EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Reliance for post-authorisation changes (PACs)

Mid-pilot review

An agency of the European Union

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Foreword

Regulatory reliance is widely used by many authorities and is frequently discussed in the context of initial authorisations where it can support earlier patient access to medicines. However, it is equally important for lifecycle management which represents a significant share of regulatory workload.

With this in mind, the European Medicines Agency together with the World Health Organization (WHO) and pharmaceutical industry, launched a pilot to improve efficiency, convergence and predictability for PACs. The pilot enables National Regulatory Authorities (NRAs) to access EMA assessments and receive aligned documentation packages through simultaneous submissions. PACs are critical for maintaining safety, manufacturing quality, and continuous improvement, but their implementation is often slowed by fragmented global regulatory requirements, lengthy timelines and uneven digital maturity. This pilot offers a practical, structured approach to address these challenges while preserving independent national decision-making.

Progress and early results

As of July 2026, 48 pilots have been initiated with EMA as a reference authority. Most pilots have focused on quality changes with potential supply impact, while a limited number of clinical variations included extension of indications or safety updates.

As committed at the outset, a mid-pilot review was conducted using the data available at the end of 2025 which covered nine finalised and eight ongoing pilots and responses from 26 NRAs surveyed on their experience; in addition, insights were discussed in a workshop with participating companies, and a regulators-only workshop. The recommendations outlined in this report are intended to support ongoing and future pilots and inform regulatory discussions, helping assess the potential transition from pilot schemes to established routine practice.

This mid-pilot review shows:

- broad international participation;
- faster approval;
- lower NRA workload and resource savings;
- high trust in EMA assessment reports;
- convergence of submission requirements;
- greater predictability, reducing shortage risks.

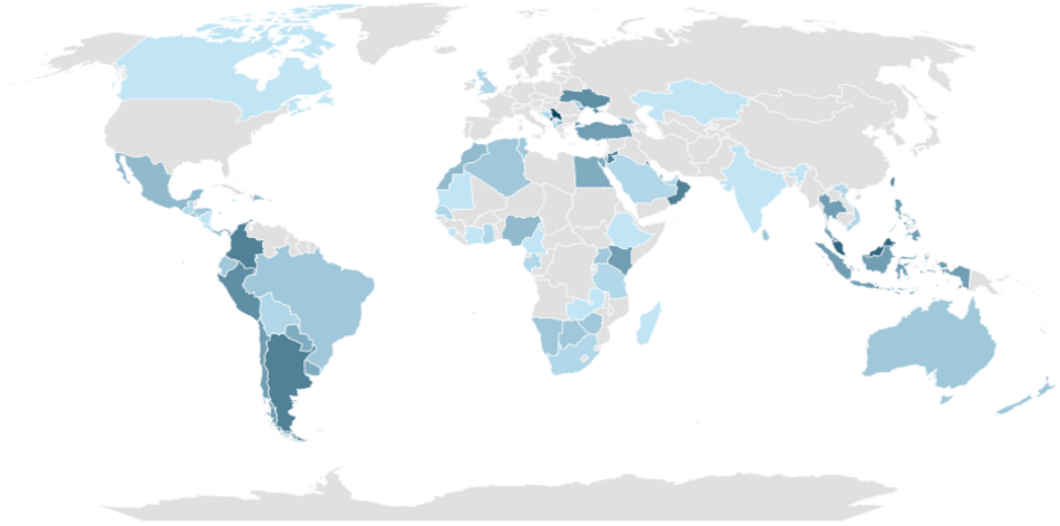
Global participation and engagement

Global engagement was strong, with 77 NRAs participating in one or more pilots by the end of 2025:

- Participating NRAs represented a wide range of regulatory maturity levels across multiple regions (Latin and North America, Africa, Asia-Pacific, Eastern Europe) reflecting broad global interest.
- Participation varied per pilot, ranging from 4 to 48 NRAs.
- Engagement across pilots was uneven: 36 NRAs declined to join, 24 NRAs always accepted participation and 53 NRAs accepting some pilot invitations but not all. This variability reflects different considerations (e.g. existing local reliance pathways, legal or policy constraints, available resources).

Overall, the pilots demonstrate global feasibility and interest, however the inconsistent participation points to the need for more targeted, data-driven advocacy and implementation support.

