country distinction that recurs throughout the workshop.

- **Technology transfer —** shared processes and training accelerate regional readiness.
- **Local resilience —** reduced dependence on external supply during emergencies.
- **Regulatory demand —** local production means local NRAs must review RNA CMC and GMP.

Regional RNA developer landscape

Several developers are advancing RNA programs across the region (listed north to south):

- **Vaxthera —** Rionegro, Colombia; a Grupo SURA vaccine developer.
- **Bio-Manguinhos / Fiocruz —** Rio de Janeiro, Brazil; a WHO mRNA technology-transfer hub.
- **Instituto Butantan / Replicate —** São Paulo, Brazil; a self-amplifying RNA (saRNA) rabies program that raises a live classification question addressed later.
- **Sinergium Biotech —** Garín, Argentina; an mRNA manufacturing partner.

A recurring thread

One question is posed repeatedly across both sessions: ***"Does your NRA have the resources and expertise to evaluate an RNA vaccine in a public-health emergency?"***

Reliance is presented as the bridge between the manufacturing-country and importing-country roles — a theme developed in Module 4 and again in Session 2, with live polling used throughout to capture where each agency stands.

Module 2 — Introduction to RNA Vaccines

Presenter: Hassan Askary, CEPI Regulatory Affairs (CMC Head)

The core technical module, covering the modality end to end: the molecule and its manufacture, the delivery vehicle, the different RNA forms, how RNA differs from other platforms, and the platform question.

What is an RNA vaccine?

The core idea is to deliver genetic instructions for an antigen and let the recipient's own cells make the protein, triggering a protective immune response. In other words, the vaccine carries a message, not the antigen itself.

- **Cell-free manufacture —** made enzymatically by in-vitro transcription (IVT), not grown in cells, unlike most biologicals.
- **Sequence-agnostic —** change the coding sequence, keep the process; this is the basis of the platform idea.
- **Needs a delivery vehicle —** RNA is fragile, so it is formulated in lipid nanoparticles (LNPs) for stability and cellular uptake.

The molecule and its manufacture

A messenger RNA construct is built from a standardized non-coding architecture — the 5′ cap, 5′ and 3′ untranslated regions (UTRs), and the poly(A) tail — surrounding the open reading frame (ORF) that codes for the antigen. It is produced by IVT: an enzymatic, cell-free reaction that transcribes RNA from a DNA template, followed by capping and purification. Because no cell culture, cell banks, or viral-clearance steps are needed for the RNA itself, the process is comparatively defined and compact.

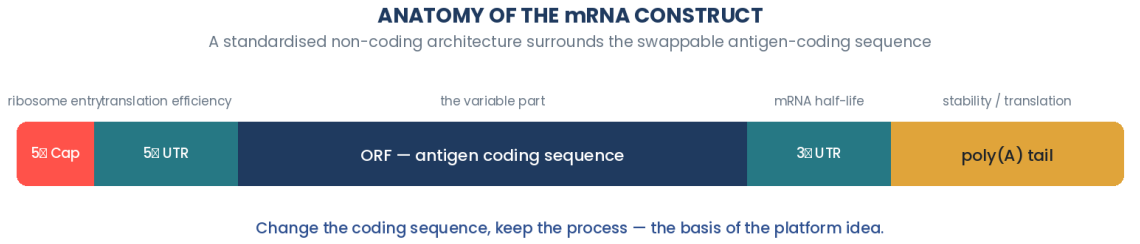


Figure 2. The mRNA construct: only the coding sequence (ORF) changes between products, while the non-coding architecture stays fixed.

The delivery vehicle: the lipid nanoparticle (LNP)

The conventional LNP uses four lipids, each with a job:

- **Ionizable lipid —** binds the mRNA and drives escape from the endosome into the cytosol.
- **Helper phospholipid & cholesterol —** give the particle structure and stability.
- **PEG-lipid —** shields the surface and controls particle size and circulation.

The mRNA is the active substance and the lipids are excipients — but the LNP shapes uptake, potency, and safety. Size, polydispersity index (PDI), encapsulation efficiency (EE%), and zeta potential are controlled critical quality attributes (CQAs).

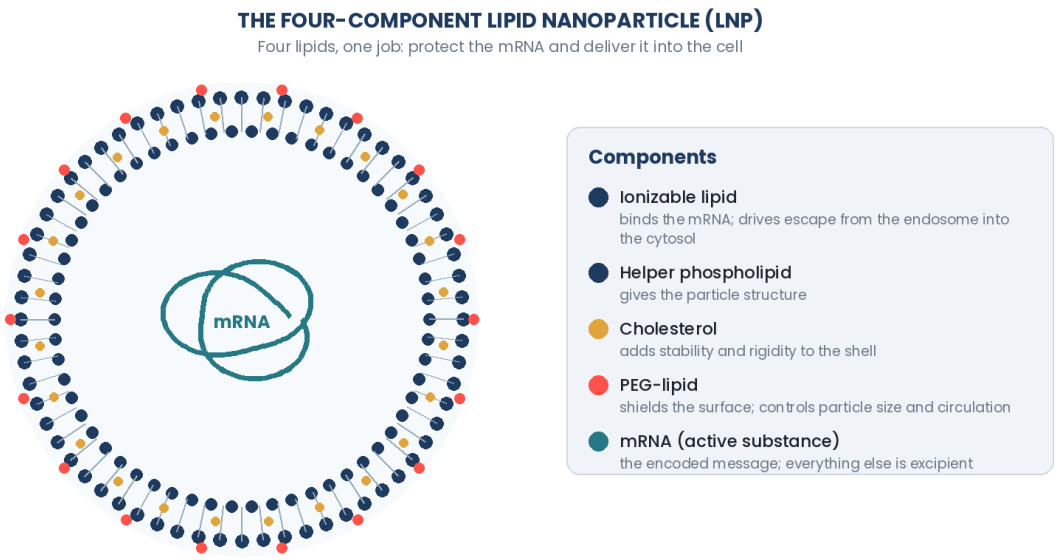


Figure 3. Schematic of a four-component LNP encapsulating mRNA, with the role of each lipid.

Why the modality adapts faster than conventional vaccines

The chemistry stays fixed; only the sequence changes. Once a process is established and validated, a new antigen can be brought online in weeks rather than the months typical of conventional cell-based platforms. Contributing factors:

- **Cell-free, defined chemistry —** no cell-culture campaigns, banks, or viral clearance for the RNA itself.
- **Small physical footprint —** a compact equipment train that is easier to deploy and transfer.
- **Rapid strain updates —** a sequence swap without re-engineering the whole process.
- **Platform leverage —** prior knowledge supports faster review of the next product.

Caveat for reviewers: the modality is “more straightforward in important ways,” but RNA retains genuine complexity — the LNP, the cold chain, and novel impurities. The speed advantage is real but not the whole story.

One modality, several RNA forms

The RNA toolkit is diversifying beyond conventional mRNA to include self-amplifying RNA (saRNA), trans-amplifying RNA (taRNA), and circular RNA (circRNA), among others. Regulators increasingly frame guidance around “RNA-based” products rather than mRNA only. Self-amplifying RNA is a particular focus: it encodes a viral replicase that amplifies the message inside the cell, potentially allowing lower doses — but it cannot form infectious particles.

How RNA differs from other vaccine modalities

Comparator platform	How RNA vaccines differ
Protein-based (subunit, conjugate)	No protein is grown or purified — the recipient's cells make the antigen; different impurity and characterization profile.
Inactivated whole-virus (e.g., CoronaVac)	No virus culture or inactivation, and no whole-pathogen antigen mix — a single defined sequence.

Comparator platform	How RNA vaccines differ
Live-attenuated	No replicating pathogen; saRNA amplifies only the message and cannot form infectious particles.
Viral-vector	No viral capsid/vector; LNP delivery avoids anti-vector immunity, easing re-dosing and updates.
Virus-like particle (HPV, HepB)	No self-assembling particle antigen; the antigen is expressed transiently in vivo.
Polysaccharide / conjugate	Not a chemistry-conjugation product; the protein antigen comes from a coded sequence, not a carrier.
DNA vaccine (closest nucleic-acid cousin)	Acts in the cytoplasm — no nuclear entry or genomic-integration concern, and no in-cell promoter transcription needed.

Defining "platform"

CEPI distinguishes several related terms that regulators often conflate:

- **Modality —** the structure of a product's active substance (e.g., RNA).
- **Common platform —** the particular type of antigen vehicle within a modality (e.g., mRNA, saRNA).
- **Regulatory platform —** a specific, well-defined process that makes products with uniform specifications and highly predictable characteristics, usually specific to a single developer's manufacturing process.
- **Platform technologies —** antigen-agnostic methods used across products, down to individual unit operations such as IVT or chromatography.

The FDA frames a related concept — the Platform Technology Designation — around common manufacturing elements shared across products.

