EMA
EUROPEAN MEDICINES AGENCY

Regulatory update from EMA

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CMC Strategy Forum Japan 2025

8-9 December 2025

Regulatory update from EMA

- Scientific guidelines
- Revision of EU variations framework
- International collaboration
- Publications

Scientific Guidelines

Scientific guidelines - EMA

- Questions and answers on BWP learnings
- Guideline on quality aspects of RNA vaccines
- Reflection Paper on tailored clinical approaches for biosimilar developments
- Guideline on the development and manufacture of human medicinal products specifically designed for phage therapy
- Revision of Guideline on Radiopharmaceuticals Based on Monoclonal Antibody Derivatives
- Revision of Guideline on epidemiological data on blood transmissible infections

Questions and answers for biological medicinal products

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Page contents

Updated on 16 June 2025:
'Raw materials and media components (3.2.S.2.3)' section

This question and answer page is developed and maintained by the CHMP Biologics Working Party (BWP) and provides agreed positions by the Biologics Working Party position on issues that can be subject to different interpretation or require clarification, typically arising from discussions or correspondence during assessment procedures of biological human medicinal products.

In order to obtain information on a topic, please click on the topics/questions. Please note that this page has been produced to provide transparency and additional information, and should be read in conjunction with the European Pharmacopoeia, CHMP guidelines on quality and other guidance documents.

Expand all | Collapse all

Guideline on quality aspects of RNA vaccines

Concept paper 2023

- 120 comments from 13 stakeholders

Draft guideline 2025

- Public consultation open until **30/09/2025**

Final guideline target: 2026

27 March 2025
EMA/CHMP/BWP/82416/2025
Committee for Medicinal Products for Human Use (CHMP)

Guideline on the quality aspects of mRNA vaccines

Draft

Draft agreed by Biologicals Working Party	February 2025
Adopted by CHMP for release for consultation	27 March 2025
Start of public consultation	31 March 2025
End of consultation (deadline for comments)	30 September 2025

Comments should be provided using this EUSurvey form. For any technical issues, please contact the EUSurvey Support.

Keywords	***mRNA, vaccine, development and manufacture, starting materials, active substance, finished product***

Reflection Paper on tailored clinical approaches for biosimilar developments

Draft reflection paper 2025

- Public consultation open until **30/09/2025**

17 March 2025
EMA/CHMP/BMWP/60916/2025
Committee for Medicinal Products for Human Use (CHMP)

Reflection paper on a tailored clinical approach in biosimilar development
Draft

Draft for internal consultation agreed by Biosimilar Medicines Working Party	21 October 2024
Consultation with MWP, BWP and SAWP	17 January 2025
Draft agreed by Biosimilar Medicinal Products Working Party	12 February 2025
Adopted by CHMP for release for consultation	17 March 2025
Start of public consultation	1 April 2025
End of consultation (deadline for comments)	30 September 2025

Comments should be provided using this EUSurvey form. For any technical issues, please contact the EUSurvey Support.

Keywords	Reflection Paper, Biosimilar, Comparative Efficacy Study, Tailored clinical approach

7 August 2025

EMA F2F multi-stakeholder workshop on tailored clinical approach for biosimilars
Agenda for the hybrid Workshop – 22 September 2025, Room 1A

Chair: René Anour – Vice-Chair: Niklas Ekman

Draft Agenda for Reflection Paper Workshop	
Intro session	
Session 1	Tailored approach: Framework and utility of Comparative Efficacy Studies (CES)
Session 2	Quality comparability: Analytical, similarity approach and statistical issues
Session 3	Clinical studies: PK, PD, and immunogenicity aspects
Session 4	Overall discussion

Scientific guidelines - ICH

- ICH Q1 & ICH Q5C Stability Testing (revision)
- ICH Q3E Extractables and Leachables (new)
- ICH Q5A Viral safety (training materials)
- ICH Q6 Specifications (revision)
- ICH M4Q Common Technical Document (CTD) – quality (revision)

ICH's Effort to Shape the Future

STEP 1

ICH M4Q(R2) defines the new structure of Module 2.3 and Module 3

STEP 2

ICH M16 (SPQS) will define Structured Product Quality Submissions

Cloud computing

Big data analytics

Knowledge management

Artificial Intelligence

Revision of EU variations framework

Revision of EU variations framework

- Aim to **improve the existing system** by incorporating experience gained and make the lifecycle management of medicines more:
  - **Efficient** for regulators and MAHs
  - **Future proof** with scientific and technological progress

- **Simplify** and enable an **agile review** of classification guideline and operational procedures.

