Control de calidad en vacunas COVID

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10º Seminario intercongresos:
Metrología y salud: un binomio de garantía para la calidad de vida

Las vacunas frente a Covid 19 son medicamentos biológicos

- Proceden de una fuente (material de partida) biológica

(en contraposición a los químicos, que se obtienen por síntesis)

- Son de difícil caracterización y control

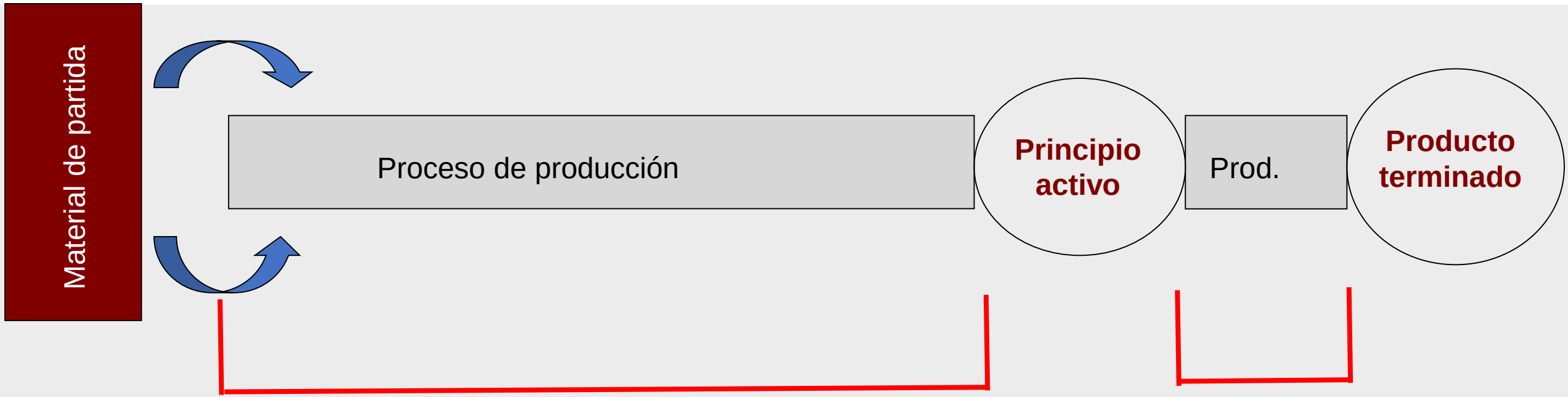
- Su calidad está relacionada con el proceso de fabricación