Can RNA function as a true platform technology?

The scientific basis is that the chemistry does not change when the antigen changes — only the coding sequence changes. The platform comprises a standardized non-coding architecture (5'/3' UTRs, cap, poly(A)), a standardized IVT process, and a conserved LNP architecture (ionisable lipid : cholesterol : DSPC : PEG-lipid). Primary variability lies in the ORF, with knock-on effects on construct length, codon composition, and secondary structure. Moderna's use of the same manufacturing platform across its COVID-19, RSV, and influenza vaccines was cited as evidence that RNA can function as a true platform technology, and regulatory flexibility was further demonstrated in SARS-CoV-2 variant updates; the open question is how far it generalizes.

The platform question

What exactly is "the platform" — the RNA, the LNP, or both? This boundary determines platform-designation scope, what data is shared vs. product-specific, and how changes are managed. It was put to participants as a live poll:

- **A — The RNA component:** the IVT process and RNA backbone.
- **B — The LNP component:** the lipid composition and encapsulation.

- **C — Both:** the integrated RNA + LNP drug product.

Figure 4. The platform question: where the regulatory boundary is drawn — RNA, LNP, or the integrated product.

What participants said

Polled live, almost all participants chose C — that the RNA and LNP together constitute the platform. The presenter then posed the harder follow-up: if the LNP is changed, is it still the same platform? The manufacturing process may be unchanged, but views diverge — the FDA and others take the position that changing the delivery system requires safety testing to be repeated, even when the underlying platform technology is unchanged. In the presenter's experience, retaining the same LNP used in the COVID-19 vaccines avoids repeat toxicology studies, whereas a change of LNP triggers a fresh clinical safety evaluation. This is the practical stake behind the boundary question, and it is revisited in Session 2.

Global regulatory perspectives on mRNA platform technologies

Status as of July 2026:

Agency / Body	Key position or guideline	Relevance to the platform approach
US FDA (draft, May 2024)	Platform Technology Designation Program, implementing §506K FD&C Act (PREVENT Pandemics Act)	Defines a platform as common manufacturing elements across products; enables leveraging of prior CMC knowledge. Being tested in practice.
EMA — human (draft guideline, Mar 2025; consultation closed Sep 2025)	Guideline on the quality aspects of mRNA vaccines (EMA/CHMP/BWP/82416/2025)	First EU text with a dedicated section on platform technology / prior knowledge for mRNA; also covers strain changes, bi-/multivalent vaccines and saRNA. Adoption pending.
EMA — veterinary (vPTMF, 2022; procedural advice Rev.1, Nov 2025)	vPTMF guideline + procedural advice for vPTMF certification	The only PTMF certification pathway currently in force (veterinary). An operational reference model for a proposed human PTMF.
Ph. Eur. / EDQM (adopted Nov 2024; published Jul 2025)	General chapters 5.36 (mRNA vaccines), 5.39 (mRNA substances), 5.40 (DNA templates for mRNA)	First harmonized quality standards for the mRNA platform and its starting materials; a common

Agency / Body	Key position or guideline	Relevance to the platform approach
		analytical baseline for regulators and control laboratories.
WHO ECBS — TRS No. 1039, Annex 3 (2022)	Regulatory considerations for the quality, safety and efficacy of mRNA vaccines	Establishes mRNA quality-control principles and recognizes common platform elements; the baseline for WHO PQ/EUL assessment and reliance.
EU pharma legislation reform (compromise texts Mar 2026; application ~2028)	New Regulation and Directive replacing Directive 2001/83/EC and Regulation (EC) 726/2004	No formal EU platform authorization pathway for human medicines is yet defined — the structural gap the PTMF framework aims to close.

Module 3 — New Horizons in RNA Technology

Novel One-Component IAJD Delivery Platform for mRNA Vaccines & Therapeutics

Presenter: Elena N. Atochina-Vasserman, M.D., Ph.D. — Penn Institute for RNA Innovation, University of Pennsylvania, presenting work from the laboratory of Drew Weissman (2023 Nobel laureate in Physiology or Medicine for the nucleoside modifications that made mRNA vaccines possible)

This scientific spotlight introduces an emerging delivery technology that regulators may encounter in future dossiers and illustrates why the "what is the platform?" question is more than academic.

Why delivery is the bottleneck

COVID-19 was a landmark for mRNA vaccines — the first successful global implementation of the technology, demonstrating safety, efficacy, and rapid development (the Pfizer-BioNTech and Moderna vaccines were designed, tested, and authorized for emergency use within a year, versus the years traditional vaccines take). A significant remaining challenge is the delivery system. Four-component LNPs are the most advanced carriers to date, but mRNA-LNP vaccines still face challenges around stability, efficacy, durability, and side effects.

Four-component LNP vs. one-component IAJD

Ionizable Amphiphilic Janus Dendrimers (IAJDs) are a single-molecule alternative to the four-lipid LNP. The contrast:

Four-component LNP	One-component IAJD
Four components (ionizable lipid, helper lipid, cholesterol, lipid-anchored PEG)	One component
Requires microfluidic (chaotic) mixing	Simple mixing on a vortex
Contains PEG (associated with adverse reactions)	No PEG
Storage at −80 °C	Stable at +4 °C for over 6 months; high encapsulation efficiency
15–19 synthesis steps	5–7 synthesis steps
Higher cost, slower production	Lower cost, fast production

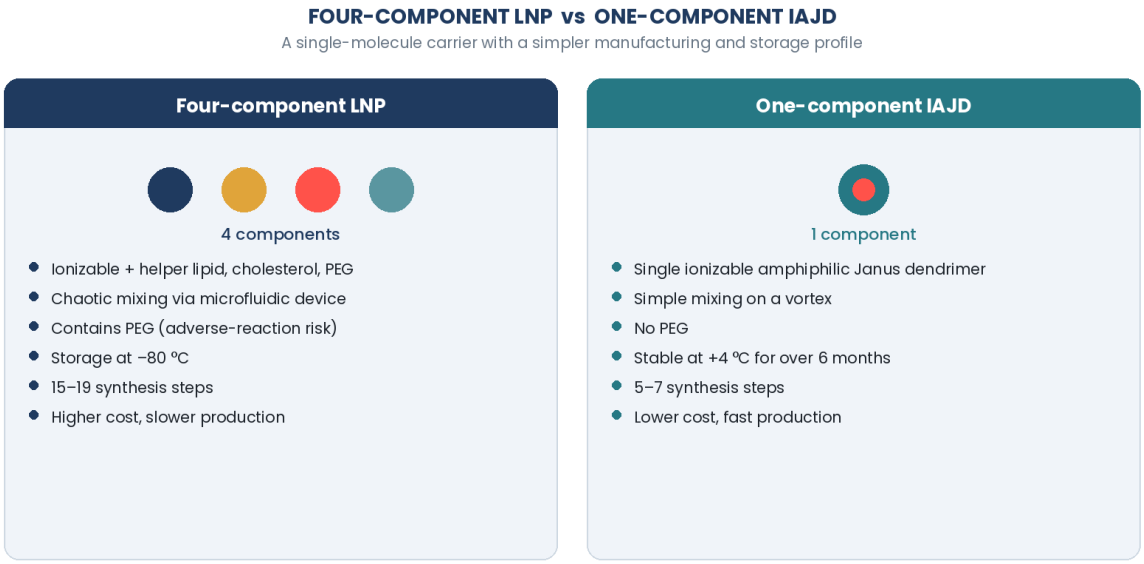


Figure 5. Four-component LNP versus one-component IAJD — composition, mixing, storage, and synthesis contrasted.

Preclinical applications

After screening and optimization using an in-vivo imaging system (IVIS), one-component IAJDs are being pursued along two branches: immunization (vaccines) and tissue-specific delivery (therapeutics).

Vaccine proof of concept — norovirus VP1 mRNA-IAJD97

An IAJD ("IAJD97") formulated with norovirus mRNA served as the proof of concept. Reported particle characteristics: size ~195 nm, PDI ~0.13, encapsulation efficiency ~96.7%, pKa ~8.22, and zeta potential ~23 mV — comparable to the Moderna and Pfizer-BioNTech LNP benchmarks. Crucially, whereas conventional LNPs distribute mainly to the liver, IVIS biodistribution of a luciferase-mRNA IAJD97 formulation (4 h post IV injection) showed expression concentrated in the spleen and lymph nodes, with lower signal in lung, liver, and heart. This preferential delivery to lymphoid tissue is thought to favor vaccine efficacy.