- **Short-term measures** which can be done independently from the review of basic legislation.

Relevant changes of the amended Variation Regulation

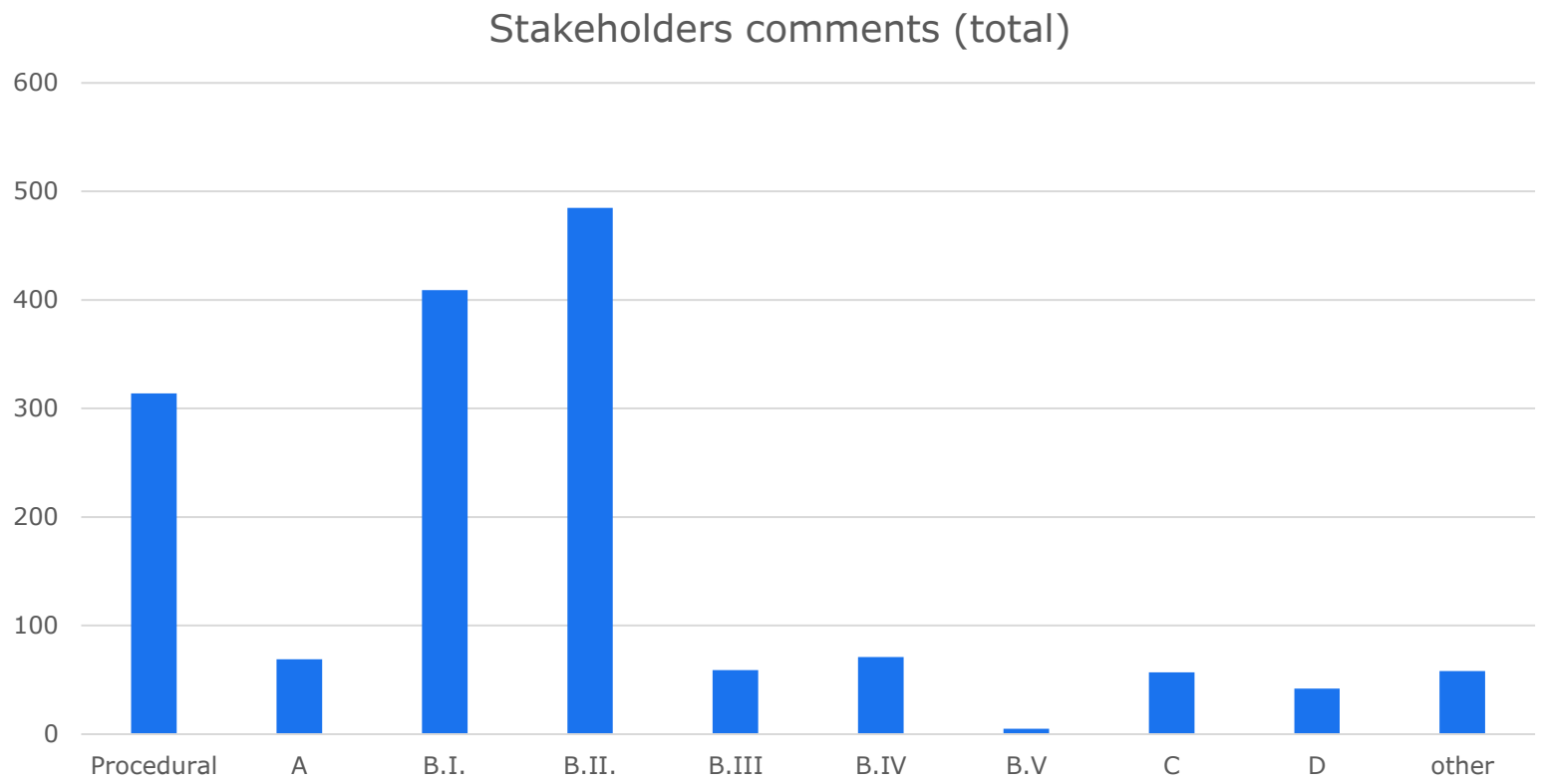
- **Efficiency gains:**
  - **Super-grouping:** less impactful for CAPs but key for the NCAs/MAHs (extended to purely NAPs).
  - **Annual update of type IA variations**: previously optional, now mandatory with exception to keep some flexibility for innovative products.
  - **Mandatory worksharing procedure**: previously optional, significant gains in terms of resources and harmonisation are expected for NAPs.
  - **Voluntary worksharing:** same variation applicable to different MA from different MAH (e.g. EoI for two MA supported by data from the same CT).

