Ignite the future - our exciting PAC reliance journey with 48 NRAs

Francesca Mangia, PhD

Associate Regulatory Program Director

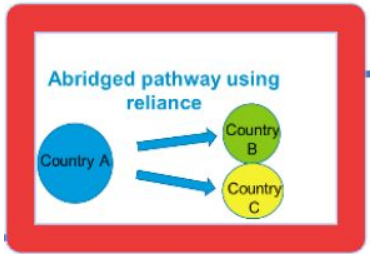
F.Hoffmann-La Roche Ltd

Roche Post-Approval Change Reliance Pilot

Major drug substance process change for mAb

Supply critical variation

- EMA - reference agency
- Unilateral reliance



- Reducing the global approval and implementation timelines for a Major DS Process change

  from 2.5 YEARS to 6.5 MONTHS to ensure the continuous supply to patients

  - **Reduce country specific requirements**

- Enhance greater **transparency** to NRAs by sharing EMA assessment report and Q&A

Pilot's Layout & Participation Criteria

One Standard Dossier

EU dossier submitted to all countries

Q&A Document

EU questions and Roche's responses document will be shared with the participating NRAs

EU Assessment Report

EU assessment report will be shared with NRAs

No Country Specific Requirements

Avoid submission of country specific requirements when justified by scientific rationale

No Testing

According to EU, for this type of change, no testing required

One Timeline for All

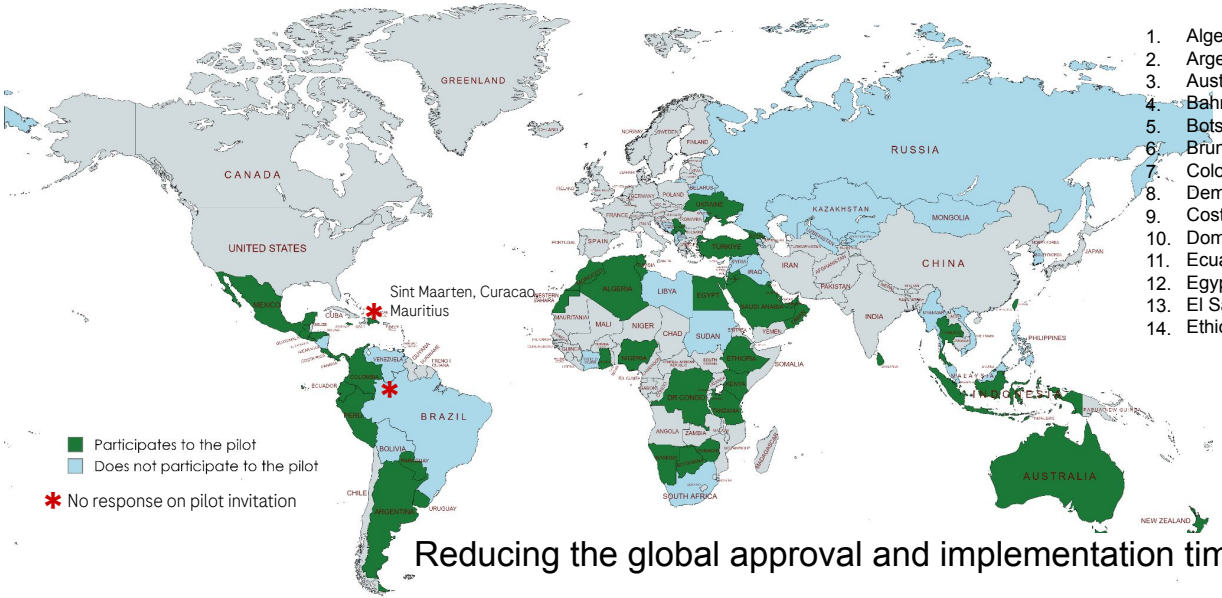
Same dossier and Q&A review timelines for all participating NRAs

