ICMRA Collaborative Hybrid Inspection Pilot (CHIP) Summary Report

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ICMRA

International Coalition of Medicines Regulatory Authorities

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1. Executive Summary

1.1. Overview of the Collaborative Hybrid Inspection Pilot (CHIP)

In June 2022, the International Coalition of Medicines Regulatory Authorities (ICMRA) launched two regulatory pilots aimed at enhancing global regulatory collaboration. The first, called the collaborative assessment pilot, focused on increasing the collaboration among global regulators in the assessments of Chemistry and Manufacturing Controls (CMC) Post-Approval Change (PAC) submissions. The second, known as the Collaborative Hybrid Inspection Piot (CHIP), was aimed at improving global cooperation in inspections of manufacturing facilities. The overall goal of both pilots was to improve collaboration and convergence among global regulators when reviewing post approval CMC changes and inspection of manufacturing facilities. This report outlines the findings of the CHIP, while a separate report will summarize the findings of the collaborative assessment pilot.

The CHIP involved cases where two global regulatory agencies[1] actively participating in a hybrid inspection of the same manufacturing facility, with one participating as the on-site lead authority and the other authority joining remotely. Additional Regulatory Authorities participated in the collaborative hybrid inspection cases as Observing Authorities without active involvement to gain experience on how this collaborative inspection could be planned and executed. The pilot focused on inspections to support post approval changes. The ICMRA CHIP team established and published the following tools to support the pilot on the ICMRA webpage;

- An inspectional protocol as guidance to participating inspectorates.
- An expectations document for participating manufacturers and sponsors.
- A timetable for undertaking and reporting on the inspection.

For each inspection, a joint inspection team was formed, comprising inspectors from the authority where the manufacturer was located and at least one inspectorate from an authority undertaking the assessment. These joint inspection teams interacted throughout the pilot, performing the inspection according to the agreed protocol, issuing the reports with an agreed set of deficiencies and following up with manufacturers on the manufacturers CAPA plan and reaching a common position on the assessment of the compliance of the facility.

Initially the pilot aimed to accept three applications over an 18-month period. Two applications were received and another preliminary application was not submitted. For the two applications, one of the manufacturing facilities was inspected twice so three joint hybrid inspections were carried out to complete the pilot. The pilot ran from July 2022 to May 2024.

[1] "Agencies" and "Authorities" inspector and investigator, Marketing Authorization Holder applicant and sponsor, are interchangeable in the document.

1.2. Summary of key findings and outcomes

The applications submitted to the pilot addressed the addition of new manufacturing sites or manufacturing capacity. Each application was assigned a lead inspectorate responsible for overseeing and managing the hybrid inspection. This was based on the location of the manufacturing facility. The lead inspectorate would carry out an on-site inspection with a supporting inspectorate participating remotely. Several regulatory authorities, including FDA, EMA, MHRA, Swissmedic, Health Canada, ANVISA, MOH Israel, PMDA and HPRA took part either as full participants or observers.

To facilitate interactions and discussions among participating inspectorates, a standardized protocol was developed. This process clarified the roles and responsibilities of participating inspectorates and set down guidelines for conducting a joint hybrid inspection, including guidelines for the crucial post-inspection follow up with the manufacturing facility. Crucially, the protocol identified the need for alignment on deficiencies and emphasised the need for a single point of contact between the joint inspection teams and the manufacturing facility.

During the CHIP process, the discussions among the regulatory authorities allowed for a consensus on harmonized lists of deficiencies to be provided to the manufacturing facility. The outcome of each pilot inspection was that the facility received fewer individual inspections, and a determination of the state of GMP compliance from the participating authorities at the same time.

On completion of each inspection, comprehensive feedback was gathered from all participants via a survey. The survey results indicated an overall positive experience, particularly among industry participants. However, it was observed that the CHIP led to an increased workload for regulators, primarily due to the additional time required for initial preparation, discussions and exchanges with other authorities.

Due to the increased resource requirements, future collaborative inspections might prioritise critical or high-impact changes for medically essential products, although early feedback on the CHIP from industry stakeholders indicated that this discouraged their participation in the pilot. Therefore, it is recommended to extend the pilot for a further year to and to consider amending the scope to make it more attractive to stakeholder participation.