Principles for the revision of the Variations Guidelines

- All categories of variations were reviewed based on **experience** acquired, the **scientific and technical progress**.
- Aim to **improve the efficiency** ensuring the protection of public health in the EU.
- When appropriate, **streamline the variation framework** (e.g. *decreasing, downgrading and simplifying the various categories of variations*).
- When possible, **future proof** the variations framework for the upcoming changes (e.g. *adapt/prepare for innovation*)
- The changes made are **compatible** with the revised Variations Regulation.

Overview of public consultation comments on draft variation guideline revision (Jun–Aug 2024)

Section	Comments
Procedural	314
A	69
B.I.	409
B.II.	485
B.III	59
B.IV	71
B.V	5
C	57
D	42
other	58
TOTAL	**1569**



Comments from **48 stakeholders** were received

Main changes

Procedural part

- **Operational details shifted** to EMA/CMDh guidance for **easiest updates** in the future.
- **Change the current code system (numbering)** to facilitate the implementation of the new framework

A. Administrative variations

- Reduction/simplification list from 8 to 5 scopes.

B. Quality variations

Review of all categories:

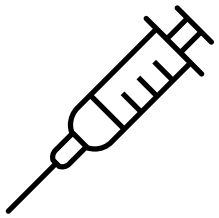
- **Downgrade** certain scopes when scientifically justified (risk/based approach).
- **Removed conditions of biological** medicinal products in certain circumstances allowing a Type IA variations.
- **Implementation of PACMP** as Type IB or Type IA also for BIO.
- **Alignment** and **consistency** between Chemicals and Biologics where appropriate
- New section on **In-house reference preparations.**
- New scopes for **Medical devices** in line with MDR.

C. Safety, Efficacy, PhV variations

- **Deletion** of scopes (C.I.9, C.I.10, as now done via Art. 57 database).
- C.I.3 **expanded to include** implementation of **PRAC signals** and **joint recommendations of EU authorities.**
- New scope for submission of **results** of assessments carried out on **target patient groups**.

D. PMF

- Reduction/simplification list from 23 to 16 scopes.



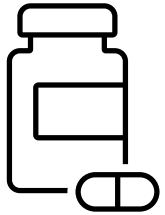
Biologicals

Risk-based decrease in categories (II -> IB, IB -> IA)

Documentation/conditions

Additional regulatory tools

PMFs



Chemicals

Alignment and **consistency** between scopes with biological

Active Substance Master Files (ASMF) / CEPs

Strengthen responsibility of MAHs (e.g. nitrosamines LLE)

Medical Devices

New scopes to align with the Medical Device Regulation

Herbals

Review of categories, documentation and conditions

Revision of EU variations framework


22 September 2025

Health and Food Safety Directorate-General

European Commission

eNews

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Commission publishes new measures for the better lifecy-cle management of medicine authorisations

The revised Variations Guidelines were published on **22 September 2025**

Official Journal of the EU - C/2025/5045

- Enter into force on **15 January 2026**
- All variation submissions from this date, for NAPs and CAPs, should follow these revised Variations Guidelines.
- EMA will issue further guidance and Q&As to support implementation.