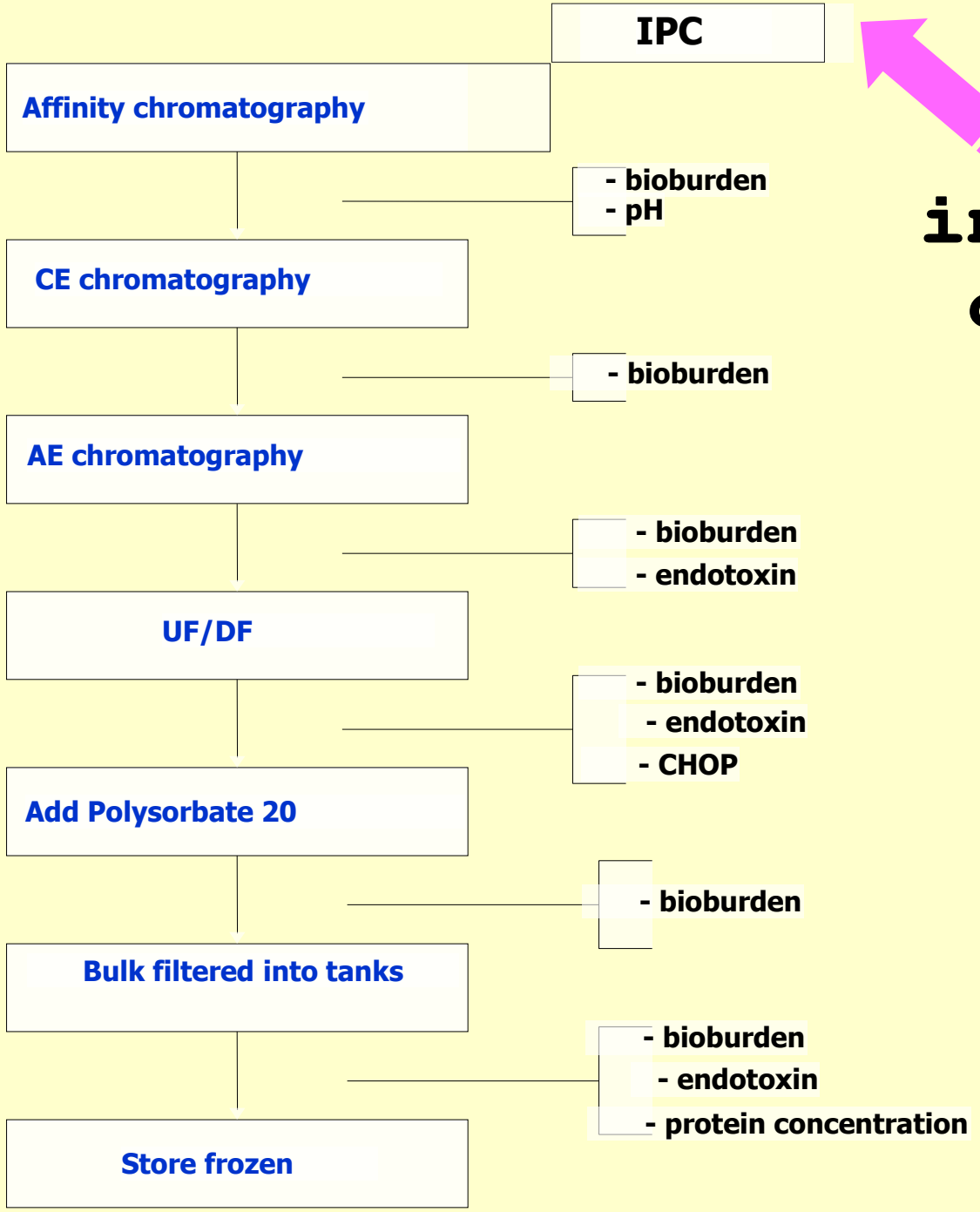
- La calidad se determina mediante una combinación de tests físico-químicos y biológicos, junto con el proceso de producción y su control

Otros aspectos relevantes de los medicamentos Biológicos

- Difícil caracterización
- Uso de reactivos de origen animal/humano
- Materiales de partida muy diversos
- Materiales de partida de origen animal/humano
- Riesgo de transmisión de patógenos (Virus, TSE)