2. Introduction

2.1. Overview of global post-approval CMC changes

Post-approval CMC changes are critical to ensuring the continued global availability of medicines to patients. Post-approval changes can encompass a wide array of areas, including the introduction of new manufacturing sites, changes in the manufacturing process, adoption of new testing methods, changes to specifications, among others. Depending on the nature of the change, supporting data may need to be evaluated by the relevant regulatory authorities before the change can be implemented on the market. However, each regional authority may have different data requirements, assessment approaches, and approval timelines. Furthermore, these changes may require separate inspections of the same manufacturing site for the same changes by more than one regulatory authority further complicating the approval process.

Consequently, it may take several years before a single modification to a medicinal product can be implemented globally, leading to logistical challenges and the necessity for manufacturers to maintain multiple product versions. This regulatory complexity poses a significant burden on the pharmaceutical industry. Furthermore, the protracted global regulatory approval times represent a risk to global availability and supply of critical medicines.

2.2. The role of ICMRA

During the July 2021 ICMRA-industry virtual workshop on enabling manufacturing capacity in the Covid-19 pandemic, collaboration in the pre-approval inspection of facilities submitted in post-approval changes was identified as a key enabler in supporting the increase manufacturing capacity of critical Covid-19 related vaccines and therapeutics. Following this workshop and in line with the publication of an ICMRA reflection paper on some of the practices applied by international regulatory authorities during the COVID-19 pandemic to enable remote oversight of good clinical practice (GCP) and good manufacturing practice (GMP) activities, ICMRA established a working group to explore ways to enhance cooperation among global regulators making use of remote methods. This group was charged with developing a pilot programme for collaborative joint hybrid inspection of facilities submitted in post approval CMC changes to allow for multiple regulatory agencies to participate in an inspection at the same time with the goal to make one regulatory decision. This will facilitate the identification of common principles for performing collaborative inspections and serve as a foundation for future international and global convergence efforts to embed reliance into inspectional processes.

The ICMRA Post-Approval Change (PAC) Sub-Working Group oversaw the establishment, implementation, and operation of the CHIP process.

3. Project Scope and Objectives

The primary aim of the pilot was to enable industry participants (or sponsors) to submit a single CMC submission to increase manufacturing capacity, and that could undergo simultaneous inspection by multiple regulatory authorities in a hybrid format. At the outset, the regulatory authorities involved committed to target COVID-19 therapeutics, but later broadened its scope to encompass other critical medicines.

The objectives of the pilot were as follows:

- Conduct GMP collaborative assessment of manufacturing facilities by combination of on-site and remote participation of GMP inspectorates using virtual and digital technology.
- Identify best virtual platforms and information technology (i.e., video) to facilitate the hybrid inspection.
- Identify best practices to prepare and conduct the hybrid inspection to ensure that both inspectorates obtain the desired information to complete respective assessments and meet their objectives.
- Develop a framework to accommodate time zone differences between the facility location and the distant inspectorates.
- Identify misalignments, differences, and potential areas for alignment or harmonization in GMP expectations.
- Provide collaboration and dialog opportunities for industry participants to understand the impact of the hybrid approach on industry.
- Develop aligned protocols and reports for performing such hybrid assessments so that the information can be easily shareable and useful to other interested ICMRA inspectorates.
- Develop methodologies for allowing easy and quick access to the final reports from the hybrid inspections.

Delivering on these objectives, the goal of the pilot was to ultimately increase the access to critical medicines for patients globally.

4. Development of the collaborative hybrid inspection process

4.1 Establishing the initial process

In order to establish the CHIP, the CHIP team undertook a number of consultations with inspectors, industry and observer authorities.

4.1.1 Fact finding survey to Health Canada and Belgium.

In order to establish the initial process, the CHIP team gathered information from inspectors from Health Canada and Belgium who had undertaken a hybrid inspection of a site during the pandemic. The CHIP team sent both inspectorates a short survey.

The responses to the survey underlined the importance of the establishment of confidentiality agreements between the participating authorities, clear rules of engagement with defined roles and responsibilities prior to any joint reinspection. The responses also recommended the use of separate virtual platforms between the inspectorates and between the manufacturer and information technology (i.e., video) to facilitate a concurrent combination of on-site and distant inspection/assessment. The importance of the role of an inspection coordinator facilitating the communication between the team and with the manufacturer was emphasized.