Roche PAC Reliance Pilot - Participating Countries

84 COUNTRIES IMPACTED BY THE CHANGE

48 COUNTRIES AGREED to participate in the pilot

57%
Acceptance Rate

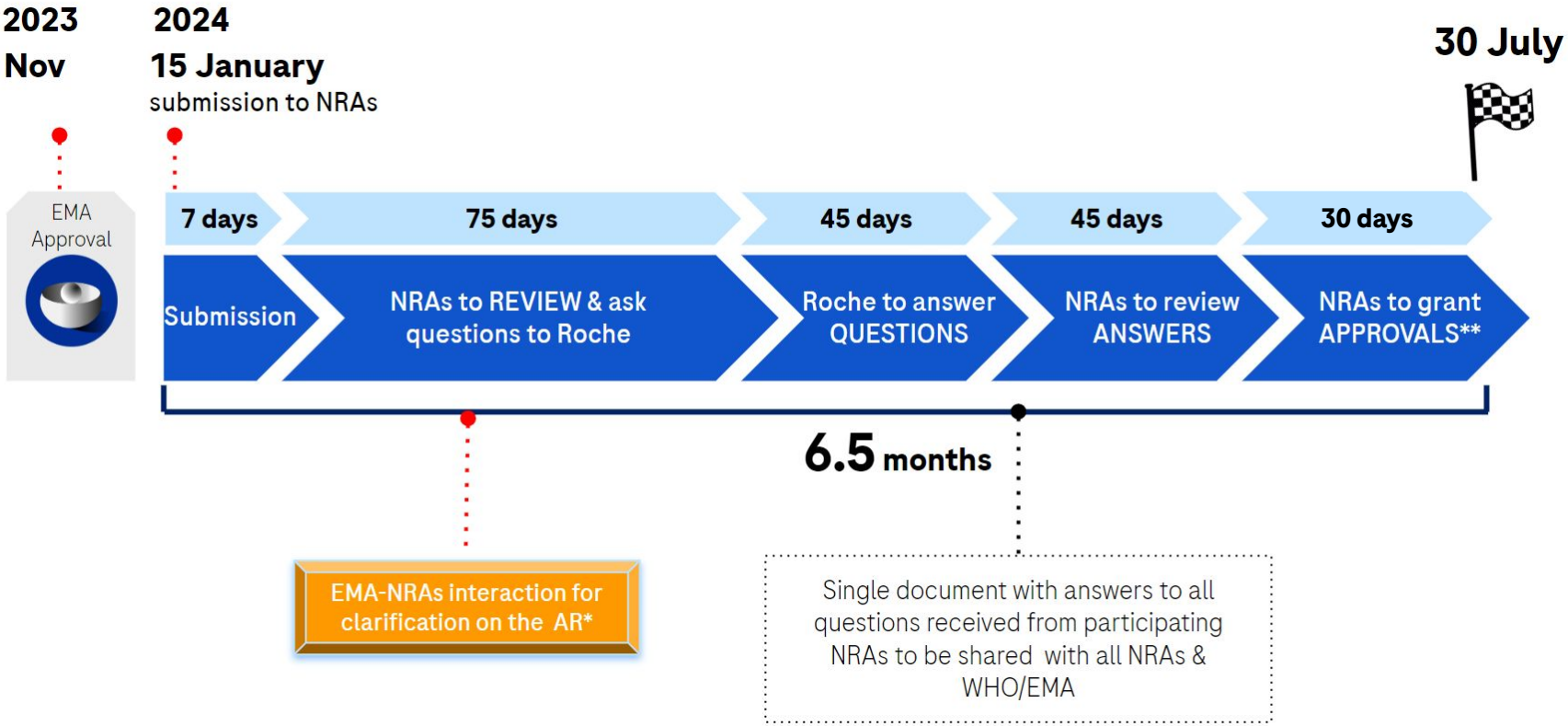


1. Algeria
2. Argentina
3. Australia
4. Bahrain
5. Botswana
6. Brunei
7. Colombia
8. Dem. Rep. of Congo
9. Costa Rica
10. Dominican Republic
11. Ecuador
12. Egypt
13. El Salvador
14. Ethiopia
15. Georgia
16. Ghana
17. Guatemala
18. Honduras
19. Indonesia
20. Israel
21. Jamaica
22. Jordan
23. Kenya
24. Kuwait
25. Mexico
26. Montenegro
27. Morocco
28. Namibia
29. New Zealand
30. Nigeria
31. Oman
32. Panama
33. Paraguay
34. Peru
35. Qatar
36. Saudi Arabia
37. Serbia
38. Sri Lanka
39. Taiwan
40. Tanzania
41. Thailand
42. Trinidad and Tobago
43. Tunisia
44. Türkiye
45. Ukraine
46. United Arab Emirates
47. Uruguay
48. Zimbabwe

Reducing the global approval and implementation timelines

From 2.5 YEARS to 6.5 MONTHS to ensure continuous supply to patients

Highlights and Timelines



*Assessment Report
**If approval not granted NRA should share rationale for refusal