Proceso de Producción de Medicamentos Biológicos





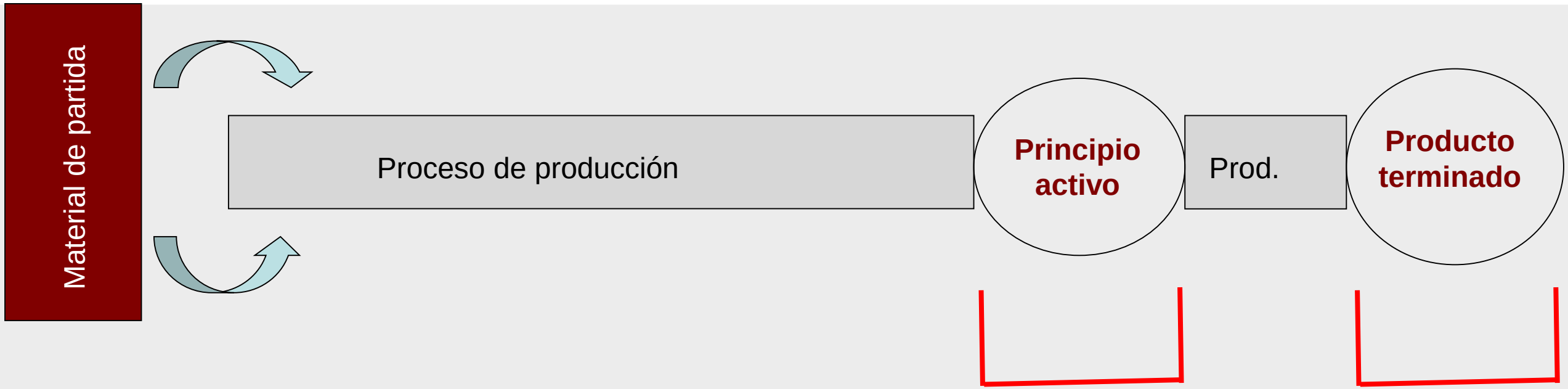
in-process controls

Comparabilidad

Table 5. Comparability studies needed following changes to the manufacturing process of a medicine produced by biotechnology

Type of manufacturing change	Expected impact	Comparability studies needed
1. Minor change (e.g. adding a more sensitive test method to characterise the active substance)	Does not affect the pharmaceutical quality of the medicine (no impact on product specifications)	Limited physicochemical studies comparing batches before and after the change
2. Significant change (e.g. changes to the cell system used to produce the active substance)	May affect product characteristics or specifications but not expected to affect safety or efficacy	Comprehensive physicochemical and functional in vitro studies
3. Major change (e.g. certain changes in the medicine's formulation)	May possibly affect safety or efficacy	Comprehensive physicochemical and in vitro functional studies complemented as needed by non-clinical and clinical studies

Proceso de Producción de Medicamentos Biológicos



ICH Topic Q 6 B
Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products

A specification is defined as a list of tests, references to analytical procedures, and appropriate acceptance criteria which are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a drug substance, drug product or materials at other stages of its manufacture should conform to be considered acceptable for its intended use.

For drug applications for new molecular entities, it is unlikely that an international or national standard will be available. At the time of submission, the manufacturer should have established an appropriately characterised in-house primary reference material, prepared from lot(s) representative of production and clinical materials.

In-house reference material: suele ser un lote bien caracterizado y fabricado con un proceso de producción representativo

ICH Topic Q 6 B
Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products

Advanced therapies
Biosimilars
Compliance
Data on medicines (ISO IDMP standards)
Fees
Medical devices
Orphan designation
Paediatric medicines
Pharmacovigilance
Plasma master file (PMF) certification
Public health threats

