Global Multi-Regulator Post-Approval Chemistry, Manufacturing, and Controls (CMC) Collaborative Assessment Cloud Solution

Market Consultation

November 4, 2024

This Market Consultation Request for Information (RFI) is issued by International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use– hereafter referred to as “ICH”. You are requested to submit a reply based on the following outlined information contained in this document.

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1.0 GENERAL INFORMATION

The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use– hereafter referred to as "ICH", is issuing this Request for Information (RFI) as a means of conducting a market consultation. This is a REQUEST FOR INFORMATION ONLY to obtain market consultation, not a Request for Proposal (RFP) and does not commit ICH to award a contract now or in the future. The purpose of this RFI is to obtain market feedback, input, and recommendations to support a more considered product for the recommended approach to implement a scalable technology solution that facilitates secure global multi-regulatory collaborative assessments. It is anticipated that if implemented, the resulting solution would create a global, secure collaborative platform for regulatory authorities which may prospectively facilitate a collaborative assessment process including interactions with sponsors. Submission of any information in response to this market consultation is purely voluntary and ICH welcomes responses from all interested parties; ICH assumes no financial responsibility for any costs incurred.

1.1 Terms & Conditions

1.1.1 Confidentiality

All material and information you share or supply in response to this RFI will remain the property of ICH. Your response will be reviewed by ICH and representatives of ICH members and observers.

By responding to this RFI, you agree that the ICH and representatives of ICH members and observers will use your information for these purposes. Please be aware that response may result in the transfer of your information to countries outside of your country of residence. These countries may have different data protection regulations compared to your country. You may withdraw your information at any time by contacting us as outlined in our privacy statement, which governs the use of your information. By providing your information, you confirm that you have read, understood, and agree to these terms.

1.1.2 Contractual Obligations

The RFI does not constitute a contractual offer by ICH capable of acceptance by respondents, nor does it create an obligation on the part of ICH to purchase services, products or equipment from any respondents submitting any information. Additionally, the ICH does not intend to hold discussions concerning this RFI with any interested parties. However, ICH reserves the right to contact respondents if additional information is required.

1.1.3 General

ICH reserves the right to withdraw or amend this RFI at any time. While this RFI is carried out under the auspices of ICH, no decision has been taken as to the governing body of a PQKM system, should one be established.

1.1.4 Disclaimer

The ICH will not reimburse respondents for any costs associated with information submitted in response to the RFI. Responders are solely responsible for all expenses associated with responding to this RFI. Responses to this RFI are not quotes and cannot be accepted by the ICH for the basis of forming a binding contract. This RFI is being issued solely for the purpose of gathering information for planning purposes. This RFI does not commit the ICH to a contract for

any supply or service. Furthermore, the ICH is not at this time seeking quotes and will not accept unsolicited quotes.

Interested parties are encouraged to respond to this RFI. If the scope of this RFI is too large or there are aspects to which your company/entity does not wish to provide a response, please feel free to provide partial/limited feedback in the areas of your specific expertise. ICH hopes to receive information from all interested parties on any aspects of this RFI that could be of benefit to the ICH. Respondents to this RFI may be requested to provide additional information/details based on their initial submittals. Respondents who submit information in response to this RFI do so with the understanding that ICH and representatives of ICH members and observers may review their materials and or data.

2.0 INSTRUCTIONS

2.1 ICH RFI Details

All correspondence regarding this RFI must be addressed to the primary contact using the email address: PQKMtaskforce@ich.org. Telephone inquiries will NOT be addressed and shall NOT contain proprietary or classified information.