Importantly the responses confirmed that all of the observations were aligned with cGMP requirements and no major differences were identified during the inspection. One difference that was noted was that national procedures for reporting were different (based on different legislative frameworks) and that report writing was difficult as some topics were solely covered by the on-site team.

The fact-finding survey responses also noted that the inspected site needed adequate resources to ensure that all questions from both the on-site inspectors and remote inspectors were responded to in a timely manner and that while, the responses were provided in a timely manner for this initial inspection, not every site may be able to accommodate the same number of requests.

The CHIP team developed and published the IMRA CHIP Implementation Plan based on this initial feedback

4.1.2 Survey to Industry

In order to establish the initial process, the CHIP team gathered information from applicants to the CHIP pilot prior to the actual inspections. The CHIP team were interested in establishing what factors were taken into account by industry when considering whether to participate in the CHIP.

The main factors identified by the applicants in the survey to participate in the CHIP were;

- Does the company have a product in scope, which meets published criteria of unmet medical need/COVID19 therapy, and relevant pre-approval inspection (PAI)? Is there an opportunity to align with an application for the Collaborative Assessment (PACMP) pilot?
- Is the process clear and well-defined, including an overview of timing, e.g., how long will the process take from application to inspection, plus which national regulatory authorities (NRAs) are expected to be involved, including as observers?
- The participating company/facility understands the following: the potential impact to the approved product in a certain region and/or a delay in the approval schedule; the possible increase in workload for inspection preparation; and that it has the experience/capability to comply with the GMP requirements for more than one NRA.

The main factors identified in the survey NOT to participate in the CHIP were;

- Complexity of managing multiple inspectorates with potential diverging requirements and interpretations; proliferation of misunderstanding
- Virtual aspects/logistic challenges (different time zone for instance)
- Potential impact on manufacturing schedules with potential risk of supply disruption impacting several markets
- Limited scope of the hybrid inspection pilot to Pre-approval and Pre-license drug inspections (PAI/PLIs, respectively)
- Existing concerns
- Diverging requirements for participating NRAs, e.g., PAI versus GMP inspections
- Lack of clarity on how the CHIP links to existing mutual recognition agreements (MRAs), for example between EU, US, UK, Japan, etc.,
- Impact of the CHIP on frequency and focus of subsequent inspections
- Confidentiality measures are in place for all documentation
- Whether translation of documents into English is required and/or if an appropriate interpreter is available to support the pilot

Industry respondents to the survey suggested to expand the scope to include products beyond those for urgent medical need. Industry respondents highlighted that such widening of the scope could minimize potential impact on supply chain and deliver practice and experience for companies and NRAs. Additionally, industry respondents recommended not to exclude vaccines from the pilot, and include routine GMP inspections withing the scope rather than restricting to prior approval inspections. The responses recommend setting the following objectives; optimization of hybrid/virtual inspection practices, promote hybrid inspections with on-site participation from the local inspectorate, include a pre-discussion amongst inspectors to identify and understand local GMP requirements and ensure there is no impact to timelines which could impact supply continuity.

Industry respondents identified the following potential challenges with hosting a collaborative hybrid inspection, and provided suggestions for how regulators could minimize these challenges;

- Alignment between participating NRAs:
    - Clarify the role, purpose and inspection interest area between and/or among inspectors and agree upfront on inspection approaches and risk classifications.
    - Different regional legal/ regulatory requirements might cause different outcomes. Provide additional information on how NRAs intend to minimize these challenges

- Communication:
    - Prepare and discuss with the host site how to share documentation, run practice session (to test IT technology and overall virtual inspection process) and check on-line system before the inspection
- Longer inspections required (e.g., more days overall).
    - Share inspection agenda in advance and define the inspectorates to be engaged, length of the process, language, time zone, etc.

As a result of this valuable feedback, the CHIP team published an updated CHIP guidance "Inspection Expectations for CHIP participants" with more detailed information aimed at addressing the issues raised in the survey responses.