COVID-19

COVID-19 vaccines

Share

Currently under rolling review

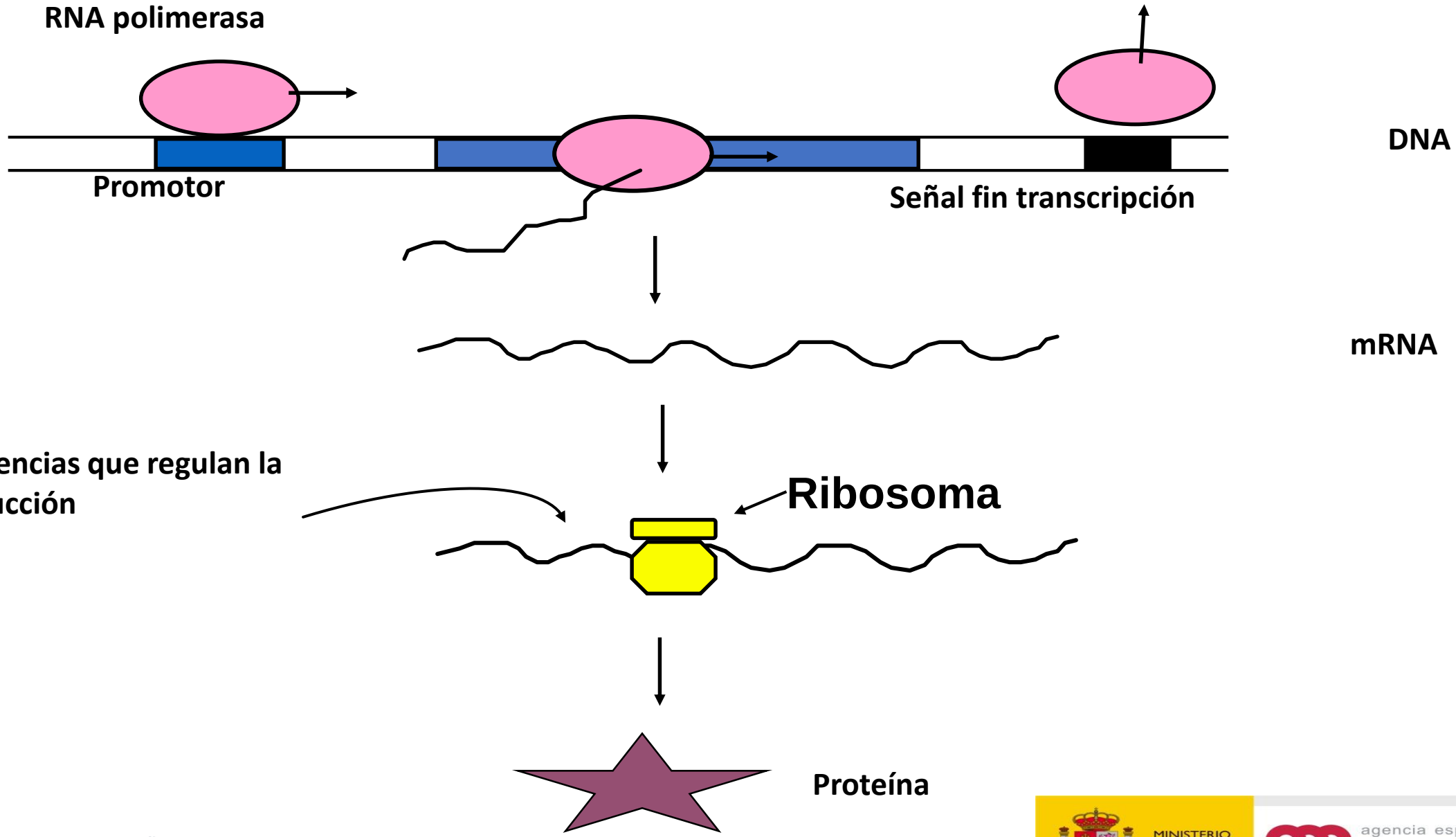
- CVnCoV
- NVX-CoV2373
- Sputnik V (Gam-COVID-Vac)
- COVID-19 Vaccine (Vero Cell) Inactivated