2.2 Response Guidelines

- 25-pages max limit (including cover page, appendix/attachments, and references)
- Submit in *one document* electronic format (25 MB limitation on e-mail applies).
- Microsoft Office or PDF format to be used.
- Please use Times New Roman font size 12 for text and font size 10 for graphics.
- Please use 1-inch margins.
- Please provide your response to the questions in Section 6.0 below.
- If you have any questions about the information in this RFI please use the attached questions template in attachment A. Please email your questions using the question template via email attachment by 4 December 2024, to the email PQKMtaskforce@ich.org.
    - Answers to all questions will be addressed to the best of our ability during the respondent information session currently planned to be held on 18 December 2024. Please note this respondent information session will **not** be recorded.
    - Any response provided to questions asked by respondents represents current thinking of the PQKM task force on that topic. It does not establish any rights for any person and is not binding on ICH or the PQKM task force.
    - Respondents understand they will not get paid or reimbursed for participation in this market consultation and respondent information session held on 18 December 2024.

Final responses should be emailed by 2:00 PM EST on 08 January 2025, if not sooner to: PQKMtaskforce@ich.org.

2.3 Key Dates

- RFI Release Date: 25 November 2024
- Submission of intent to respond: 04 December 2024 2:00 PM EST
- Questions due to ICH: 04 December 2024 2:00 PM EST
- Respondent Information Session: 18 December 2024
- RFI Submissions Due Date: 08 January 2025 2:00 PM EST

3.0 BACKGROUND

ICH partnered with the International Coalition of Medicines Regulatory Authorities (ICMRA), International Pharmaceutical Regulators Programme (IPRP), and Pharmaceutical Inspection Co-operation Scheme (PIC/S) to develop a vision for building the data infrastructure to support a global regulatory Pharmaceutical Quality Knowledge Management (PQKM) capability to ultimately enable better availability of high-quality medicines. The shared vision of the four organizations for the development of this global capability was outlined in a Joint Reflection Paper.

Within the joint reflection paper, these organizations committed to developing a multi-year work plan. This work plan identifies specific harmonization or convergence projects that the four organizations will undertake in a coordinated and prioritized manner, focusing on work to be initiated in the annual period 2023 to 2027.

Additionally, ICH develops and publishes international guidelines that seek to harmonize technical and scientific requirements for pharmaceutical registration. More detailed information on these efforts relevant to PQKM are linked below:

- ICH M8 eCTD v.4.0
- ICH M8 Expert Working Group (EWG)/ Implementation Working Group (IWG)
- ICH M4Q(R2) EWG
- Future ICH Guideline on Structured Product Quality Submissions (SPQS) mentioned in the PQKM work plan and M4Q(R2) Concept Paper
- ICH Q10
- ICH Q12
- Medical Dictionary for Regulatory Activities (MedDRA)

In support of this harmonization work, ICH agreed to establish the PQKM task force aimed at understanding the foundation needed to establish and govern a secure standardized technology platform for PQKM. The PQKM work is focused on Post Approval Chemistry, Manufacturing and Controls (CMCs) submissions due to the similarities in global regulatory requirements for CMC and quality submissions and relevance to urgent drug supply chain needs. More information around the creation and background of the PQKM task force can be found here.

4.0 NOTIONAL VISION AND PHASED APPROACH

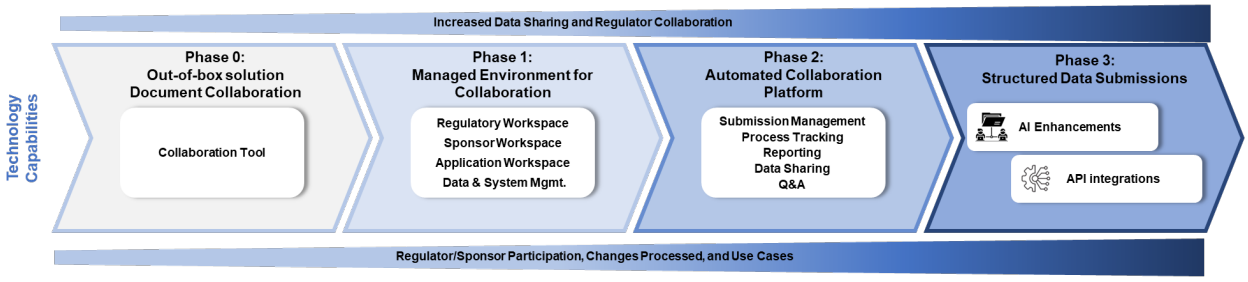
The ultimate vision is to develop a global PQKM solution that can support collaboration between regulatory authorities and sponsors. It is anticipated that the solution will drive improvements in the form of productivity gains through process efficiencies, facilitating information sharing among regulators, promoting better pharmaceutical quality management by sponsors, thus reducing the risk of drug shortages, and improving access to quality medicine for patients globally. The scope is post-approval CMC submissions with potential scalability to other regulatory activities and use cases.