- **Safety —** even at doses up to 30 µg (about 30× the ~1 µg vaccination dose), the only finding was minor lymphocyte depletion in the spleen; there was no organ pathology and no significant increase in IL-6, AST, or ALT versus naïve animals — i.e., no structural abnormality or systemic inflammation.
- **Humoral immunity —** a prime/boost schedule (days 0 and 28, IV or IM) elicited potent neutralizing antibody titers by day 60, comparable to an SM102 LNP benchmark — and comparable results were seen for norovirus, influenza, and HIV immunogens, confirming the platform is immunogen-agnostic.
- **Cellular immunity —** strong antigen-specific $CD4^+$ and $CD8^+$ T-cell responses (IFN-γ, IL-2, TNF-α) and increased follicular helper T (Tfh) and germinal-center B (GCB) cells.
- **Stability —** the luciferase mRNA-IAJD formulation stayed robust for ~16–20 weeks at +4 °C (a standard refrigerator), remained detectable out to 40 weeks at +4 °C, and held up for ~8 weeks at room temperature — a major advantage over the −80 °C requirement of conventional LNPs.

Formulation optimization with stabilizers

IAJD97 was combined with low levels of stabilizers (S1–S5, ~0.1–0.5 mol%), mixed microfluidically, and dialysed from acetate (pH 4.0) into PBS (pH 7.4). Stability of stored formulations was tracked out to 20 weeks at +4 °C and at room temperature, read out by luciferase signal in spleen and lymph nodes.

Beyond norovirus — influenza and HIV

As broader proof of principle (1 µg/mouse, IM), IAJD-formulated vaccines against influenza (PR8) and HIV envelope (11MUTB) elicited neutralizing responses and strong antigen-specific T-cell responses broadly comparable to an SM102 LNP benchmark. (These data were marked confidential in the presentation.)

Tissue-specific therapeutic delivery to the lung

The platform can be tuned for organ targeting. Anatomically, the human airway branches ~23 times from the trachea to the alveolar sacs; the first ~16 generations are conducting airways and the last ~7 are the respiratory (gas-exchange) zone — creating a clinical need to target specific airway regions.

- **Lower-lung targeting (IAJD34) —** an IV luciferase mRNA-IAJD34 formulation delivered mRNA specifically to the lower regions of the lung, with expression concentrated in lung tissue over heart, liver, and spleen (Meshanni et al., Nature Communications, 2025).
- **Acute lung injury (TGF-β mRNA-IAJD34) —** in a bleomycin-induced injury model, TGF-β mRNA-IAJD34 reduced markers of injury and inflammation in bronchoalveolar lavage (total protein, percent neutrophils, IL-6, and IP-10) relative to empty-IAJD controls.
- **Upper-airway targeting (IAJD97pII, intranasal) —** intranasal delivery peaked at ~24 h and produced significant staining in nasal ciliated columnar epithelial cells and lung bronchoalveolar epithelial cells, indicating extensive mRNA delivery to nasal and upper-airway epithelium.
- **Intranasal H5N1 influenza vaccine —** an intranasal H5N1 mRNA-IAJD produced systemic neutralizing responses comparable to intramuscular delivery and generated serum IgG, with far less lung inflammation on histology than an mRNA-LNP comparator — conventional four-component LNPs caused severe lung inflammation when given intranasally, attributed to interference with lung surfactant. The study is ongoing, with bronchoalveolar lavage samples to be analyzed for IgG and IgA.

Discussion. April Hernandez noted that CEPI is actively evaluating mucosal vaccines and finds this intranasal/mucosal work of significant interest.

Take-home

One-component IAJD97, formulated with mRNAs encoding immunogens for norovirus, influenza, and HIV, serves as a proof of concept for a novel and efficient platform for vaccine delivery — with a manufacturing profile (fewer synthesis steps, no PEG, refrigerator-stable, vortex mixing) that could ease production and cold-chain constraints if it advances clinically. All data to date are preclinical (mouse models), with studies ongoing.

Key references: Ona N. et al., … Atochina-Vasserman EN (2026), *Science Advances*; Meshanni M. et al., … Atochina-Vasserman EN, *Nature Communications* 16:1806 (2025).

Module 4 — Regulatory Considerations

Presenter: April Hernandez, CEPI Regulatory Affairs (Americas)

Three linked topics that frame how NRAs prepare to review RNA vaccines: emergency review capacity, product classification, and the manufacturing-country vs. importing-country roles.

Topic 1 — NRA emergency review capacity

A structured self-assessment lets an NRA evaluate its readiness to review — and to inspect, or rely on inspection of — RNA vaccines under emergency tempo, and to identify where investment is needed. A companion self-assessment tool (provided in English and Spanish) was distributed to every participating agency for internal use, so each can turn this framework into an actionable list of gaps and training needs. The deliverable is deliberately actionable rather than a critique: for each of six domains, an NRA scores itself, identifies its top gaps, and commits to a concrete remediation action. The pattern is Score → Gap → Remediation.

Figure 6. The six domains of NRA emergency-review readiness, each worked through as Score → Gap → Remediation.

Domain 1 — Scientific expertise

- **What good looks like:** At least one reviewer per functional area (CMC, nonclinical, clinical) who has actively reviewed an RNA product or completed structured training. Competencies include RNA sequence identity, capping and poly(A) analytics, LNP characterization (DLS/NTA, encapsulation), immunology of endogenous expression, and biodistribution/shedding evaluation.
- **Common gaps:** Single points of expertise, limited succession planning, few reviewers with active LNP experience.
- **Remediation options:** Structured training (WHO, ICDRA, CEPI-supported), secondments to reference NRAs, joint review with regional partners, tabletop exercises.

Domain 2 — Analytical infrastructure

- **What good looks like:** Choose a model and know it: in-house testing, designated third-party/OMCL-style labs, or oversight-only (reliance on manufacturer or reference-NRA release data). Methods to access: identity (RT-PCR/sequencing), integrity (capillary electrophoresis), capping (LC-MS), residual DNA (qPCR), LNP size (DLS/NTA), encapsulation (RiboGreen), potency (cell-based expression assay).
- **Common gaps:** LC-MS and cell-based potency assays are the most frequently missing capabilities.

- **Remediation options:** OMCL-style regional labs, reliance on reference-NRA release, formal agreements with academic labs, WHO EQAS participation.

Domain 3 — Legal & regulatory authority

- **What good looks like:** A clear legal basis for emergency authorization, explicit authority to accept reliance and reference-NRA decisions, defined lot-release powers, and post-market surveillance mandates that hold up under emergency tempo (EUA/EUL-equivalent, reliance and Collaborative Registration Procedure mechanisms, conditional/time-limited approvals).
- **Common gaps:** Legal ambiguity about what can be accepted from reference authorities; emergency pathways needing legislative change; post-market surveillance authority lagging deployment.
- **Remediation options:** Interim regulations or emergency guidance; formal reliance agreements (WHO CRP); standing MOUs with reference NRAs; documented delegated authority. The preferred end-state is a disease-agnostic legal basis for emergency authorization (rather than COVID-specific interim guidance) plus, with sponsor approval, access to unredacted reference-NRA reports.

Domain 4 — Operational systems

- **What good looks like:** Rolling-review capability with documented triggers and stopping rules; defined timelines with escalation paths; case-tracking that holds up under load; delegated decision authority that avoids single-point bottlenecks; acceptance of partial/rolling submissions.
- **Common gaps:** Paper-based tracking that doesn't scale; single-thread workflows that can't parallelize; limited decision authority below senior leadership; unclear governance for expedited decisions.
- **Remediation options:** SOPs for rolling review; case-management systems (WHO templates or lightweight tools); documented delegated authority; standing crisis-response governance activated on trigger.

Domain 5 — Collaboration mechanisms

- **What good looks like:** Formal reliance agreements with reference NRAs, active participation in regional/global regulator forums, WHO listed-authority status where applicable, and standing information-sharing channels (reliance/CRP in routine as well as emergency use, PAHO NRAr work-sharing, bilateral MOUs, ICDRA/ICMRA membership).
- **Common gaps:** Collaboration that is ad-hoc rather than formalized; reliance used only in emergencies; information-sharing that lags because channels aren't standing.
- **Remediation options:** Formalize informal relationships into MOUs; join WHO CRP; participate in PAHO NRAr and joint assessments; assign named liaison staff per reference NRA.

Domain 6 — RNA GMP inspection readiness

- **What good looks like:** The NRA can inspect, or credibly rely on inspection of, the RNA drug substance and the LNP drug product against RNA-specific GMP criteria — assessing RNase control and segregation, qualifying microfluidic LNP encapsulation (mixing, in-line particle sizing), ultra-cold-chain and excursion monitoring, and oversight of RNA analytics.
- **Common gaps:** Conventional checklists omit RNA/LNP specifics; few inspectors have seen an RNA facility; over-reliance on desk assessment; unclear split of inspection duties across NRAs.
- **Remediation options:** RNA-specific inspection aide-memoire; joint or observed inspections with reference NRAs; PIC/S participation; inspector training (WHO, PIC/S, CEPI); reliance on reference-NRA inspection reports.