Marketing authorisation application submitted

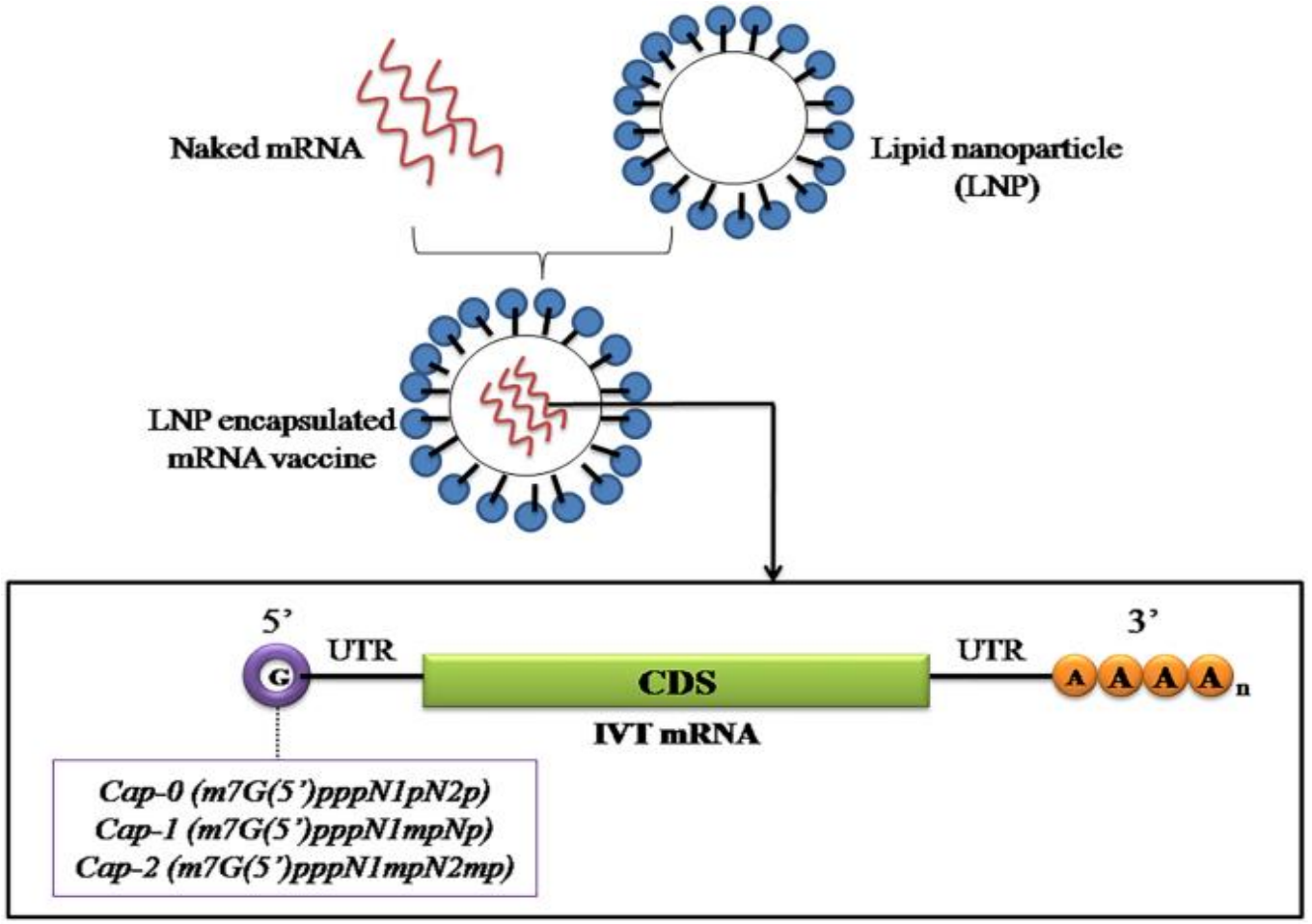
No marketing authorisation applications currently under evaluation