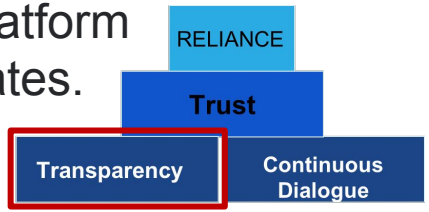
Handling potential Questions & Answers transparently

Q & A were shared via a Accumulus Synergy Accumulus synergy

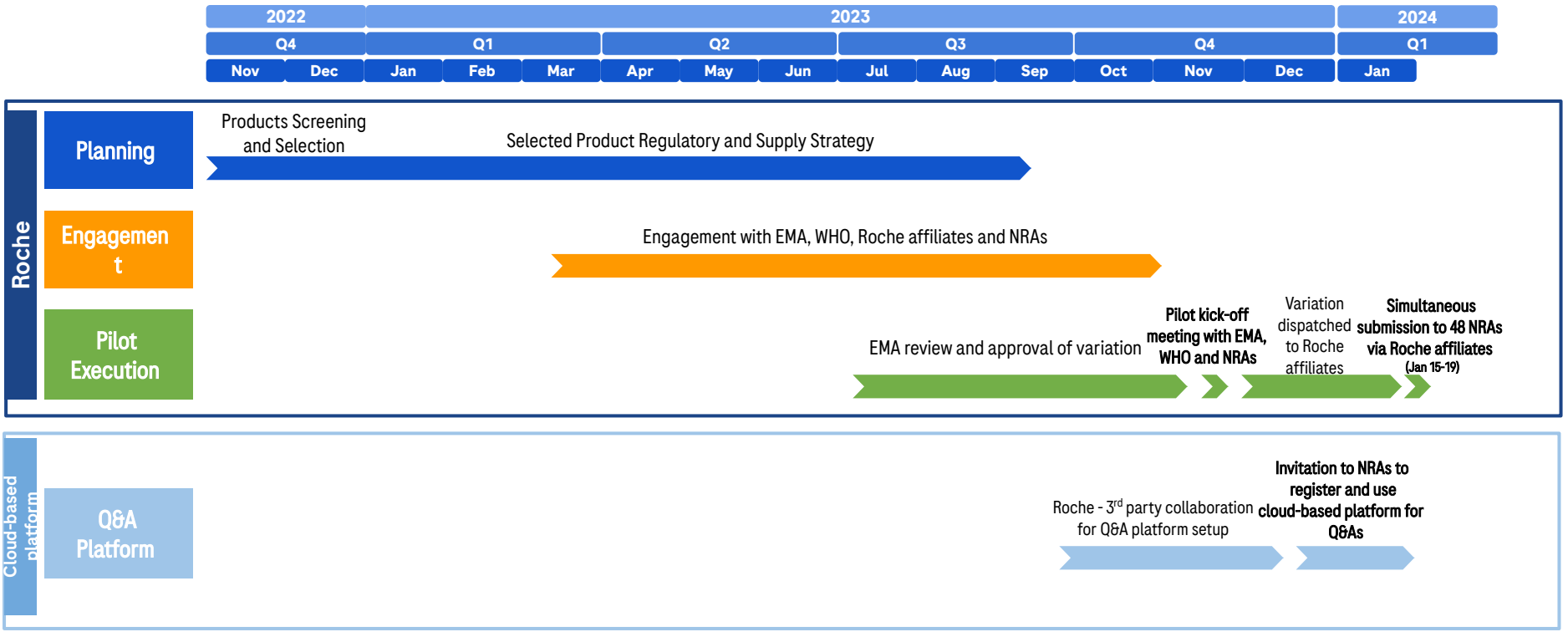
Roche

- **A first-of-its-kind, cloud-based data and information exchange platform** supporting regulatory interactions between Life Sciences Organizations and Global Health Authorities
- This tool is a proposal for **greater visibility and transparency**. All participating NRAs were able to see the questions real-time from other NRAs

Each NRA could choose whether to use the Accumulus Q&A platform or issue Q&As following its standard process via Roche affiliates.