Topic 2 — Product classification considerations

The category a product falls into determines the review pathway, the dossier expectations, and the inspectorate involved. A recurring question from reviewers is whether an RNA product can integrate into the host genome and what risk that carries — a concern that weighs especially on how self-amplifying RNA is classified.

- **Vaccine pathway —** a biological product for the prevention of infectious disease; typically reviewed by the vaccines division with standard requirements for prophylactic biologicals.
- **Advanced-therapy / gene-therapy pathway —** a product that alters or acts on the host's genetic material; requires additional considerations (biodistribution, persistence, shedding, insertional risk) and often a different inspectorate.

The decision is not always obvious: novel modalities (saRNA, taRNA, circRNA) sit at the boundary, and jurisdictions have taken different views. The classification cascades through everything — which regulation and guidance applies, which committee reviews, and which inspectorate handles GMP.

Regional case: the Butantan / Replicate saRNA rabies vaccine

RBI-4000 — a self-amplifying RNA rabies vaccine from Instituto Butantan (Brazil) with Replicate Bioscience (USA) — puts the classification question on the table for Latin American NRAs. Because saRNA encodes a viral replicase that amplifies RNA in the cell, some jurisdictions read this as a gene-therapy characteristic while others treat it as a vaccine with novel-modality considerations. Biodistribution and shedding studies may be expected beyond conventional-vaccine levels, and the CMC package will include replicase-specific attributes. For ANVISA and other regional NRAs, this decision will set an important precedent.

How to approach the decision

- **Look to precedent —** how reference NRAs (FDA, EMA, Health Canada) have classified similar novel RNA products.
- **Consider intended use and mechanism —** prophylaxis against infectious disease supports a vaccine classification; therapeutic intent or a genome-modifying mechanism supports gene-therapy classification.
- **Engage early —** novel-modality products benefit from early scientific advice, before pivotal studies, to lock in the classification and pathway.
- **Document the reasoning —** record the rationale, since downstream questions all reference it.

Topic 3 — Manufacturing-country vs. importing-country NRA roles

Reliance pathways distribute the review burden between the manufacturing-country and importing-country NRAs, which carry different responsibilities. Regulators should recognize which role they play for each product; the reliance flow carries reports, decisions, and inspection findings from the manufacturing side to the importing side.

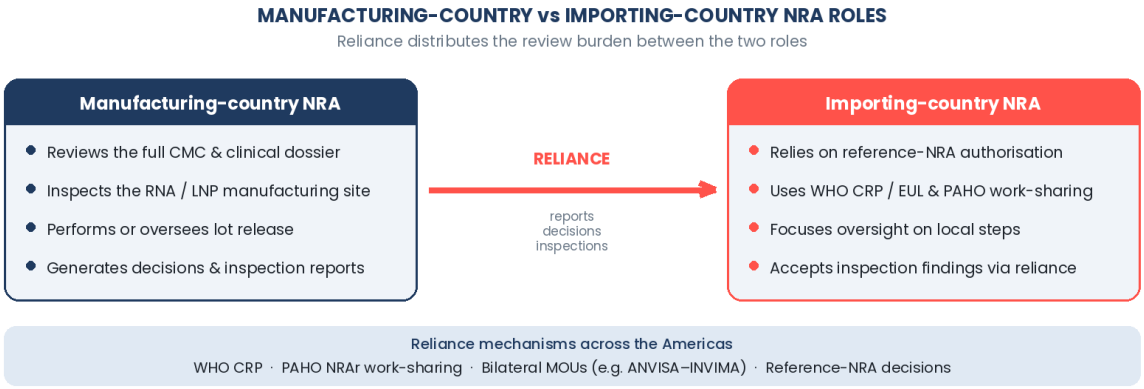


Figure 7. How reliance distributes the review burden between manufacturing-country and importing-country NRAs.

- **Manufacturing-country NRA —** the primary reviewer: full CMC, non-clinical, and clinical review; local GMP inspection; lot release for the domestic market; and domestic post-market surveillance. In the region this describes ANVISA with Fiocruz and Butantan (Brazil), ANMAT with Sinergium (Argentina), and INVIMA with Vaxthera (Colombia).
- **Importing-country NRA —** relies on the manufacturing-country and reference-NRA assessments; GMP inspection may be waived under reliance. It still owns local labeling and patient-information requirements and coordinates post-market surveillance. Many Caribbean and Central American countries currently sit in this position.

Reliance mechanisms across the Americas:

- **WHO Collaborative Registration Procedure (CRP) —** a reliance framework for products with WHO Emergency Use Listing or prequalification.
- **PAHO NRAr work-sharing —** a regional network coordinating NRA authorities across Latin America and the Caribbean.
- **Bilateral MOUs —** e.g., ANVISA–INVIMA information-sharing and similar arrangements that support faster review.
- **Reference-NRA decisions —** authorization and inspection reports from FDA, EMA, Health Canada, and other WHO-listed authorities that reliance-based NRAs can use to accelerate their own reviews.

Timing matters: these mechanisms should be established before an emergency, not during one — including advance agreement with sponsors for access to non-redacted reports.

The framing question that recurs: *"What must a manufacturing-country NRA do versus an importing-country NRA?"* It returns in Session 2 (Emergency Development and GMP Inspections), in the closing takeaways, and in each NRA's own score-to-gap-to-remediation self-assessment — because the two roles need different capabilities and different investments.

Key Takeaways

- **RNA vaccines carry a message, not the antigen.** The recipient's cells make the protein; the RNA is the active substance and the LNP is a set of excipients that nonetheless shapes uptake, potency, and safety.
- **The platform's speed comes from a fixed process with a swappable sequence — but complexity remains.** The LNP, cold chain, and novel impurities keep RNA products genuinely complex, even as strain updates are fast.
- **"What is the platform?" is a consequential regulatory choice.** RNA, LNP, or both — the answer sets designation scope, what data is shared vs. product-specific, and how changes are managed.
- **The delivery field is still evolving.** One-component IAJDs illustrate that carriers with very different manufacturing, storage, and composition profiles may appear in future dossiers — reinforcing why classification and platform boundaries matter.
- **Emergency readiness is measurable and improvable.** The six-domain framework turns readiness into a concrete Score → Gap → Remediation plan spanning expertise, analytics, legal authority, operations, collaboration, and inspection.
- **Classification cascades through the whole review.** Especially for saRNA (e.g., RBI-4000), the vaccine vs. gene-therapy decision determines pathway, dossier, and inspectorate — so engage early and document the rationale.
- **Reliance is the bridge.** Manufacturing-country and importing-country NRAs have different jobs; WHO CRP, PAHO NRAr, bilateral MOUs, and reference-NRA reports let importing NRAs review faster without duplicating everything.

Action items for participating NRAs

Coming out of Day 1, each participating agency was asked to:

- **Complete the self-assessment tool** (English or Spanish) across all six readiness domains to surface internal gaps and training needs.
- **Prioritize the domains** — scientific expertise, analytical infrastructure, legal/regulatory authority, operational systems, collaboration mechanisms, and GMP inspection readiness — that most need strengthening.
- **Document the agency's classification approach** for novel RNA modalities, including saRNA, and check it against reference-NRA precedent.
- **Audit existing reliance mechanisms and MOUs** with reference NRAs and identify what must be formalized before the next public-health emergency.

CEPI, in turn, will gather these self-assessment outputs to shape a regional training program.

Bridge to Session 2

Day 1 closed with an open Q&A (no questions were raised) and a preview of Day 2. Session 2 features two vaccine manufacturers sharing their perspectives and a presentation by María Teresa Ibarz of PAHO. It builds on this technical foundation to cover developing frameworks in an emergency, international frameworks and Emergency Use Listing (EUL), RNA/mRNA guidances (WHO TRS 1039 and the EMA draft guideline), product-specific GMP inspection, and CEPI tools and a way forward — returning throughout to the manufacturing-country vs. importing-country question and to reliance as the connecting thread.

Selected References & Resources

- WHO ECBS. *Evaluation of the quality, safety and efficacy of mRNA vaccines for the prevention of infectious diseases: regulatory considerations*. TRS No. 1039, Annex 3 (2022).
- EMA. Draft *Guideline on the quality aspects of mRNA vaccines* (EMA/CHMP/BWP/82416/2025), Mar 2025.
- US FDA. *Platform Technology Designation Program for Drug Development* (draft, May 2024), implementing §506K FD&C Act.
- Ph. Eur. / EDQM. General chapters 5.36, 5.39, 5.40 (adopted Nov 2024; published Jul 2025).
- Ona N. et al., … Atochina-Vasserman EN (2026). *Science Advances* — norovirus, influenza, and HIV mRNA-IAJD vaccine studies.
- Meshanni M. et al., … Atochina-Vasserman EN (2025). *Nature Communications* 16:1806 — lung-targeted mRNA-IAJD34 delivery and acute lung injury.