Authorised for use in the European Union

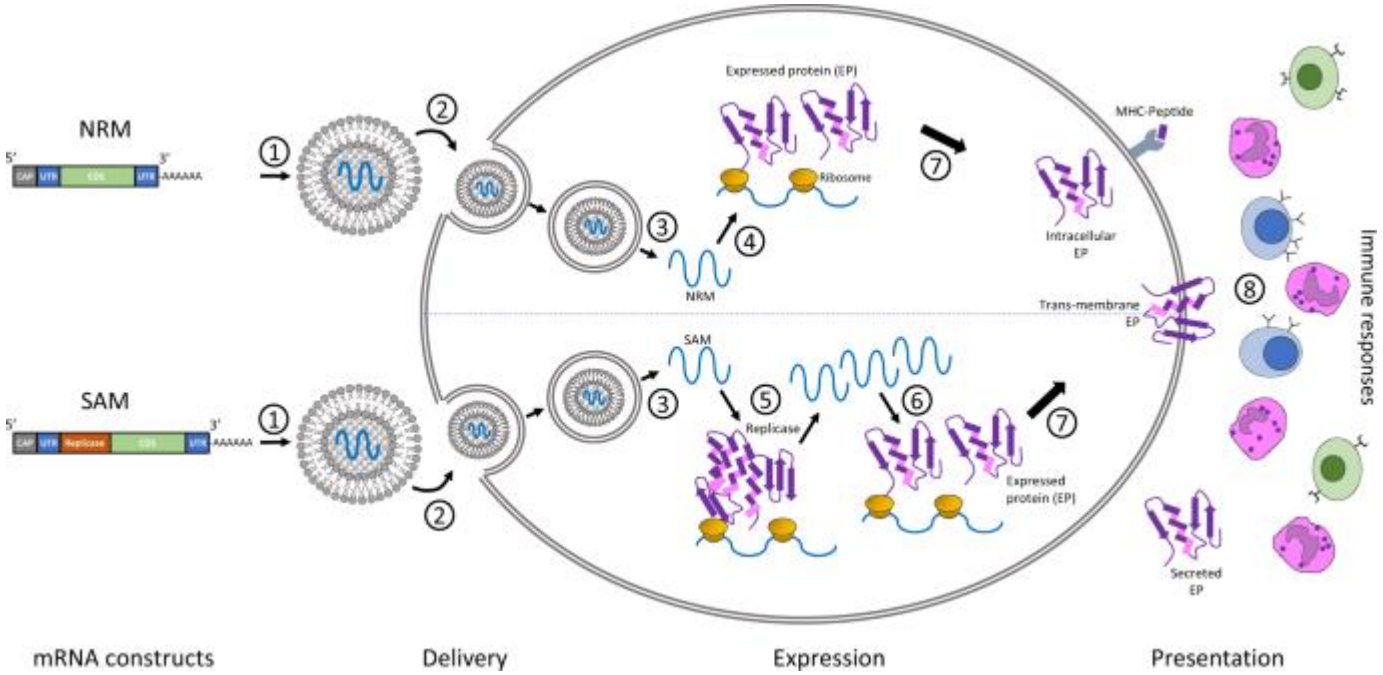
- Comirnaty
- COVID-19 Vaccine Moderna
- Vaxzevria (previously COVID-19 Vaccine AstraZeneca)
- COVID-19 Vaccine Janssen


RNA polimerasa
Promotor
Señal fin transcripción
DNA
mRNA
Secuencias que regulan la traducción
Ribosoma
Proteína

Vacunas de RNAm



Vacunas de RNAm



REVIEW ARTICLE OPEN

The promise of mRNA vaccines: a biotech and industrial perspective

Nicholas A. C. Jackson[1]*, Kent E. Kester[2], Danilo Casimiro[2], Sanjay Gurunathan[2] and Frank DeRosa[3]

npj Vaccines (2020)5:11; https://doi.org/10.1038/s41541-020-0159-8

Especificaciones en vacunas de RNAm para Covid

Comirnaty

Product specification (taken from EPAR)

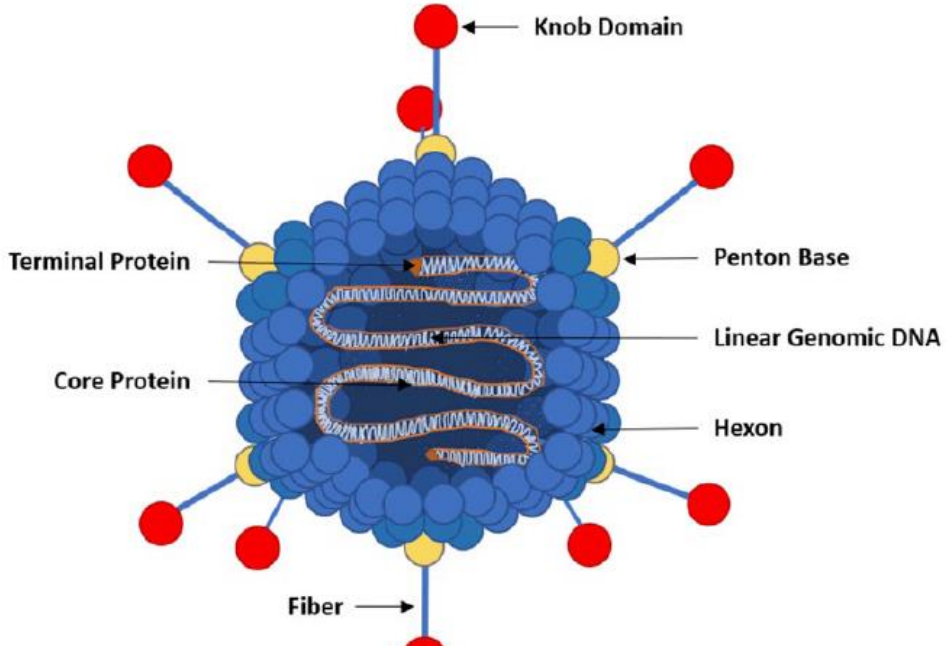
Appearance (Visual), Appearance (Visible Particulates), Subvisible Particles (Ph. Eur.), pH (Ph. Eur.), Osmolality (Osmometry), LNP Size (Dynamic Light Scattering), LNP Polydispersity (Dynamic Light Scattering), RNA Encapsulation (Fluorescence assay), RNA content (Fluorescence assay), ALC-0315 content (HPLC-CAD), ALC-0159 content (HPLC-CAD), DSPC content (HPLC-CAD), Cholesterol content (HPLC-CAD), extractable volume (Ph. Eur.), Lipid identities (HPLC-CAD), Identity of encoded RNA sequence (RT-PCR), Potency / in Vitro Expression (Cell-based flow cytometry), RNA Integrity (Capillary Gel Electrophoresis), Bacterial Endotoxin (Ph. Eur.), Sterility (Ph. Eur.) and Container Closure Integrity (Dye incursion).