Figure 1: participating countries overview



Colours represent the level of engagement, with darker blue indicating higher participation and lighter blue indicating lower participation. Grey areas indicate no participating countries or no data available at the time of analysis.

Approval timelines

Applicants and regulators reported faster review and approval timelines, particularly for complex variations.

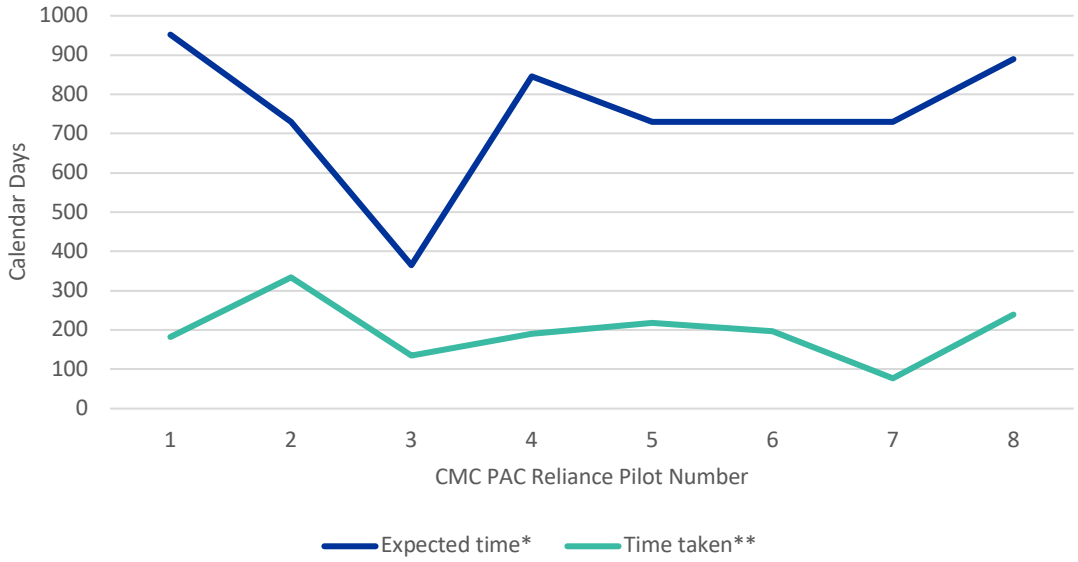
For the CMC pilots, applicants reported 80% of participating relying NRAs granted approvals in less than half of the expected overall approval time when not using reliance.

Nearly 80% of NRAs also reported faster review and approval timelines compared with standard national procedures, enabled by:

- use of EMA assessment reports as the primary scientific basis;
- elimination of duplicate questions already resolved at EU level;
- more predictable, near-concurrent submissions across countries.

The feedback on timelines from both the industry and NRAs is presented below.

Figure 2: feedback on PAC pilot timelines from industry.

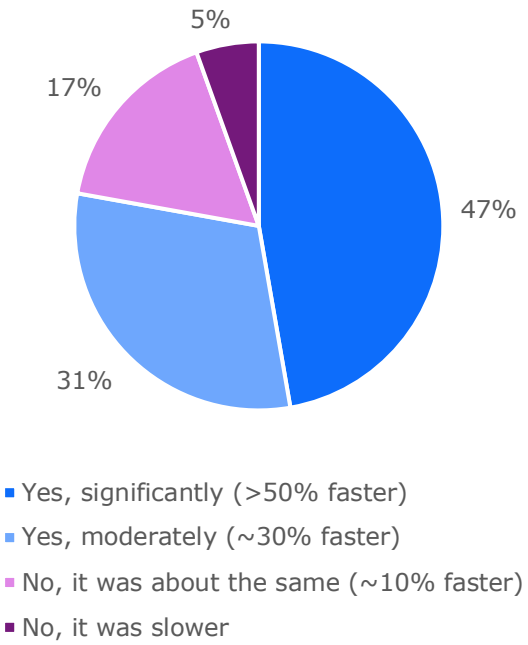


* Based on applicant experience - to receive all participating NRA approvals without the use of reliance.

** Time taken to get 80% approvals from participating NRAs

Figure 3: feedback on PAC pilot timelines from NRAs.