Commission publishes new measures for the better lifecycle management of medicine authorisations

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International Collaboration

ICMRA Collaborative Assessment Pilot – Overview

- **Scope**

Multi-agency collaborative assessment of Post Approval Change Management Protocols (PACMPs)

Focused on medically important treatments, including chemical and biological products, but excluding vaccines

- **Application Process**

14 applications received

Prioritised based on impact to supply of critical medicines & potential for agreed regulatory approach

- **Pilot implementation**

5 proposals accepted

Identical submissions sent to all participating agencies

ICMRA Pilot cases

Application	Product	Indication	Proposed change	Lead Authority	Participating Authorities	Observer Authorities
Pilot Case 1	Monoclonal antibody	Follicular lymphoma	Additional active substance manufacturing site and additional QC testing site	EMA	FDA	PMDA
Pilot Case 2	Small molecule	Hyperkalaemia	Additional drug product manufacturing site	FDA	EMA	PMDA, Health Canada, HSA, ANVISA
Pilot Case 3	Small molecule	Non-small cell lung cancer	Additional active substance manufacturing site	PMDA	FDA, EMA, MHRA, Swissmedic	HSA, Health Canada, TGA
Pilot Case 4	Antibody drug conjugate	Metastatic triple-negative breast cancer	Additional active substance intermediate manufacturing site and additional QC testing site	FDA	EMA, MHRA, Swissmedic	Health Canada
Pilot Case 5	Monoclonal antibody	Multiple cancer indications	Improvements to the manufacturing process	EMA	FDA, PMDA, Health Canada	HSA, Swissmedic

Lead Authority

- Assess application
- Propose IRs
- Coordinate all activities
- Lead on project calls
- Consolidates IRs
- Applicants' main contact

Participating Authorities

- Conduct independent assessment
- Participate in discussion meetings
- Propose IRs

Observer Authorities

- Participate in discussion meetings
- Cannot raise IRs

Key achievements

Streamlined Timelines

- Agreed a common **120 day assessment timetable**
- **Near-simultaneous approvals** — a global first!

Overall duration (days)	Max difference in approval dates between participating authorities
115	0
118	0
105	0
122	2
119	12

Efficiency & Harmonisation

- **88% of all assessment IRs** harmonized via intensive discussions
- Harmonisation achieved across all sections of Module 3
- **~25% reduction** in total IRs due to collaborative review meetings
- All 5 collaborative assessments completed successfully with **harmonised outcomes**
- No increase in standard expectations → the regulatory bar remained unchanged
- **Positive feedback** from industry and regulators (based on survey results)
- Increased resource requirements, especially for regulators

Regional Specificities

- Some region-specific IRs (e.g. method transfer data, validation report requirements)
- A few region-specific administrative questions (e.g. applicant forms, GMP documentation)

Key Benefits of Collaborative Assessment

Benefits for industry

- Harmonized 120 day approval timeline across multiple jurisdictions
- Alignment on CMC data requirements across regions
- Increased predictability
- Faster implementation of global manufacturing changes
- Agile response to market shifts and capacity demands
- Reduced risk of divergence in global dossiers

Benefits for regulators

- Enhanced knowledge sharing among global authorities
- Deeper insight into regulatory practices of other agencies
- Builds trust and confidence for future reliance and work-sharing
- Supports international harmonisation and convergence

Benefits for Patients

- Increased availability of critical medicines through accelerated global approvals
- Assessment outputs support reliance in low- and middle-income countries