Moderna

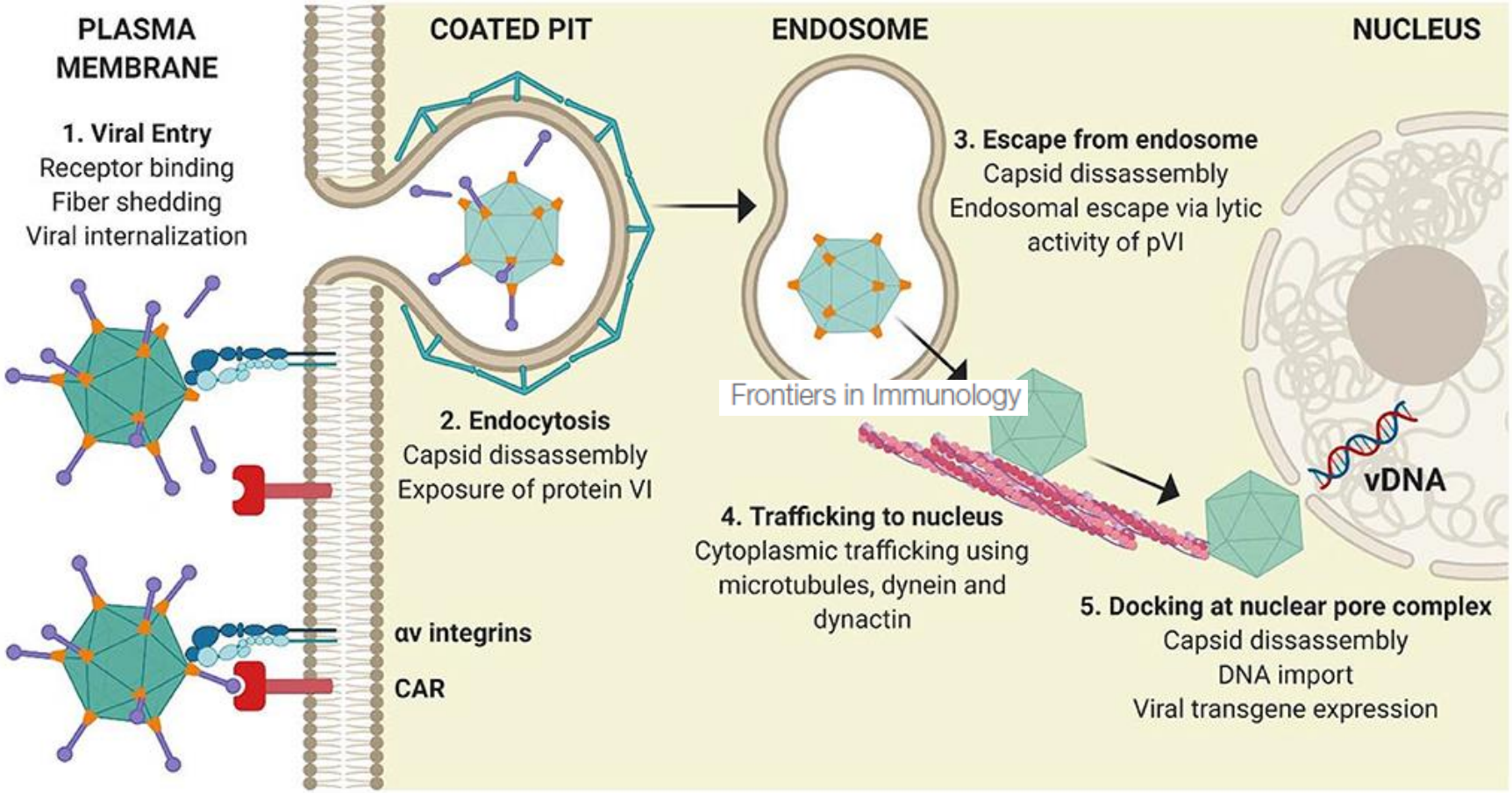
Finished product specifications (taken from EPAR)