Prepared as a Workshop Report from the Session 1 (Day 1) presentation materials and the Day 1 Zoom AI meeting summary — CEPI RNA Vaccine Regulatory Workshop, 28–29 July 2026. Some datasets referenced in Module 3 were marked confidential in the original presentation; all IAJD results are preclinical.

CEPI · REGULATORY PATHWAYS IN THE DEVELOPMENT OF RNA VACCINES

Session 2 (Day 2) — Workshop Report

Day 2 of a two-day workshop, delivered online on 29 July 2026 · two hours · five modules plus a closing · Q&A woven throughout (~5 minutes per topic). Simultaneous interpretation was provided in English, Spanish, and Portuguese.

How to use this report. This report consolidates all Session 2 presentations into one reference document and follows the running order of the day: a recap of the Session 1 foundations, an industry view of the mRNA "revolution" and platform economics, a regional developer's manufacturing and regulatory journey (Fiocruz – ANVISA), PAHO's evidence on emergency-authorization practice in the Americas, RNA-specific GMP inspection, and a closing way-forward. A glossary and reference list are at the end. It is a companion to the Day 1 report.

Session 2 Agenda at a Glance

Session 2 turns from the science toward its regulation. It keeps returning to one framing question from Day 1 — is your NRA a manufacturing-country or an importing-country authority, and what does each role require? The five modules and closing are:

Time	Module	Presenter
10:00–10:15 (15 min)	Opening & Recap of Session 1	April Hernandez (CEPI)
10:15–10:40 (25 min)	The mRNA Vaccine Revolution: core principles, safety, and regulatory pathways of platform technologies	Dr. Sanjay Singh (Founder & CEO, ImmunoScript Life Sciences)
10:40–11:05 (25 min)	The Fiocruz development process and the regulatory relationship with ANVISA	Patrícia Neves (HUBRNA — Bio-Manguinhos/Fiocruz)
11:05–11:30 (25 min)	Strengthening regulatory preparedness in the Americas: lessons from COVID-19 and emerging expectations	María Teresa Ibarz M. (Quality & Regulation Unit, PAHO)
11:30–11:50 (20 min)	Product-specific and GMP inspections	April Hernandez (CEPI)
11:50–12:00 (10 min)	Closing & Way Forward	April Hernandez (CEPI)

Learning objectives

By the end of Session 2, participants should be able to:

- **1.** Re-state the Session 1 foundations — the mRNA molecule, cell-free manufacture, the RNA family, the platform-boundary question, and the six-domain readiness self-assessment.
- **2.** Explain how development and review compress under emergency: phased trials, an EUA bridge, a strain-change variation pathway, and continuous pharmacovigilance.

- **3.** Draw lessons from a licensed indigenous mRNA program (GEMCOVAC) and a regional developer (Fiocruz) on platform economics, thermostability, and the NRA relationship.
- **4.** Interpret PAHO's regional evidence (2024 mapping) on emergency-authorization mechanisms and the central place of reliance.
- **5.** Identify what makes RNA/LNP GMP inspection different, where conventional checklists fall short, and what inspectors are actually finding.
- **6.** Commit to concrete next steps: run the readiness self-assessment, formalize reliance, build RNA-specific inspection criteria, and engage the CEPI tools and mRNA hub.

Module 1 — Opening & Recap of Session 1

Presenter: April Hernandez, CEPI Regulatory Affairs (Americas)

A fast recap, not new material: re-orient everyone to the Session 1 foundations, then re-post the framing question that runs through Day 2. Session 2 then adds three working modules — development under emergency, reliance in the Americas, and product-specific GMP inspection — each returning to the manufacturing-country vs. importing-country distinction.

What Session 1 established

- **The molecule —** the mRNA construct (5′ cap, UTRs, antigen ORF, poly(A) tail), each element deliberate; only the coding region changes between products.
- **The manufacture —** cell-free in-vitro transcription then LNP formulation; sequence-agnostic and faster to adapt.
- **The RNA family —** standard mRNA, self-amplifying RNA, and circular RNA: one diversifying platform whose regulatory questions rhyme.
- **The platform question —** RNA, LNP, or both — the boundary shapes what data can be shared and how post-approval changes are managed.
- **Readiness & roles —** the six-domain self-assessment, product classification, and the two NRA roles.

mRNA in plain terms

An overview of RNA was covered for a second time because it anchors the whole workshop: mRNA is a short-lived instruction, not a drug that lingers. The vaccine delivers the message; the person's own cells make the antigen. It moves through four beats — deliver (the LNP carries mRNA into the cytoplasm, staying outside the nucleus), translate (ribosomes read it and build the antigen), display (the immune system learns to recognize the antigen; no live virus is involved), and clear (the mRNA is broken down within days). Three reassurances follow: it never enters the nucleus, never alters DNA, and is cleared within days.

Why this makes a fast, adaptable platform

- **Plug-and-play —** swap the coding sequence, keep the process; a new antigen does not mean a new manufacturing method.
- **Sequence-agnostic —** no cell culture and no eggs; the same cell-free chemistry makes any construct, so scale-up is faster.
- **Transient & non-integrating —** expression is temporary and the genome is untouched, giving a well-characterized safety profile.

For an NRA: platform knowledge carries across products — much of the process review can be reused when only the sequence changes. This is the idea that justifies platform-based regulation, and the thread the rest of Day 2 builds on.

Module 2 — The mRNA Vaccine Revolution

Presenter: Dr. Sanjay Singh, Founder & CEO, ImmunoScript Life Sciences (India). Core principles, safety, and regulatory pathways of platform technologies. Some material was presented as confidential.

An industry perspective on why mRNA behaves as a platform, how it has been regulated in practice, its safety story, and a concrete example of an indigenous program licensed outside the US and EU.

Four generations of vaccine technology

Each generation trades biological complexity for speed and adaptability. mRNA (4.0) is synthetic — it carries the cell's own message to make the antigen — which is why it is the fastest to design and manufacture.

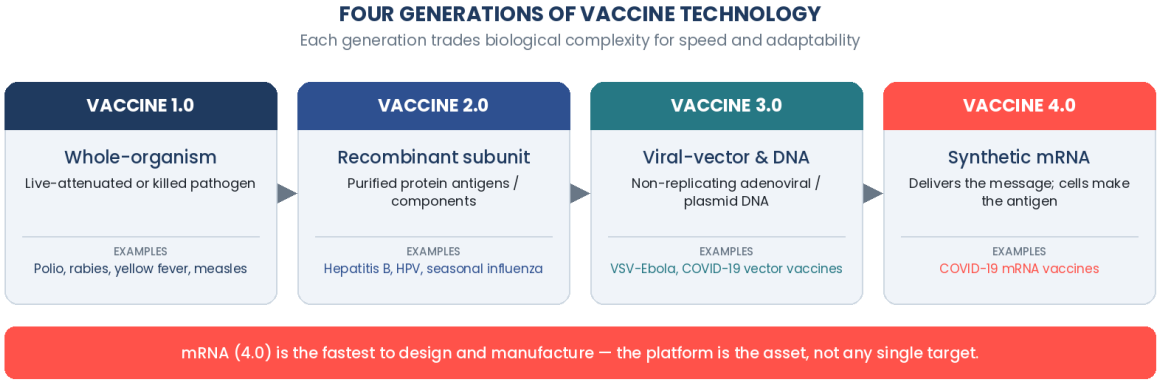


Figure 1. Four generations of vaccine technology, from whole-organism vaccines to synthetic mRNA.

The regulatory journey

The talk traced four stages: strict progression through Phase I–III before licensure; an Emergency Use Authorization that bridged early rollout ahead of full Biologics License Application approval; a platform advantage whereby seasonal strain updates use a streamlined, flu-shot-style variation pathway rather than a fresh dossier; and continuous pharmacovigilance tracking real-world outcomes.

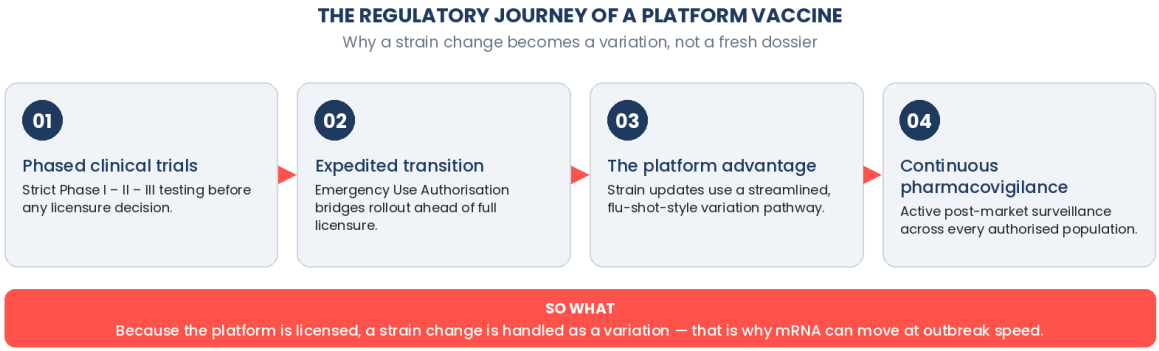


Figure 2. The regulatory journey — because the platform itself is licensed, a strain change is a variation, not a fresh dossier.