Question: Do you believe the pilot helped to accelerate review and approval timelines for this post-authorisation change compared to your standard process for similar changes without reliance?



Some regulatory authorities noted that reliance could help reduce variation backlogs, and several NRAs prioritised assessment of these PAC variations over their existing backlogs, but others mentioned files are still processed in 'first-in, first-out' queues limiting prioritisation even when reliance is used.

Resource savings

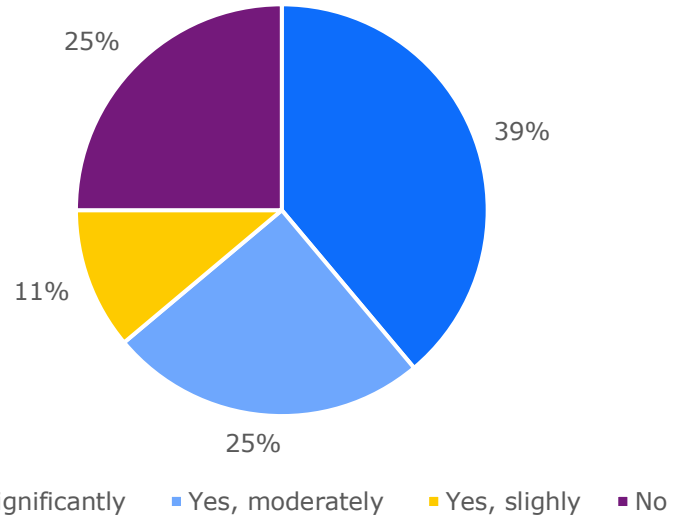
Applicants and regulators experienced efficiency gains through access to EMA assessment reports and reduction in questions.

Reliance allowed NRAs to use resources more strategically while building capacity. 75% of NRAs reported saving resources as access to EMA ARs reduced duplication of work and the need to ask questions. In about half of the pilots, an optional online collaboration platform was used.

Some NRAs reported initial additional effort (meetings, coordination) but noted this would proportionally decrease as familiarity with this reliance process increases.

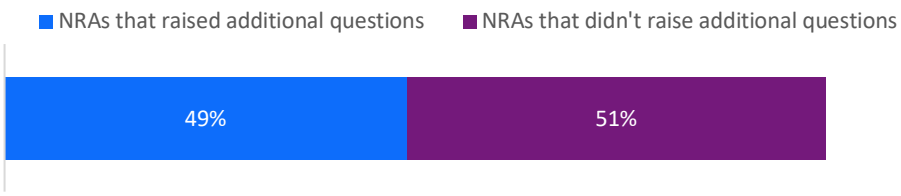
Figure 4: feedback from NRAs on resource saving.

Question: Did participation in this pilot result in any potential resource savings for your NRA (such as reduced staff time or a decreased need for human resources)?



Level of reliance was measured by applicants by the additional questions raised by NRAs, which were fewer than anticipated and mostly focused on understanding complex CMC variations and local requirements. These findings also point towards convergence in assessment, while supporting capacity-building.

Figure 5: feedback from industry on the number of questions raised during the PAC pilots.

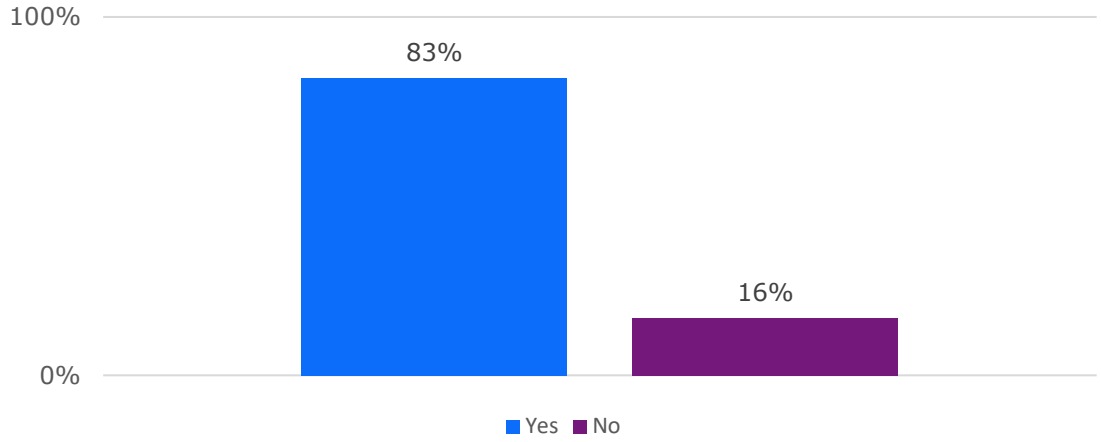


Reliance models

NRAs applied different approaches to reliance depending on their regulatory context, experience and available resources. Trust in EMA documentation was high: 83% of NRAs found EMA assessment reports sufficiently detailed to support their national decision making.