The PQKM task force assumes this solution will be implemented in phases. Under all phases, it should be assumed that the solution will support collaborative assessments in line with current laws and regulations in the regions of the regulatory authorities of the PQKM governing body.

The solution is assumed to align with the following principles:

- Scale to support a larger and more diverse set of sponsor submitters and regulatory authorities who will engage in international regulator collaboration beyond the initial PQKM scope, which may require more robust and scalable technology.
- Follow state-of-the art security practices and leverage advanced technology capabilities.
- Be compliant with constantly evolving relevant regulatory changes in different regions of the PQKM governing body and incorporate process improvements.
- The solution will be able to store assessment results in support of data sharing agreements.
- Enable increasing global regulator participation to support international collaboration.
- Support potential solution shift from document submission to data submission.
- Ensure that data security is compliant with the relevant laws and regulations in the regions of the PQKM governing body and is consistent with increases in data sensitivity (e.g., intellectual property or personal data) that may come with expanded use cases.

The PQKM task force expects the PQKM scope to be implemented in a phased approach. This could include the implementation and evolution of technology capabilities in alignment with the scope expansion and harmonization capabilities improvements. This notional phased approach is visualized below in Figure 1.



	Phase 0	Phase 1	Phase 2	Phase 3
Process Scope	• Post Approval CMC – High public health value submission • Pilot Participants	• Post Approval CMC – Expanded Scope • Public Health Emergency Collaboration • Incremental expansion to other Members	• Expansion to use cases beyond PQKM • Collaborative Hybrid Inspection Pilot (C.H.I.P.) Inspections • Incremental expansion to health regulators and sponsors	• Further harmonization of technical standards and business processes
Harmonization Capabilities	• ICH Q10 • ICH Q12 • Point-to-point NDA/CC • Sponsor Authorization Letter • One Recommended Timeline	• Solution Specific MoU • Terms & Conditions for the solution • M4Q(R1)	• ECTD common standard adopted • SPQS • M4Q(R2)	• Continued convergence of regulatory practices

*The evolution from phase to phase will be determined and guided by direction of the participating regulatory authorities.

Figure 1: Notional Phased Approach to achieve PQKM Vision

Phase zero above refers to the current state with incremental improvements that are underway. The current solution is based in a collaborative file sharing tool with manual integration to legacy regulator's environments and managed in a decentralized way. While this supports the current process and activities, it is understood that this may not be scalable for a global solution.

The first phase could consist of centralizing the phase zero pilot process under a governing body (to be determined), standardizing the provisioning and use of these tools, establishing formal governance and technical capabilities, and centralizing harmonization efforts into a 'Business Operation' function.

The second phase could see the adoption of new harmonization capabilities and more robust technology through quality submission management, process tracking, reporting, improved data sharing by incorporating ICH requirements such as M4Q(R2) and potentially SPQS.

Once established, advanced technology, such as automation via Artificial Intelligence (AI), could be introduced to help reduce time and improve quality within the system as the solution moves into further phases of maturity and extended use. The evolution from phase to phase will be determined and guided by direction of the participating regulatory authorities.