Pilot extension

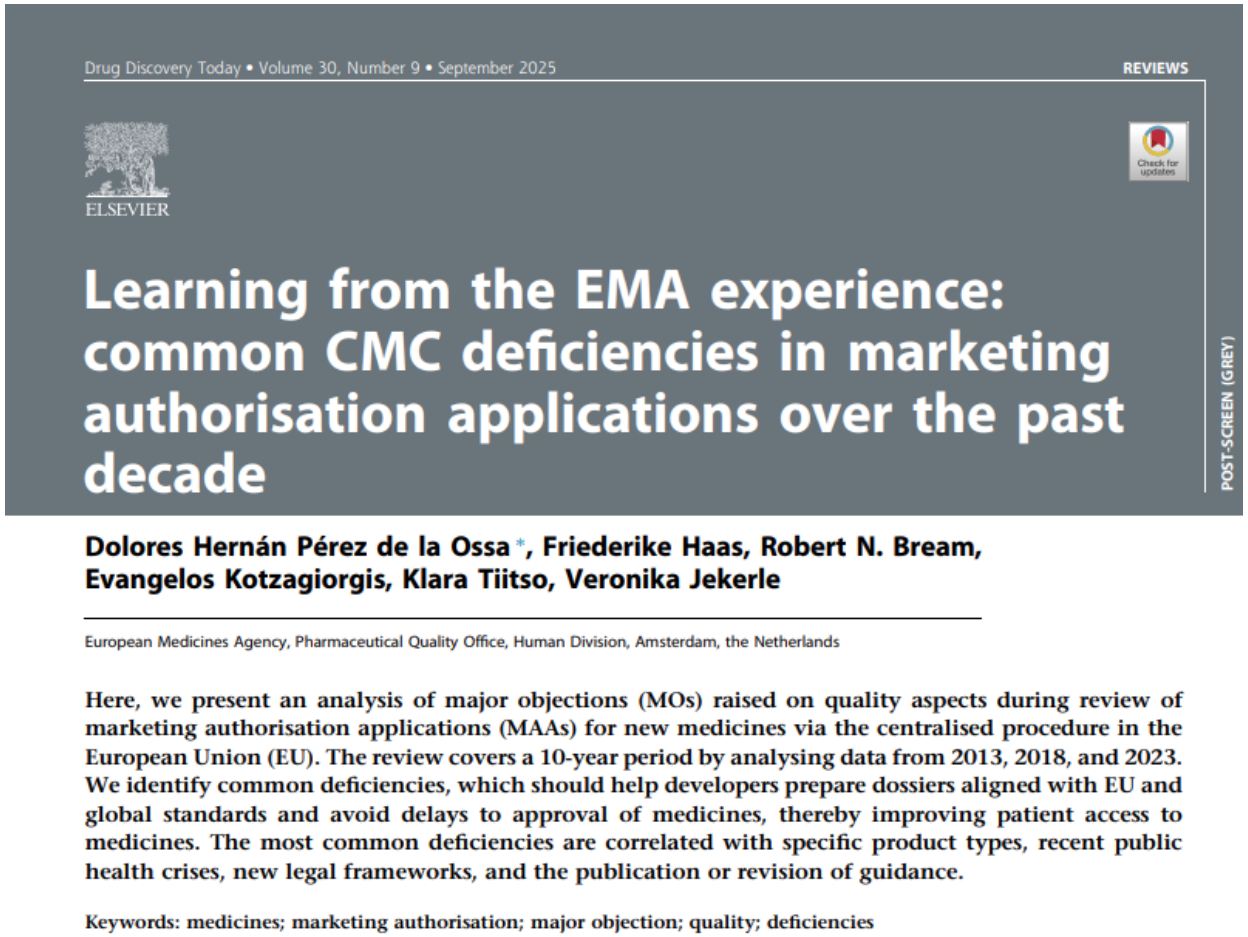
Based on positive results and feedback, pilots have been extended for **1 extra year.**

- A detailed report is now publicly available

Scope includes:

- ✓ High impact changes for medically important treatments
- ✓ Innovative manufacturing technologies
- ✓ PACMPs that impact supply
- ✓ Generics and biosimilars

Publications



Drug Discovery Today • Volume 30, Number 9 • September 2025 REVIEWS

ELSEVIER

POST-SCREEN (GREY)

Learning from the EMA experience: common CMC deficiencies in marketing authorisation applications over the past decade

Dolores Hernán Pérez de la Ossa *, Friederike Haas, Robert N. Bream, Evangelos Kotzagiorgis, Klara Tiitso, Veronika Jekerle