So what: because the platform is what gets licensed, a strain change is handled as a variation. That single regulatory fact is why mRNA can move at outbreak speed.

Safety profile and clinical success

- **Expected reactogenicity —** mild, temporary effects (fatigue, sore arm, short-lived fever) consistent with a working immune response.

- **Modified nucleosides —** chemical modification of the mRNA minimizes unintended innate inflammation without blunting immunogenicity.
- **Exceptional efficacy —** over 90% protection against the initial strains, with sustained reductions in hospitalization and ICU admission.
- **Rare-event tracking —** low-risk, manageable transient myocarditis identified early and mitigated through label and dosing guidance.

So what: reactogenicity is expected and self-limiting; the rare events are known, tracked, and manageable. Regulators licensed the platform on exactly that distinction.

India's indigenous mRNA pathway — GEMCOVAC

GEMCOVAC-19 was India's first indigenously developed mRNA vaccine, granted DCGI emergency use authorization in June 2022; the Omicron-specific booster GEMCOVAC-OM followed in 2023. It became the world's first thermostable mRNA COVID-19 vaccine to reach authorization — stable at 2–8 °C, enabling rural distribution without the ultra-cold chain that the Pfizer and Moderna products require — and the first developed wholly outside the US or EU.

- **Regulatory adaptation —** DCGI mirrored global EUA frameworks while weighting local feasibility and manufacturing readiness.
- **Conditional approval —** granted against a commitment to ongoing pharmacovigilance and real-world safety data.
- **Strategic impact —** validated India's biotech ecosystem and set a precedent for oncology and infectious-disease mRNA programs.

Democratizing the platform, and the outlook

Barriers to wider access — raw-material supply, scalability, ease of manufacturing, and ultra-low-temperature logistics — are being addressed through thermostable (2–8 °C) formulations, adsorption chemistry that is readily scalable, a self-amplifying mRNA approach that allows lower doses, backward integration, and regional-hub technology transfer. Because the platform is disease-agnostic (you “change the plasmid” and keep the process), pipelines now extend to rabies, influenza, Nipah, and Ebola, alongside personalized oncology — all in development, not yet authorized. The asset is the speed of iteration: new target sequences can be synthesized and scaled within days of a genome being published.

Module 3 — The Fiocruz Development Process & the ANVISA Relationship

Presenter: Patrícia Neves, Head of RNA Products Development, Bio-Manguinhos/Fiocruz (HUBRNA), Brazil

A regional developer's account of building an end-to-end RNA platform — and the regulatory relationship with ANVISA that goes with it. Bio-Manguinhos/Fiocruz was selected by WHO/PAHO in 2021, through a global call, as a partner institution in the mRNA technology-transfer program to expand development, production, and access to RNA vaccines in low- and middle-income countries.

A Brazilian RNA platform

The program works across both self-amplifying RNA and conventional mRNA constructs, and has fully developed more than 20 combinations of ionizable lipids and constructs in-house. Its proprietary LNP is presented as a draw for partners. Preclinical results reported robust T-cell responses, high titers of neutralizing antibodies, reduced viral load, and full protection in the model used. The non-replicating mRNA platform is the subject of a patent (PCT_BR_2025_050533) and received the Denis Barbosa Award for Intellectual Property and Public Interest.

Manufacturing

Fiocruz reports the first GMP area for RNA products in Latin America, spanning naked-RNA drug substance, encapsulation, and fill-and-finish drug product, together with housing/utilities, and supported by toxicology studies.

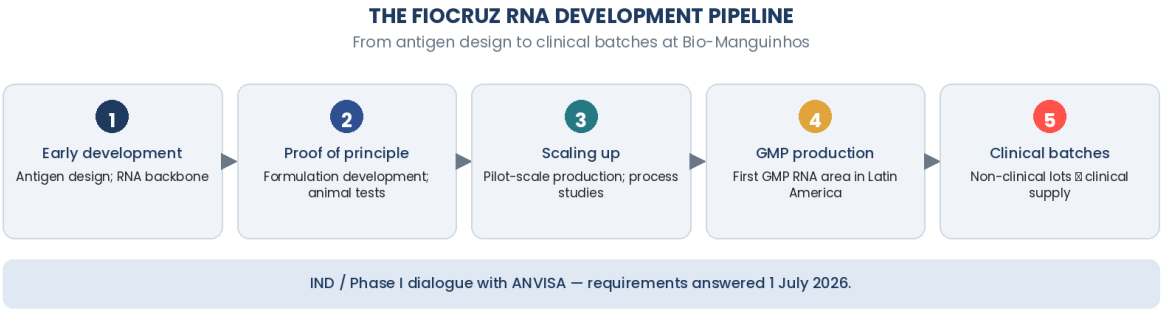


Figure 3. The Fiocruz RNA development pipeline, from antigen design to clinical-batch production.

Quality, regulatory development, and the ANVISA dialogue

On the quality side, the team described its analytical control strategy, drug-product quality-control status, and documentation status. On the regulatory side, an ongoing dialogue with ANVISA supports an Investigational New Drug / Phase I request, with the agency's requirements answered on 1 July 2026 — a concrete example of the manufacturing-country NRA relationship in action.

Portfolio and regional role

The RNA portfolio spans the technology-readiness levels (TRL 1–9) and includes RNA-COVID, tuberculosis, thermostability work, leishmaniasis, an Oropouche vaccine, yellow fever, Mpox, and therapeutic programs such as anti-PD-1 RNA and in-vivo CAR-T, alongside synthetic RNAi. Fiocruz positions itself as a hub for the Latin American RNA innovation ecosystem, funded through a mix of partners including CEPI and the Medicines Patent Pool.

Module 4 — Strengthening Regulatory Preparedness in the Americas

Presenter: María Teresa Ibarz M., International Consultant, Quality & Regulation Unit, PAHO
How the regulatory landscape has evolved since COVID-19, and what is expected for the next emergency — grounded in two regional mapping exercises.

Lessons from H1N1 and COVID-19 (2020 mapping)

Earlier work identified recurring gaps in readiness: regulatory frameworks built on a traditional approach; an absence of requirements and procedures based on risk criteria; a lack of clarity in the roles and responsibilities of the staff in charge; exception pathways applied without regard to the type of medical product, its origin, or its regulatory impact; and, overall, a lack of regulatory preparedness for emergencies. (Anchored in WHO TRS 1004 (2017) and PAHO's 2021 recommendations.)

The 2024 mapping

A follow-up study analyzed 22 countries across Latin America and the English-speaking Caribbean over August 2023–August 2024, examining when emergency regulations were issued, which authorization mechanisms were established, which risk criteria were applied, and what information was available on NRA websites.

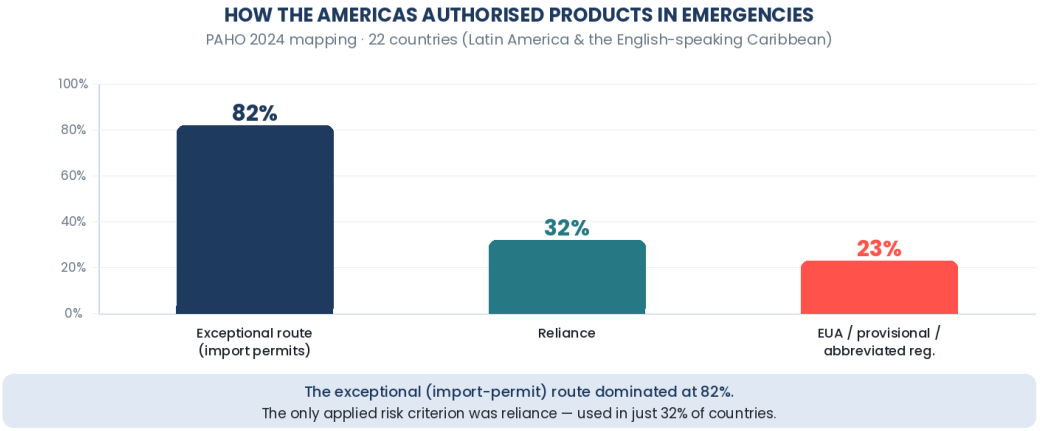


Figure 4. Authorization mechanisms used for emergencies in the Americas (PAHO 2024 mapping).