Figure 6: feedback from NRAs on usefulness of EMA assessment reports.

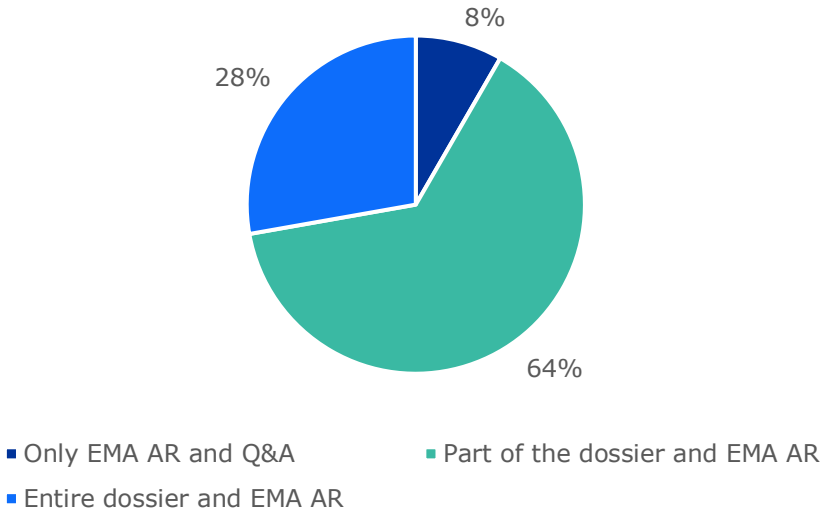
Question: Did you find EMA's Committee for Medicinal Products for Human Use (CHMP) assessment report and approval letter sufficiently detailed to inform your own decision-making process?



Most NRAs generally relied on EMA assessment reports as the main scientific basis, while still doing a verification and country specific checks rather than a full independent assessment. However, some NRAs still requested more specific information and reviewed the entire dossier with the EMA assessment reports.

Figure 7: feedback from NRAs on review conducted.

Question: How did you conduct the review in this reliance pilot? Please describe the data reviewed.



Convergence of requirements

The impact of reliance depended on how it was implemented in practice.

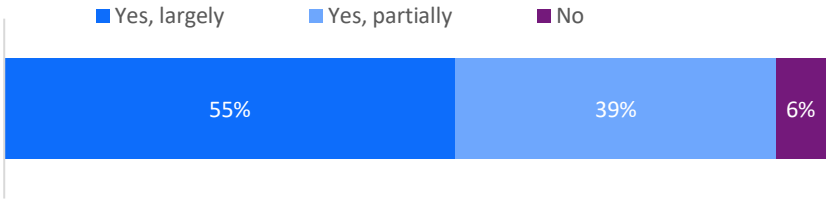
Across pilots, applicants submitted a core data package with aligned changes reflected in the common technical document (CTD) dossier available to all NRAs, including EMA assessment report, approval (for type II variations)/notification (for type IB variations) and highlighting any dossier differences.

Common data packages were used across NRAs, and reliance was applied even when NRAs operated under different classification frameworks.

Full harmonisation is not easy, but reliance can significantly reduce fragmentation, by enabling authorities to align more closely around a shared scientific assessment. In some pilots, NRAs accepted to waive specific countries requirements (e.g. administrative declarations, additional batch data, batch records, chromatograms…) enabling more convergence.

Figure 8: feedback from NRAs on dossier convergence.

Question: Did your NRA find it feasible to align country-specific requirements to EMA?