4.1.3 Feedback from Observers during the Pilots

The CHIP team also invited feedback from Observing authorities during the pilots via an Observing Authority Questionnaire and Comment Form with the aim to assist in improving the process toward eventual operationalization. Comments were intended to be a reflection of the CHIP process, not the technical aspect of the inspection. One survey was completed by PMDA during the pilot. The survey responses made recommendations for use of software to record web conferencing and identified some problems experienced by observing authorities such as sound and video quality during the facility tour and that sometimes it was not clear what documents were being discussed on site. Time differences was noted as an issue and it was recommended that in the case of large time differences, each authority must have a system in place that allows investigators to get adequate rest.

Positive impressions from the the hybrid inspection included the ability for remote authorities to carry out inspections without having to visit the production site. In addition, the broad outlines of the inspection were clearly understood. However, this approach relies heavily on trust in the lead authority, since remote authorities have less information available compared to on-site joint inspections.

A negative impression from the the hybrid inspection was the difficulty for remote authorities to reach an agreement with the lead inspectorate on the inspection plan. This is because the information available to the remote inspectorate is limited compared to that of the lead inspectorate. It is also desirable for the lead inspectorate to keep the remote inspectorate fully informed about the results and to provide feedback after each inspection day.

The following suggestions for improvements were received from the observer inspectorate:

- Chatting function that allows real-time consultation only among authorities may be useful.
- In this inspection, no cameras were brought into the filling room (Grade B) and the observing authority could not understand the structure of the filling room and filling booth. If it is difficult to bring a camera into a Grade B area during the facility tour, it would be helpful to ask the manufacturer to film those areas in advance to obtain sufficient information on the structure of the isolator or RABS, and the manufacturing process of the product.
- Information about areas where web cameras and microphones can be brought in and where they cannot be shared in advance between the manufacturer and all participating authorities.
- When multiple authorities (on-site and remote authorities) conduct an inspection simultaneously, it is desirable to decide in advance the areas to be inspected and the

documents and records to be checked. (We understand that changes may occur depending on the situation. Even in that case, it is desirable to share the understanding on how the changes will be handled in advance.)

4.2. Development of an agreed timetable

A key requirement for the success of the pilot was to reach agreement on a harmonised inspection timetable which could be adopted by all participating regulatory authorities. Given the differing legal and regulatory processes in force in the various regions, development of an agreed synchronised timeline was a considerable challenge. Nonetheless, it was possible to agree on a standardised timetable among all regulatory authorities. This standardized timetable offered clarity and predictability to industry stakeholders while providing a structured framework for undertaking the inspection. A 150-day schedule with interim milestones was developed, outlined in Table 1.

Following an agreed inspection date, there was a period of preparation when inspection teams could prepare to undertake the inspection, and then a 14-day test period was included to carry out any technical checks to ensure that the hybrid inspection could take place. Following the inspection, there was a clear set of steps and a timeline for the inspection of the facility, a CAPA plan and finalisation of the assessment of the GMP compliance of the manufacturer and/or adherence with any application timelines. The timeline allowed for flexibility to accommodate strict deadlines dictated by lead and participating authorities' legal frameworks (for instance, under current EU regulations, EU inspectorates must issue a GMP certificate or a statement of non-compliance with GMP within 90-days of the inspection). Each participating regulatory authority adjusted its internal inspection timelines to align with the ICMRA collaborative inspection timeline, while considering region-specific requirements or procedures, such as internal clearance processes. The inspection process was required to conclude within 90-days from the day of the inspection start.