Appearance (visual), mRNA identity by reverse transcription/Sanger sequencing, total RNA content by anion exchange chromatography, purity and product-related impurities by RP-HPLC, % RNA encapsulation by absorbance assay, in vitro translation (methionine labelling), lipid identity by UPLC-CAD (SM-102, cholesterol, DSPC, PEG2000-DMG), lipid content by UPLC-CAD (SM-102, cholesterol, DSPC, PEG2000-DMG), lipid impurities by UPLC-CAD (% individual impurities and sum of impurities), mean particle size and polydispersity by DLS, pH, osmolality, particulate matter, container content (USP), bacterial endotoxin (Ph. Eur. 2.6.14, kinetic chromogenic method) and sterility (Ph. Eur. 2.6.1)

Vacunas de Adenovirus



Vacunas de Adenovirus



Factors Which Contribute to the Immunogenicity of Non-replicating Adenoviral Vectored Vaccines

*Lynda Coughlan**†

Frontiers in Immunology May 2020 | Volume 11 | Article 909

Especificaciones en vacunas de Adenovirus para Covid

Vaxzevria

Finished Product specification (taken from EPAR)

Appearance, color, clarity, visible particles, pH, and polysorbate 80, extractable volume, sub visible particles, and osmolality. The potency tests of infectivity and the purity tests of DNA to protein ratio and viral particle to infectivity ratio. Also performed are identity by qPCR, viral particle concentration by anion exchange chromatography, and the safety tests of sterility, container closer integrity testing and endotoxin.

Janssen

Finished Product specification (taken from EPAR)

Appearance (degree of coloration, clarity, and visible particles), identity by (ID)-PCR and virus protein fingerprinting by RP-HPLC, potency with transgene expression by quantitative ELISA and infectious units by QPA, quantity (virus particles) by VP-qCR, purity (aggregates average hydrodynamic radius and polydispersity) by DLS, safety tests (sterility, bacterial endotoxins, container closure integrity) and general tests (pH, osmolality, extractable volume, and polysorbate 80 concentration).

Control de calidad en vacunas Covid: Conclusiones

- Las vacunas frente a la Covid 19 son medicamentos biológicos

- Su control incluye: control de los materiales de partida, control del proceso de producción, caracterización, control de cada lote de principio activo, control de cada lote de producto terminado, control de estabilidad

- El control de cada lote debe incluir tests para parámetros generales, cantidad, identidad, pureza e impurezas y potencia

- Se necesita establecer un lote representativo como estándar de referencia

¡Muchas gracias!

MINISTERIO DE SANIDAD
agencia española de medicamentos y productos sanitarios