- **Emergency regulations —** 64% of countries did not change their regulations for emergencies; 32% submitted new ones. Only 36% had updated after 2021, while 64% retained pre-2021 (pre-COVID-19) rules.
- **Authorization mechanisms —** the exceptional route (import permits) dominated at 82%; reliance was applied in 32% of countries and EUA / provisional / abbreviated registration in 23%. The only risk criterion actually applied was reliance.
- **Other findings —** acquisition ran through varied pathways (PAHO Revolving Fund, donations, and direct/bilateral procurement) that carry different levels of risk; and no NRA website had a dedicated section on emergency procedures, standards, requirements, or response times.

Key recommendations

The study recommends applying risk and probability criteria according to the source of acquisition; revising regulatory frameworks to include differentiated, risk-based mechanisms; establishing simplified pathways for

quality-assured products through reliance; reducing the use of import authorizations that carry no risk criterion; and improving the transparency of NRA websites — supported by a proposed risk matrix. (Reference: Pombo ML, Ibarz MT, Mata A, Marin D. Rev Panam Salud Publica 2025;49:e129.)

Module 5 — Product-Specific & GMP Inspections

Presenter: April Hernandez, CEPI Regulatory Affairs (Americas)

What makes RNA-vaccine facilities different — and where existing biologicals inspection checklists fall short. RNA facilities introduce hazards and controls that traditional vaccine inspections were never designed to catch: different hazards (ubiquitous RNases, organic solvents, ultra-cold storage), different equipment (microfluidic mixers and inline sizing rather than bioreactors and chromatography skids alone), and different analytics (nanoparticle sizing and RNA-integrity assays many QC labs have not run).

RNase control — the organizing principle

RNases are everywhere — on skin, surfaces, and equipment — and a single contamination event can degrade a batch and destroy potency, so RNase control organizes the whole facility. Inspectors should verify it is designed in, not bolted on: segregated, dedicated equipment with validated RNase decontamination; environmental monitoring tuned to RNase and bioburden, not only classical particulates; staff decontamination protocols (gowning, glove discipline, workflow) that treat the operator as the main RNase source; and RNase-free consumables, reagents, and water with documented supplier qualification.

Cold chain

The inspection focus is validated storage across the whole chain, continuous excursion monitoring, and lot-release rules honoured at both the manufacturer and every receiving site.

Qualifying the LNP encapsulation suite

- **Microfluidic mixer qualification —** flow rates, mixing ratio, and shear are critical process parameters; qualify the equipment and its operating ranges, not just the output.
- **Inline particle-size monitoring —** real-time size and polydispersity control during formulation, with defined action limits.
- **Solvent (ethanol) control —** ethanol is a process-related impurity of particular relevance for LNPs; characterize and control its removal.
- **Encapsulation efficiency —** un-encapsulated mRNA is unstable, so percentage encapsulation is a controlled critical quality attribute.

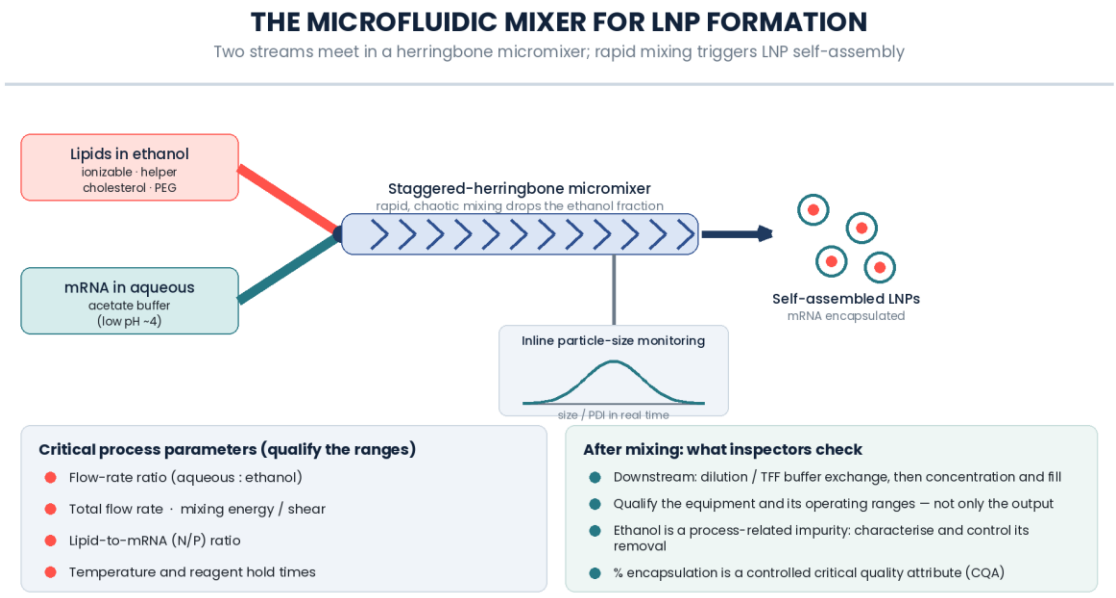


Figure 5. How the microfluidic mixer forms LNPs — converging inlets, a herringbone mixing channel, and inline particle sizing.

Analytics — where existing checklists fall short

Four analytical areas go beyond the conventional panel: DLS/NTA for LNP size, distribution, and zeta potential; capillary electrophoresis for RNA integrity, fragment sizing, and percent-intact transcript; potency bioassays (cell-based or cell-free expression) with qualified reference standards; and impurity/adduct analysis (IP-RP-HPLC and mass spectrometry) for double-stranded RNA, residual DNA template, and RNA-lipid adducts. Reference-standard availability is often the binding constraint — potency and integrity assays are only as good as the standards behind them.

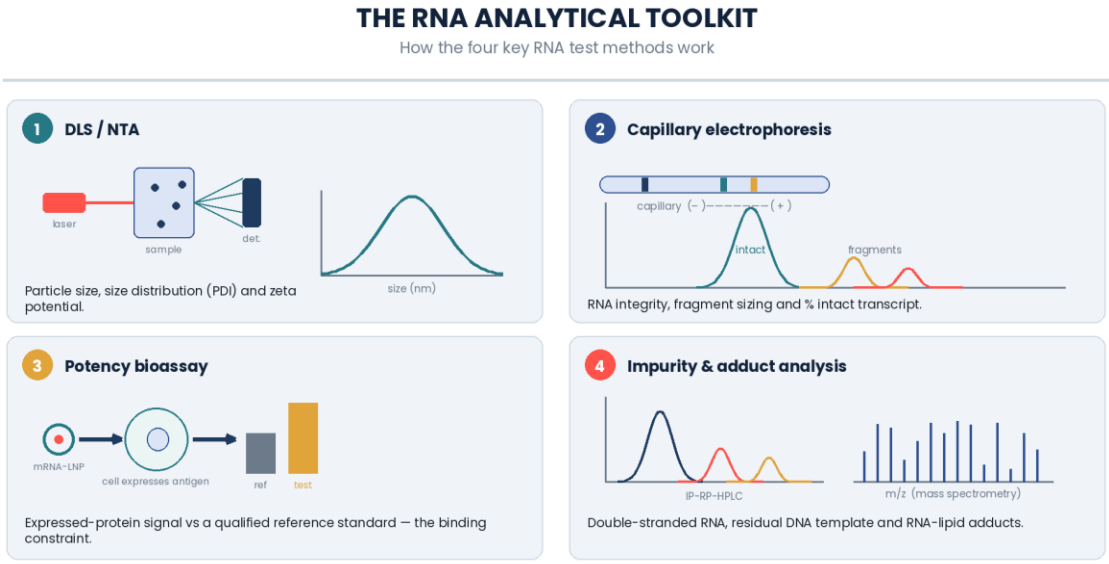


Figure 6. The RNA analytical toolkit — how the four key test methods work.

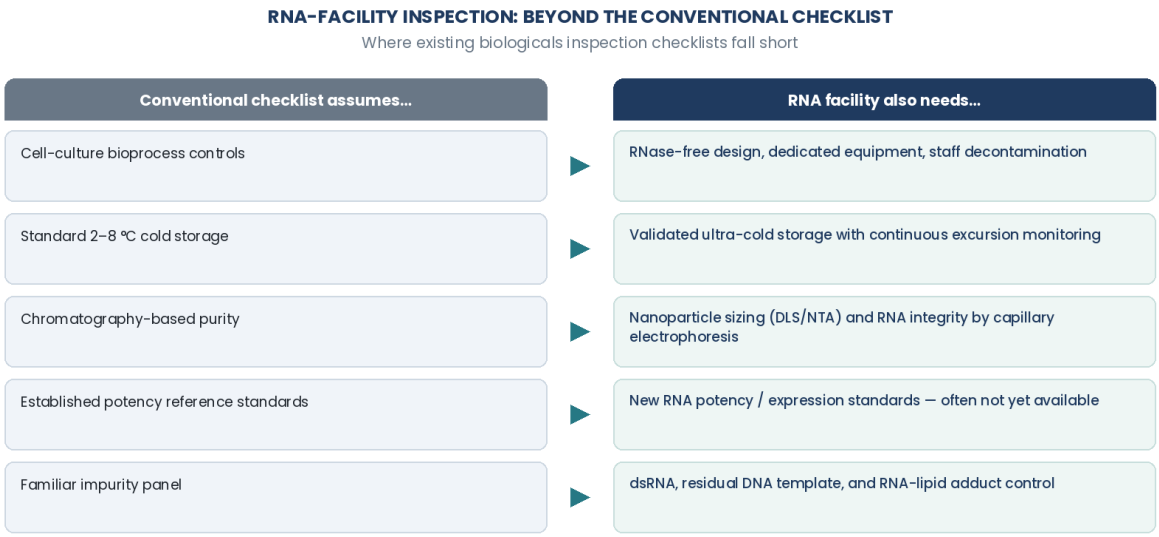


Figure 7. Mapping the gaps — what a conventional checklist assumes versus what an RNA facility also needs.