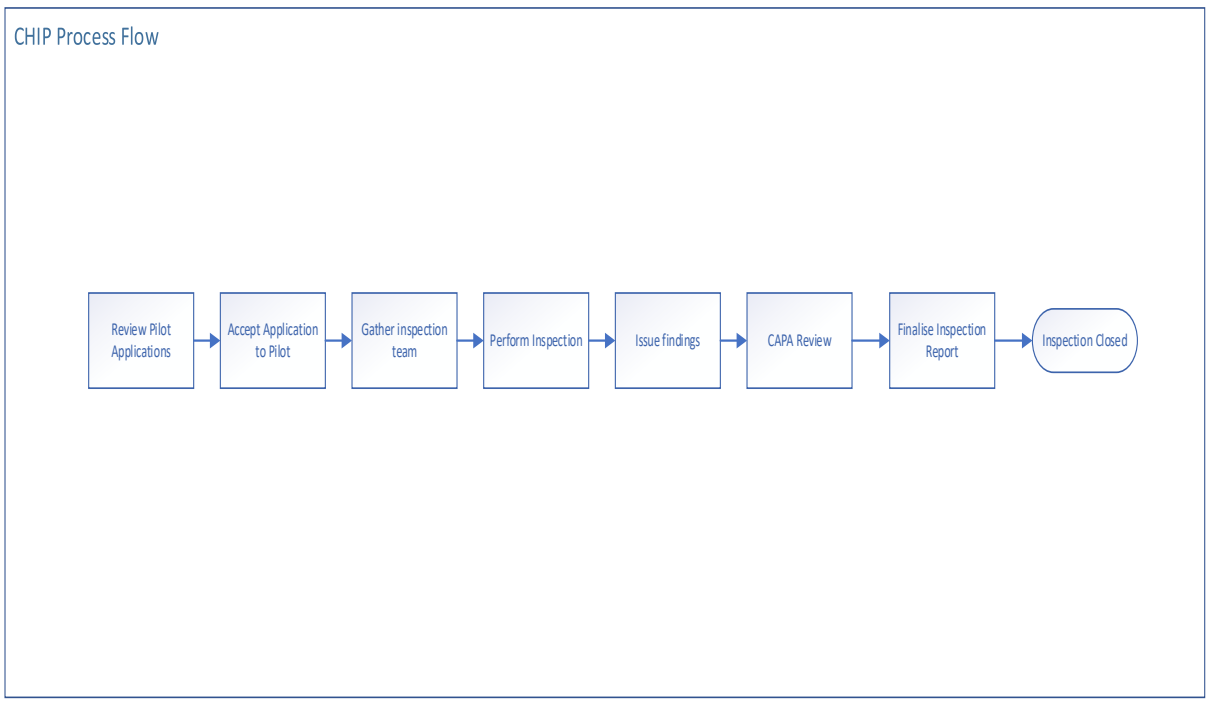
4.3 CHIP Co-ordinating Officer

The CHIP co-ordinating officer was the inspection facilitator appointed by the lead inspectorate with responsibility to ensure good communication and information sharing between the regulators on a continuous basis. This avoided redundancy and duplication of work, discussions, documentation review, etc. This support was crucial to facilitate the conduct of a multi-agency inspection. The coordinating officer was able to accommodate inspectors working in the local site time zone and the remote team’s time zone and was able to debrief with the on-site and the remote team.

Table 1 Agreed Timetable for a Collaborative Hybrid Inspection.

Activity	Timeline (calendar days)
Pre-inspection planning between inspectorates.	30 - 60 days before the start of the inspection
Communication with the manufacturer to test IT and communication capabilities	7 - 14 days prior to the inspection
Start of the inspection	0
Close-out meeting to provide the manufacturer with a consolidated list of observations	5 - 8 days after initiating the inspection
RAs receive CAPAs	30 days after close-out meeting
Engagement with manufacturer to clarify CAPA plan(s), if necessary	10 days post receipt of CAPAs from the manufacturer
Preliminary inspection report reviewed by the RAs	60 days post inspection
Final inspection report(s) sent by RAs (GMP certificate or equivalent issued/ or statement of GMP Non-Compliance, if applicable) to manufacturer.	90 days post inspection

Figure 1 CHIP Process Flow



5. Applications received and criteria for acceptance into the pilot programme

The call for applications was opened in June 2022, and two proposals were received in total. An overview is provided in **Table 2**. The applications were to increase the manufacturing capacity in their respective supply chains.

Table 2 Overview of the applications received

Application Number	Details of change
Application 1	Addition of a new Drug Product manufacturing facility
Application 2	Addition of a Drug Substance manufacturing/analytical testing facility

There were two applications for the addition of new manufacturing facilities for drug product. The other application was for the addition of a new drug substance manufacturing facility.