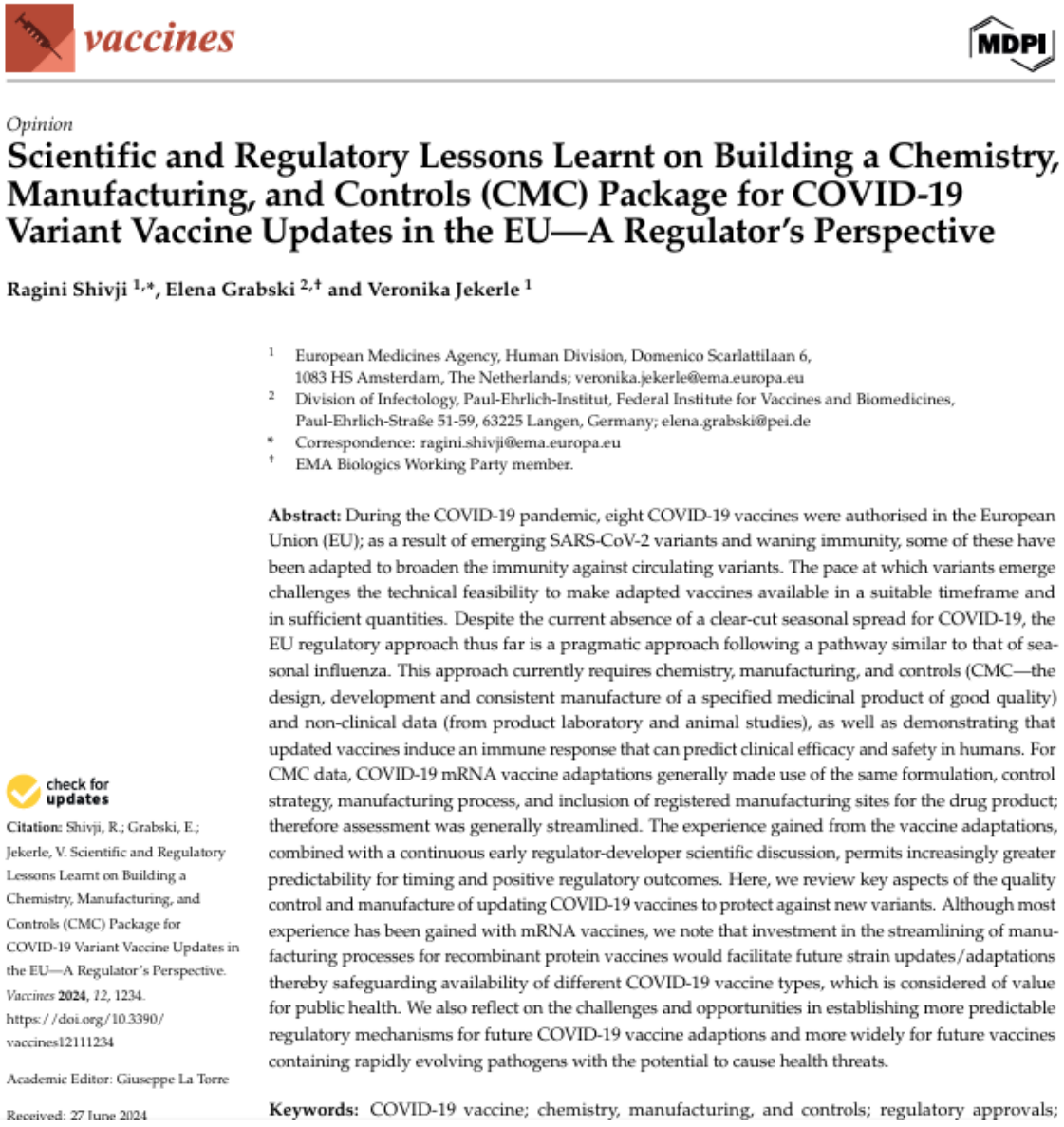
European Medicines Agency, Pharmaceutical Quality Office, Human Division, Amsterdam, the Netherlands

Here, we present an analysis of major objections (MOs) raised on quality aspects during review of marketing authorisation applications (MAAs) for new medicines via the centralised procedure in the European Union (EU). The review covers a 10-year period by analysing data from 2013, 2018, and 2023. We identify common deficiencies, which should help developers prepare dossiers aligned with EU and global standards and avoid delays to approval of medicines, thereby improving patient access to medicines. The most common deficiencies are correlated with specific product types, recent public health crises, new legal frameworks, and the publication or revision of guidance.