5.0 OVERVIEW OF SOLUTION COMPONENTS

The PQKM task force identified 3 key components for the technical solution which are business process, capabilities, and governance. This section provides more information about each.

5.1 Business Process

The PQKM task force identified enhanced opportunities for technology enablement and global transparency by leveraging existing processes used by previous pilot efforts, in particular those conducted under the ICMRA PQKM strategic initiative. The ICH PQKM task force has developed a notional global regulatory submission collaboration process to illustrate the potential future workflow of post approval CMC submissions, with identical parallel submissions to each of the participating regional regulatory authorities' local systems. All communications between regulators and sponsors could be managed through the envisioned technology solution, providing a single place to assess and support a collaborative, flexible management environment. A technology-enabled solution could support a streamlined process to make sure that regulators are able to collaborate on an equivalent workflow.

The high-level Phase 1 notional process is depicted in the Appendix. (*Figure 4 High-level overview of a Phase 1 collaborative review process flow*).

5.1.1 Personas

There are three primary user roles depicted in the process and are described below. Additional administrative roles may be included as well.

Sponsor: The sponsor initiates the submission with the regional regulatory authorities' legacy systems and then also submits the necessary files to the PQKM global solution authorizing their information to be shared amongst the regulators involved in the collaborative assessment.

Lead Regulator: The Lead Regulator of the collaborative assessment of the PQKM submission is responsible for managing the submission milestones and consolidating all questions (information requests) from all the participating regulatory authorities to be sent to the Sponsor for additional response and subsequent regulatory review. The Lead Regulator may post a joint regulatory assessment report to the solution platform as regulations allow.

Participating Regulator: Participating regulators are responsible for collaborating with the Lead Regulator and other participating regulatory authorities to conduct the regulatory pharmaceutical quality assessment of the post approval CMC submissions.

5.2 Solution Capabilities

To support the envisioned PQKM solution from its implementation to its end state, the following set of technology and business capabilities may be needed. Please note, the capabilities listed below are anticipated to be phased in over time and may not be available in the initial solution.

5.2.1 Technology Capabilities

- A secure solution that allows for workflow automation, Application Programming Interface (API) integration, and interoperability and is flexible enough to adhere to diverse regional regulations and global standards. There is no mandate to require each regional regulatory authority's decision to be harmonized.
- The technology solution should have the highest possible security standards, including cyber defense, digital identity, and data privacy and protection.
- Data and records management: each regional regulatory authority has its own legal regulations and guidelines around data residency and the retention of records, and this will need to be accommodated in the technology solution. It is important to state that transitory records do not have a strict retention requirement, while master records would need to be locally retained in the regional regulatory authority's systems. The solution will likely contain commercial information, intellectual property including manufacturing process information, and limited personally identifiable information (PII). The PQKM technology solution is not envisioned to contain patient or clinical trial data.
- As the solution scales, it should store additional data types for collaboration purposes (e.g., product and facility data)
- Provide ability for strict data management and governance: data provisioning, data integration with various sources systems, document management, and utilization of advanced analytics tools.
- Implementation of scalable and customizable workspaces with user-friendly interfaces and desktop accessibility, where each entity has its own workspace and allows for global collaborative assessment for a given submission. Please refer to the Notional Solution Architecture in Figure 2.
- Federated role-based access management.
- Integration of next-generation technology for workflow automation such as automated document comparisons, automated submission eligibility checks, automated lead regulatory assignment and workload balancing, and Outlook calendar integrations.
- Scalability and performance that includes redundancy and failover mechanisms ensuring high availability and performance monitoring.