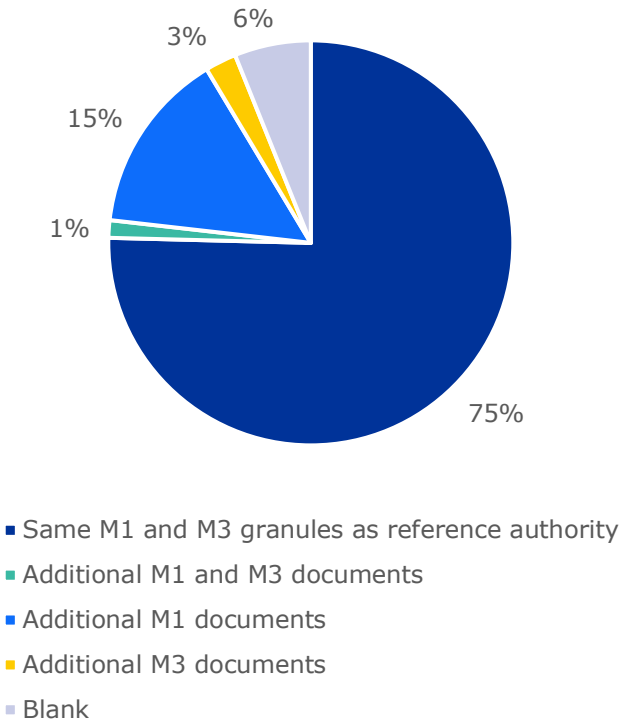


NRAs described successes and challenges encountered in aligning requirements as follows:

- **Successes encountered by NRAs when aligning requirements:**
    - existing national requirements already aligned with EMA requirements;
    - acceptance of alternative documents in place of national requirements;
    - risk based approach to waive national documentation.
- **Challenges encountered by NRAs when aligning requirements:**
    - legal constraints requiring additional documentation;
    - insufficient internal capacity/expertise to adapt documentation;
    - other challenges, including ensuring the product is the same.

In most cases, NRAs could align with EMA/Reference country requirements and accept a single core data package as shown below.

Figure 9: feedback from industry on dossier convergence.



Additional documentation requests – beyond core data package (CTD dossier).

EMA, WHO and industry will continue monitoring and evaluating the pilot data, with a further analysis planned based on the evidence available at the end of 2026. In the meantime, NRAs and industry are encouraged to focus on the specific recommendation in the following two sections.

Recommendations for NRAs

1. **Strengthen predictability and convergence.**
    1.1. Formalise reliance pathways and designate reliance focal points for the NRA, where possible.
    1.2. Promote greater convergence of requirements while maintaining appropriate flexibility.
2. **Build capacity.**
    2.1. Develop practical reliance guidance for assessors and industry.
    2.2. Strengthen peer-to-peer learning and knowledge exchange.
3. **Maximise efficiency and measure impact.**
    3.1. Make greater use of EMA assessment reports and scientific opinions to streamline decision-making, shorten timelines, and reduce workload.
    3.2. Systematically collect evidence to demonstrate and monitor the impact of reliance approaches.
4. **Efficient tracking system and predictable timelines.**
    4.1. Ensure that reliance variations are monitored under a fast-track process where possible, potentially considering two variation processes/queues (standard versus reliance).
    4.2. Planned for defined timelines for variation when reliance is used for the evaluation.

For more information, see the meeting report 'Regulators-Only Workshop on Reliance for Post-Approval Changes (PACs)' available in the EMA website at Reliance for post-authorisation changes: pilots for the pharmaceutical industry.

Recommendations for industry

1. **Promote convergence and build capacity.**
    1.1. Use a standardised core variation package, ensuring dossier transparency and highlighting any differences compared to the reference dossier.
    1.2. Participate in reliance implementation workshops.
    1.3. Provide comments to WHO/national PACs guidelines and promote use of ICH Q12 (e.g PACMPs).
2. **Raise awareness on reliance pilot benefits.**
    2.1. Share outcome of CMC and clinical PACs pilots in conferences and through trade associations.
    2.2. Promote implementation of reliance by companies (through use of unilateral, regional, collaborative pathways and multi-NRA pilots).
3. **Maximise efficiency and measure impact.**
    3.1. Continue to explore use of digital technology to streamline process.
    3.2. Continue to collect evidence to demonstrate and monitor the impact of reliance approaches on efficiencies and approvals.
    3.3. Optimise process and transition to sustainable routine practice.

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