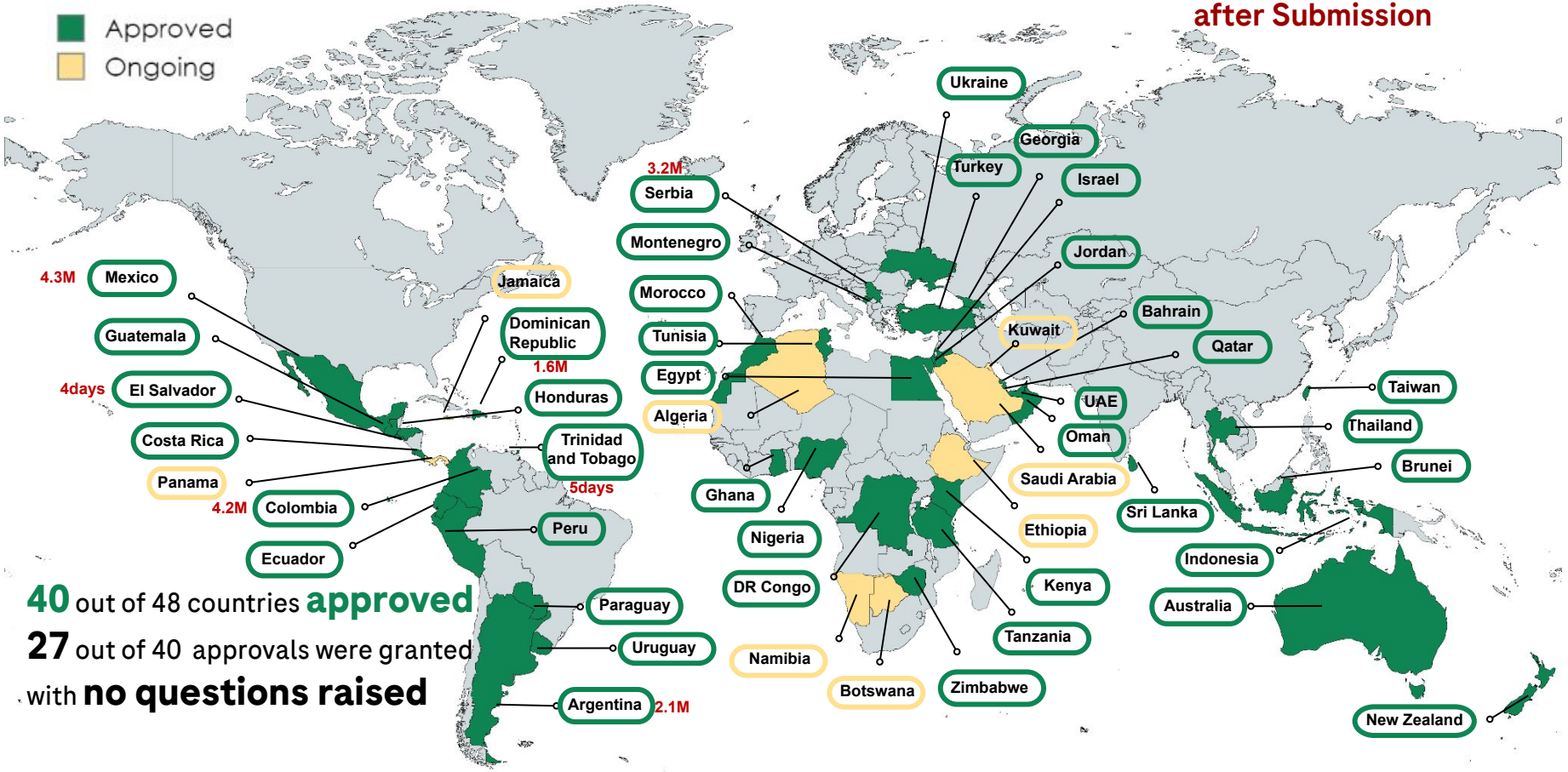
Roche PAC Reliance Pilot Journey



Current Status (as of August, 7th '24) - Approvals

83%

Approvals 6.5M after Submission



- **40** out of 48 countries **approved**
- **27** out of 40 approvals were granted with **no questions raised**

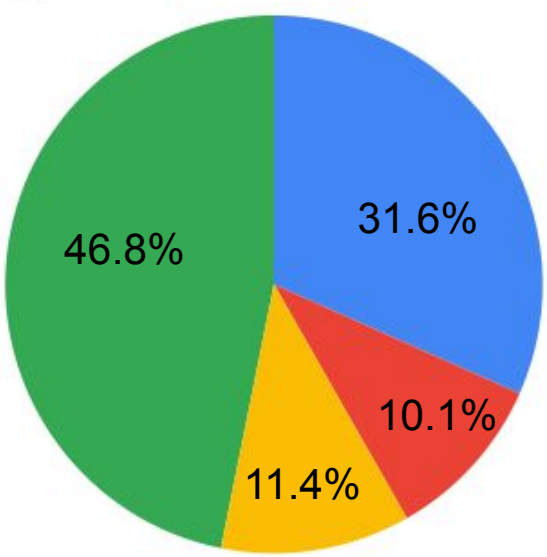
Current Status - Overview of Questions Received