5.2.2 Business Capabilities

- Document lifecycle management (e.g., including document upload/download/ viewing/editing, version control, automatic document deletion post regulatory decision).
- Collaborative workspaces that keep data compliant to regional (legal) storage requirements, dashboarding for submission checks, application status, regulatory availability, timeline management, and ability for making payments.
- Collaborative review workflows with a relevant workspace view on pre-submission checks (e.g., submission eligibility), application status and progress, timeline and deadlines, application and amendment changes, dialogue functionality (e.g., chat), and language translation options.
- Adherence to legal agreements and clear responsibilities: continuously evolving regulatory legislation and foreseen adoption of the solution by additional regulatory

members as the solution scales would require a high degree of technical agility as well as compliance monitoring capabilities. Herewith, in-depth policy and regulatory analysis is highly recommended during all steps of solution realization. Given cross regulatory involvement, the solution should comply with international standards (e.g., GDPR, IIP, ISO 27000, EU AI Act), and strict policies and legislations of each regulatory authority.

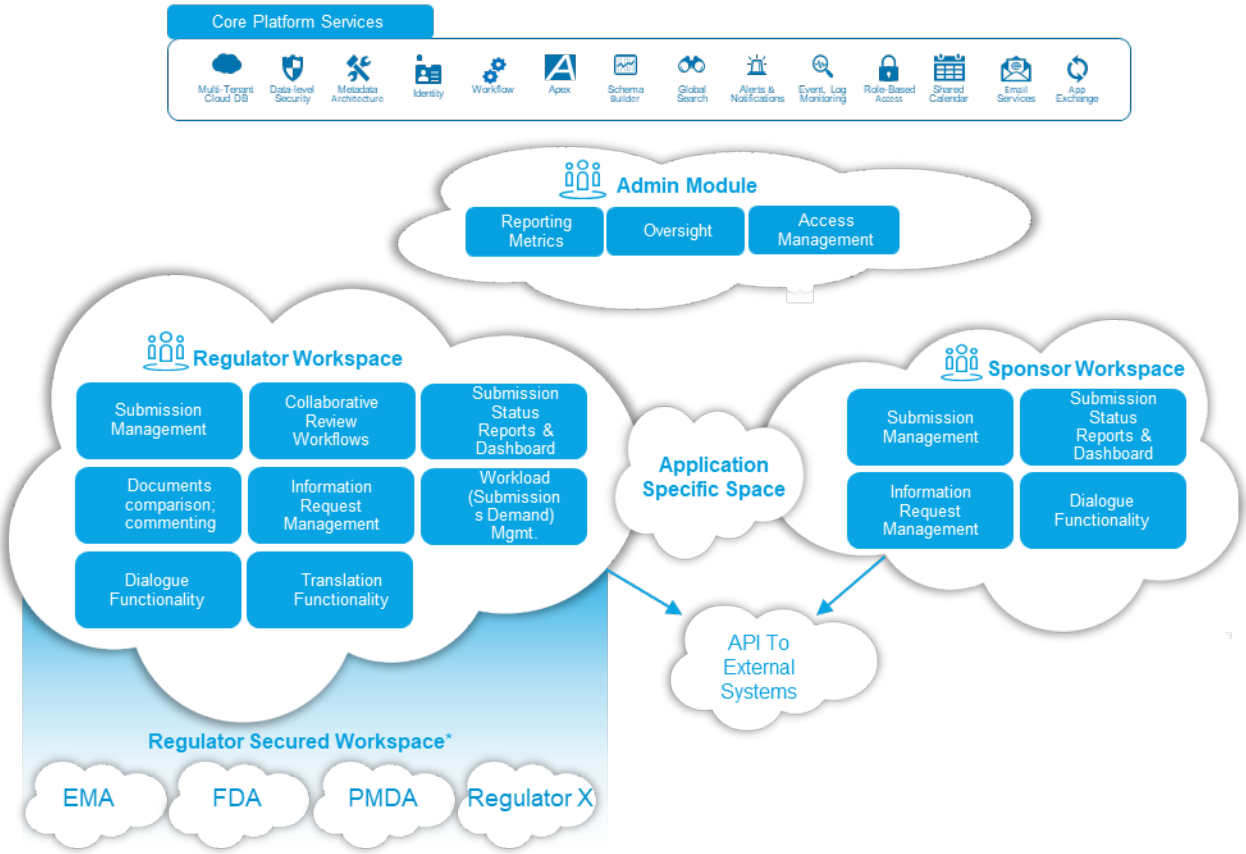


Figure 2: Notional Solution Architecture of possible workspaces set-up for each Regulatory Authority and Sponsor