What inspectors are finding

Across FDA and EMA inspections of mRNA-vaccine sites, the citable observations cluster into four themes:

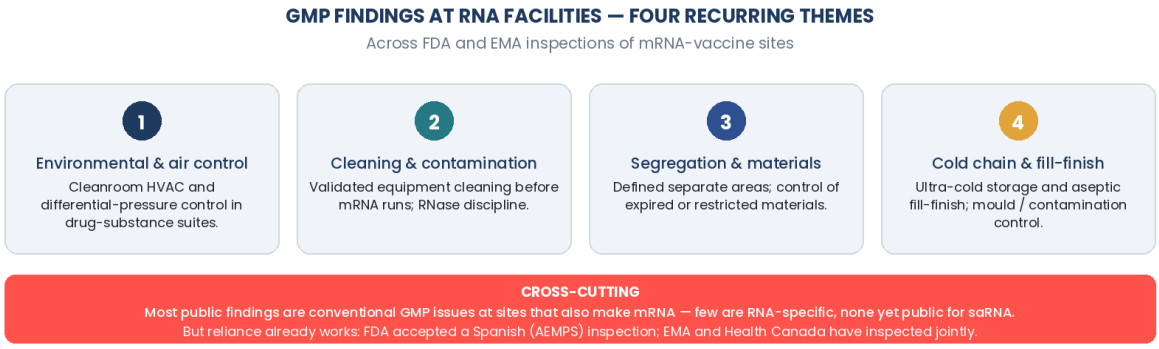


Figure 8. The four recurring themes in published GMP findings at RNA facilities.

Cross-cutting point: most public findings are conventional GMP issues at sites that happen to make mRNA — few are RNA-specific, and none are yet public for saRNA. Crucially, reliance already works in practice: the FDA accepted a Spanish (AEMPS) facility inspection, and the EMA and Health Canada have inspected jointly.

Findings you can cite, by facility

Facility (role)	Agency · year	What was cited (paraphrased)
Moderna — Norwood, MA (mRNA drug substance)	FDA Form 483 · Sep 2023	Equipment not cleaned before drug-substance runs; expired/restricted materials in DS; Grade C cleanroom air handling judged inadequate.
Catalent — Bloomington, IN (fill-finish)	FDA Form 483 · Sep 2022	Observations at bivalent fill-finish; the site was not initially added to the EUA pending FDA review.

Facility (role)	Agency · year	What was cited (paraphrased)
Pfizer (ex-Hospira) — McPherson, KS (fill-finish)	FDA 483s (repeat)	Mold and microbial-contamination control and cleaning/disinfection — general aseptic issues, not RNA-specific.
Spikevax pharmacovigilance system	EMA + Health Canada (joint) · 2021	5 major / 5 minor findings with CAPA endorsed — a joint-inspection and reliance example.
mNEXSPIKE (reliance record)	FDA SBRA · 2025	FDA accepted a Spanish AEMPS facility inspection as roughly "voluntary action indicated" — a reliance example.

Note: a Form 483 records an inspector's observations, not a final GMP determination. Sources: FDA 483s/EIRs (fda.gov), EMA EPAR assessment reports, and the FDA Summary Basis for Regulatory Action.

Key Takeaways

- **RNA is a platform, not a product.** The chemistry is fixed and the sequence changes — enabling weeks-not-months adaptation, and letting much of a process review carry across products.
- **Draw the platform boundary deliberately.** Whether the platform is the RNA, the LNP, or both decides what data is shared vs. product-specific and how post-approval changes are managed.
- **The frameworks converge.** WHO TRS 1039, the EMA draft guideline, and WHO EUL are used together, not in isolation.
- **Guidance is going RNA-based.** saRNA is already licensable (Kostaive); expect broader, RNA-based expectations rather than mRNA-only rules.
- **Inspection is genuinely different.** RNase control, ultra-cold chain, and nanoparticle analytics exceed conventional biologicals checklists — and reference-standard availability is often the binding constraint.
- **Reliance is the force-multiplier.** It lets importing-country NRAs act quickly on trusted reference decisions — and the region's own evidence shows it is still the exception, not yet the norm.

The thread that tied both sessions together

Every module returned to the same question: is your NRA a manufacturing-country authority — owning the full dossier, GMP inspection, and release at source — or an importing-country authority that relies on the work of others and focuses effort on local decisions? Reliance is the bridge between these two roles, and the practical answer for most NRAs in the region.

Way forward

Four concrete next steps were proposed for each agency:

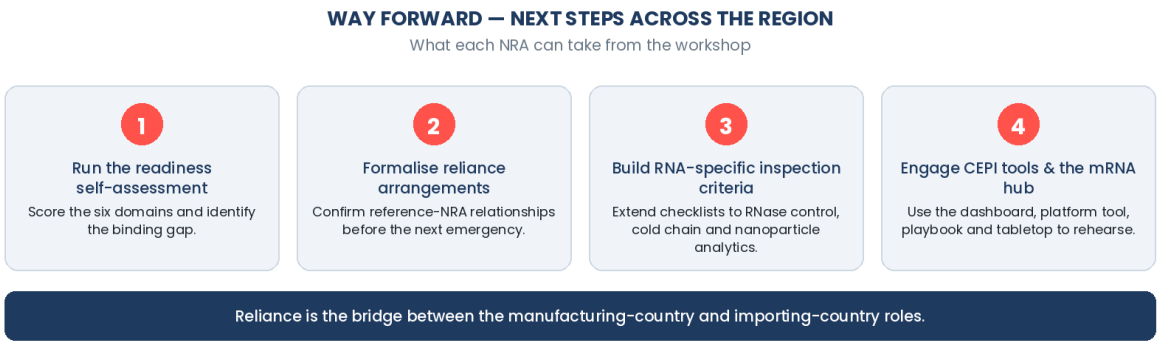


Figure 9. Way forward — four next steps for NRAs across the region.

- **Run the readiness self-assessment** across the six domains and identify the binding gap.
- **Formalize reliance arrangements** — confirm reference-NRA relationships and work-sharing before the next emergency.
- **Build RNA-specific inspection criteria** — extend biologicals checklists to cover RNase control, cold chain, and nanoparticle analytics.
- **Engage the CEPI tools and mRNA hub** — use the dashboard, platform tool, playbook, and tabletop exercises to rehearse the dialogue.

Selected References & Resources

- Pombo ML, Ibarz MT, Mata A, Marin D. *Autorización de vacunas en situaciones de emergencia en países de las Américas, agosto 2024*. Rev Panam Salud Publica 2025;49:e129.
- WHO. *Guidelines on regulatory preparedness for provision of marketing authorization of human pandemic influenza vaccines in non-vaccine-producing countries*. TRS No. 1004 (2017).
- PAHO. *Recommendations on Regulatory Processes and Aspects related to the Introduction of Vaccines during the COVID-19 Pandemic and Other Emergencies* (2021).
- WHO ECBS. Regulatory considerations for mRNA vaccines. TRS No. 1039, Annex 3 (2022); EMA draft *Guideline on the quality aspects of mRNA vaccines* (2025).
- FDA Form 483s / EIRs (fda.gov, ORA Electronic Reading Room); EMA EPAR assessment reports; FDA Summary Basis for Regulatory Action.
- DCGI / CDSCO authorization records for GEMCOVAC-19 and GEMCOVAC-OM (Gennova).
- Fiocruz non-replicating mRNA platform patent, PCT_BR_2025_050533.
- Referenced primary literature as cited in the presentations: *Nature* 654:892–901 (2026); *The Lancet* 408(10551):275–288 (2026).

Prepared as a Workshop Report from the Session 2 (Day 2) presentation materials — CEPI RNA Vaccine Regulatory Workshop, 28–29 July 2026. Some material (ImmunoScript; Fiocruz) was marked confidential or proprietary in the original presentations; guest data are reproduced as presented. A companion to the Day 1 report.