Keywords: medicines; marketing authorisation; major objection; quality; deficiencies

- Analysis of major objections (MOs) raised on quality aspects during review of marketing authorisation applications (MAAs) via the centralised procedure.
- 10-year period 2013-2023
- Discusses evolution in types of medicinal product authorised and identifies common deficiencies.
- The most common deficiencies are correlated with specific product types, recent public health crises, new legal frameworks, and the publication or revision of guidance.

Ref: https://www.sciencedirect.com/science/article/pii/S1359644625001576



vaccines

MDPI

Opinion

Scientific and Regulatory Lessons Learnt on Building a Chemistry, Manufacturing, and Controls (CMC) Package for COVID-19 Variant Vaccine Updates in the EU—A Regulator's Perspective

Ragini Shivji [1,*], Elena Grabski [2,†] and Veronika Jekerle [1]

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† EMA Biologics Working Party member.

Abstract: During the COVID-19 pandemic, eight COVID-19 vaccines were authorised in the European Union (EU); as a result of emerging SARS-CoV-2 variants and waning immunity, some of these have been adapted to broaden the immunity against circulating variants. The pace at which variants emerge challenges the technical feasibility to make adapted vaccines available in a suitable timeframe and in sufficient quantities. Despite the current absence of a clear-cut seasonal spread for COVID-19, the EU regulatory approach thus far is a pragmatic approach following a pathway similar to that of seasonal influenza. This approach currently requires chemistry, manufacturing, and controls (CMC—the design, development and consistent manufacture of a specified medicinal product of good quality) and non-clinical data (from product laboratory and animal studies), as well as demonstrating that updated vaccines induce an immune response that can predict clinical efficacy and safety in humans. For CMC data, COVID-19 mRNA vaccine adaptations generally made use of the same formulation, control strategy, manufacturing process, and inclusion of registered manufacturing sites for the drug product; therefore assessment was generally streamlined. The experience gained from the vaccine adaptations, combined with a continuous early regulator-developer scientific discussion, permits increasingly greater predictability for timing and positive regulatory outcomes. Here, we review key aspects of the quality control and manufacture of updating COVID-19 vaccines to protect against new variants. Although most experience has been gained with mRNA vaccines, we note that investment in the streamlining of manufacturing processes for recombinant protein vaccines would facilitate future strain updates/adaptations thereby safeguarding availability of different COVID-19 vaccine types, which is considered of value for public health. We also reflect on the challenges and opportunities in establishing more predictable regulatory mechanisms for future COVID-19 vaccine adaptions and more widely for future vaccines containing rapidly evolving pathogens with the potential to cause health threats.

check for updates

Citation: Shivji, R.; Grabski, E.; Jekerle, V. Scientific and Regulatory Lessons Learnt on Building a Chemistry, Manufacturing, and Controls (CMC) Package for COVID-19 Variant Vaccine Updates in the EU—A Regulator's Perspective. *Vaccines* **2024**, *12*, 1234. https://doi.org/10.3390/vaccines12111234

Academic Editor: Giuseppe La Torre

Received: 27 June 2024

Keywords: COVID-19 vaccine; chemistry, manufacturing, and controls; regulatory approvals;

- Reviews key aspects of the **quality control and manufacture** of updated COVID-19 vaccines to protect against new variants.
- Continuous **early regulator-developer scientific discussion** permits increasingly greater predictability for timing and positive regulatory outcomes.
- Reflects on the **challenges and opportunities** in establishing more predictable regulatory mechanisms for future COVID-19 vaccine adaptions and for future vaccines containing rapidly evolving pathogens with the potential to cause health threats.

Ref: https://pubmed.ncbi.nlm.nih.gov/39591137/

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- Publications

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Thank you

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