The following are a few examples of the types of records one could expect in the system:

- "Dialogue" questions/answers/review comments.
- Personal identifiers of regulator and sponsor roles e.g., users name and contact information, time and date of "Dialogue" originated by user.
- Documents attachments e.g., Amended submission documents, Dossiers, Collaborative Report, Decision Letters.
- Status of submissions.
- System/audit logs.

The PQKM task force's assumption is that 1) initial submissions would still be made to local/ regional regulatory systems (for the foreseeable near-term solution phases at least), where sponsors are still responsible to make sure that the complete submission package is in the given regulator's eCTD format and is complete and available to that regulatory authority, and 2) followed

by the submission of select module(s) (e.g., eCTD Modules 2 and 3) documents to the PQKM solution by the sponsor. The notional data sharing flow is displayed in Figure 3 below.

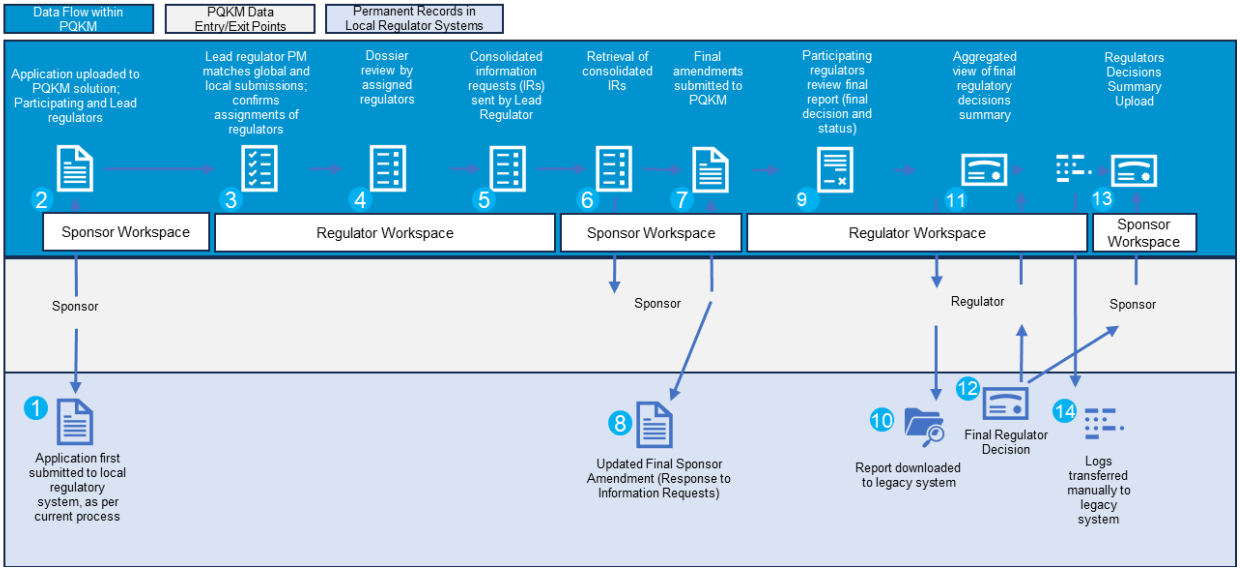


Figure 3: Notional data flow between local regulatory systems and the PQKM solution

5.3 Governance and Operations

The ICH PQKM task force identified that governance and operations of a global submission solution (i.e., the platform to support sponsor CMC/PAC submissions with request for collaborative assessment by multiple identified regulatory authorities) would need to be managed by a trusted third party rather than by either an individual regulatory authority or sponsor. The need for a trusted third party is to accommodate both sponsor and regulatory authorities' needs within a technical solution while accounting for necessary differences across a broad set of stakeholders.