14 COUNTRIES issued questions

85 Total **QUESTIONS**

Questions Categories

Technical
Clarifying
Country Specific Document
Administrative



Success Factors

Transparency and Dialogue: same variation package as EMA, EMA's Q&As and unredacted assessment report

Support from EMA and WHO, strong advocates for reliance around the globe

Choice of product and supply critical variation: This medicine is used for treating life-threatening diseases and involves a major supply-critical variation with high public health and business impact.

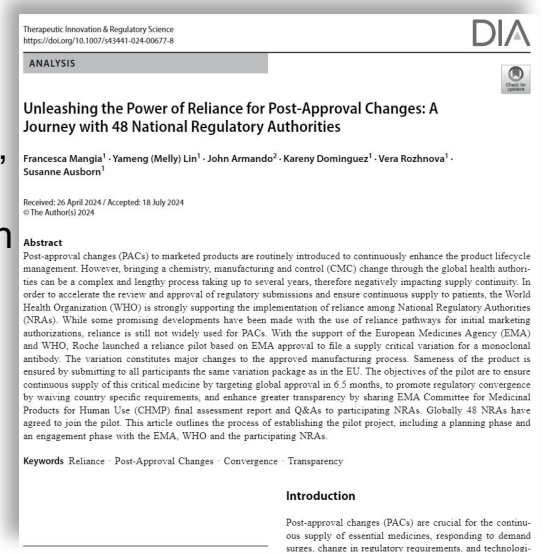
Overall product strategy, especially the impact of the pilot on change implementation, should be continuously and carefully assessed.

Regulatory affiliates of each participating company, which operate in the countries impacted by this variation, play a crucial role as the primary contact with their respective NRAs.

Conclusion

- **57% participation rate** → Strong interest and willingness of many NRAs across the globe to bring reliance into action for PACs
- **83%** of NRAs **approved in 6.5 months**
- **Transparency** is key in building trust with regulators
- Applying reliance throughout the lifecycle of the product, including PACs, represents a contribution towards global convergence and harmonization

*You want to know more about the Roche PAC Reliance Pilot? Check out our latest **publication on TIRS** (LINK)!*



Therapeutic Innovation & Regulatory Science
https://doi.org/10.1007/s43441-024-00677-8

DIA

ANALYSIS

Unleashing the Power of Reliance for Post-Approval Changes: A Journey with 48 National Regulatory Authorities

Francesca Mangia[1] · Yameng (Melly) Lin[1] · John Armando[2] · Kareny Dominguez[1] · Vera Rozhnova[1] · Susanne Ausborn[1]

Received: 26 April 2024 / Accepted: 18 July 2024
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Abstract

Post-approval changes (PACs) to marketed products are routinely introduced to continuously enhance the product lifecycle management. However, bringing a chemistry, manufacturing and control (CMC) change through the global health authorities can be a complex and lengthy process taking up to several years, therefore negatively impacting supply continuity. In order to accelerate the review and approval of regulatory submissions and ensure continuous supply to patients, the World Health Organization (WHO) is strongly supporting the implementation of reliance among National Regulatory Authorities (NRAs). While some promising developments have been made with the use of reliance pathways for initial marketing authorizations, reliance is still not widely used for PACs. With the support of the European Medicines Agency (EMA) and WHO, Roche launched a reliance pilot based on EMA approval to file a supply critical variation for a monoclonal antibody. The variation constitutes major changes to the approved manufacturing process. Sameness of the product is ensured by submitting to all participants the same variation package as in the EU. The objectives of the pilot are to ensure continuous supply of this critical medicine by targeting global approval in 6.5 months, to promote regulatory convergence by waiving country specific requirements, and enhance greater transparency by sharing EMA Committee for Medicinal Products for Human Use (CHMP) final assessment report and Q&As to participating NRAs. Globally 48 NRAs have agreed to join the pilot. This article outlines the process of establishing the pilot project, including a planning phase and an engagement phase with the EMA, WHO and the participating NRAs.

Keywords Reliance · Post-Approval Changes · Convergence · Transparency

Introduction

Post-approval changes (PACs) are crucial for the continuous supply of essential medicines, responding to demand surges, change in regulatory requirements, and technologi-









Thank you!