Governance incorporates both strategic and operational aspects. The strategic capability includes providing the vision, priorities, and objectives for a technical solution while the operational is the day-to-day management and technical oversight of the solution. For purposes of this market consultation, it can be assumed that a governing body would provide the necessary strategic and operational governance structure for procuring the services required to develop and operate a technical solution.

In the context of operating a global PQKM solution, it can be assumed that the governing body for PQKM would be establishing a new operation with limited staffing during the near-term phases. In the near-term phases it can be assumed that the governing body would seek to procure a managed service that may include program management, solution development, operations and maintenance, security operations, and financial management for collecting potential fees for platform use. As the program management capability of the governing body is established and matures, portions of the managed service may be insourced to the governing body.

6.0 RFI QUESTIONS

6.1 Establish

6.1.1: Based on the notional vision and phased approach described in section 4.0 and assuming each of the early phases will take a minimum of 12 months for the technical solution, what approach would you recommend implementing the solution? If you don't feel a phased approach is necessary or have an alternate phased approach and timeline, please explain.
6.1.2: Describe in detail your proposed target solution architecture for the solution considering desired capabilities, existing constraints regarding existing national/regional laws, regulations, and security policies especially around submission requirements, handling of commercially confidential information, handling of personal data including data residency requirements.
6.1.3: What approach do you recommend to handling data protection, information security, and records management?
6.1.4: Please describe your ideal interaction model with the program office.
6.1.5: What approach do you recommend for compliance with the various privacy, cyber, and data residency requirements of the solution's stakeholders, in particular various regional regulatory authorities?
6.1.6: Do you have an existing solution today that demonstrates how you meet all or some of the identified capabilities without custom development? If so, please describe what capabilities you are able to demonstrate.

6.2 Run

6.2.1: Describe your approach to security operations for the solution.
6.2.2: What approach do you recommend ensuring the solution is continuously compliant with changing regional regulations and functional requirements?
6.2.3: Assuming you are operating this solution, how would you measure/monitor success? How would you collect and report on these measures?
6.2.4: What successful protections have you seen put in place to address data breaches, both for compliance and liability purposes?
6.2.5: Please describe your approach for end user support of the solution.

6.3 Evolve

6.3.1: Describe your approach to enabling new functional capabilities. How would you engage with stakeholders through this process?
6.3.2: What risks and challenges do you foresee to the evolution of the solution and how would you mitigate them?
6.3.3: How would you bring technical innovation to the solution over time?

6.4 General

6.4.1: Based on the information provided in Section 5.3, the governing body may lack technology support that it may wish to insource over time. How would you design a managed service to support a new capability and operation?
6.4.2: What experience do you have in building, operating, and transferring aspects of a managed service to a client?
6.4.3: Are there other innovative governance models you would recommend for this solution other than what is described in Section 5.3? If so, please describe.

6.4.4: Have you implemented similar solutions before? Please describe the project, your approach, and key outcomes.
6.4.5: What challenges have you seen while implementing similar solutions? How do you address these challenges?
6.4.6: What best practices do you recommend in terms of cost recovery for this type of multi-stakeholder solution?
6.4.7: Do you recommend any additional capabilities beyond those listed under section 5.2? If so, please provide them and explain why.
6.4.8: Based on the information provided above and your proposed solution, what minimum resources and skillsets would you expect the governing body to provide for you to successfully implement, run, and evolve this solution?
6.4.9: Based on the information provided above and your proposed solution, what resources and skillsets would you recommend to successfully implement, run, and evolve this solution?
6.4.10: Based on your solution and the information provided, please describe the team structure and roles you would recommend putting in place to manage the solution over its lifecycle.

7.0 APPENDIX

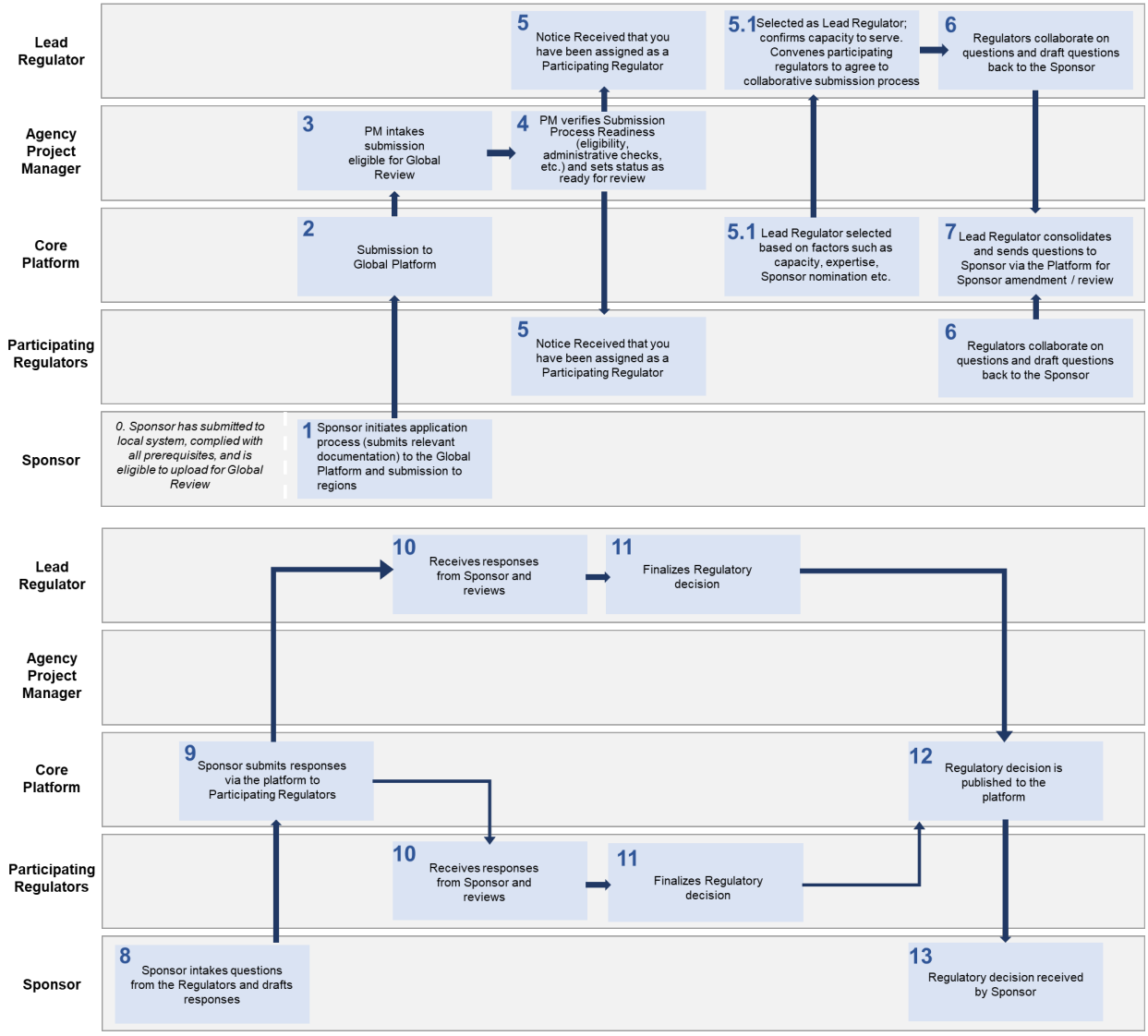


Figure 4: High-level overview of a Phase 1 collaborative review process flow