The applications were also reviewed against additional manufacturer specific criteria established for the CHIP;

- Each manufacturer agreed that the participating NRAs will share information to support the collaborative hybrid inspection;
- Each manufacturer agreed to the application and availability of technology to enable remote facility tours;
- Each manufacturer agreed to provide the platform for document sharing. This included direct access to documentation, electronically or otherwise, by inspectors, and in formats which can be downloaded/printed as required and, if feasible, in 'searchable' form;
- Each manufacturer agreed to safeguard the privacy and confidentiality of all parties;
- Each manufacturer agreed that the working language of the inspection would be in English and, if requested would provide competent translation services to support the timely availability of information and documentation to the inspection team

5.1. Details of the applicants and regulatory authorities

Details of the participating companies, products, and regulatory authorities for the two accepted applications are shown in Table 3.

Table 3 Participating companies and regulatory authorities

Applicant	Lead Inspectorate	Participating Inspectorates	Observers
Gilead	US FDA	Health Canada	EMA HPRA PMDA MOH Israel MHRA
Roche	Swissmedic	US FDA	EMA Health Canada Regierungspraesidium Tuebingen
Gilead	US FDA	Health Canada	No observer

The post approval changes covered the following areas, inter alia, new manufacturing facilities, new quality control testing facilities, and changes to the drug substance manufacturing process. There were three participating regulatory authorities involved in the inspection team covering lead and supporting inspector roles, USFDA, Health Canada and Swissmedic, and observing regulatory authorities included EMA, FDA, PMDA, Health Canada, Swiss Medic, MHRA, Israeli Ministry of Health, and HPRA.

5.2. Collaborative Inspection Team and Roles

To facilitate a streamlined assessment process and maximize efficiency, each inspection was conducted on site by a lead regulatory authority, supported by participating and observing regulatory authorities who joined the inspection remotely. Inspectors from each of these regulatory authorities together comprised the team. The lead authority coordinated all activities, including leading inspection preparation calls, leading the on-site inspection and collaborating with participating remote inspectors and consolidating lists of questions/information requests and preparing and agreeing the final list of deficiencies and their final classification, and sending the final inspection report to the manufacturer.

Observing regulatory authorities observed the opening and closing meetings, and could watch the entirety of the inspection, as technology allowed, and review documents requested during the inspection. Any questions from observers were directed to the CHIP Inspection co-ordinator. Collaboration between inspectorates and the manufacturer was facilitated through the use of a dedicated Microsoft Teams Channel. A separate channel was used to facilitate communications between participating authorities.

5.3 The inspection report and CAPA review process.

The inspection report and review process evolved with experience gained throughout the pilot programme.

The first CHIP pilot saw the issuance of separate reports by both USFDA (Lead Inspectorate) and Health Canada (participating inspectorate), The list of observations at the close of the inspection was a single compiled list where it was identified which observations were common between the two inspectorates and where they were not due to difference in regulatory requirements. Health Canada identified a small number of additional observations concerning requirements for their national market.
The CAPA provided by the manufacturer consisted of a single response addressing the issues identified by both inspectorates. Throughout the post inspection interactions with the manufacturer, both USFDA and Health Canada coordinated with each other to make sure each inspectorate was informed and aware of what was taking place and were aligned in actions taken.

Based on that first experience, Swissmedic as the lead inspectorate worked together with FDA as the participating inspectorate to develop a common approach in the second CHIP pilot. Swissmedic as the lead inspectorate was the main voice to communicate with the inspected company there was one common list of deviations and one common inspection report signed by both inspectorates. One CAPA plan was shared and assessed by both agencies. After finally accepting the company's CAPA, the inspection was formally closed by Swissmedic on behalf of all inspectors (Swissmedic and FDA).

The third CHIP pilot was a follow up inspection to the first CHIP pilot and the inspection report and CAPA review was handled in a similar manner to the first pilot.

For each pilot, the formal decision/approval on the submitted variation was then done by each agency following their national marketing authorization procedures.

6. Survey Results

Following the completion of each of the three pilots, a survey was sent to each participating sponsor and manufacturer and participating and observing regulatory authorities. The survey used a five-point Likert scale, ranging from strongly agree to strongly disagree. The results are presented visually with the following colour codes: strongly agree (dark blue), agree (blue), neutral (grey), disagree (orange), and strongly disagree (red). The percentage of responses in each category is shown below with graphs centred on the x-axis around neutral responses. Positive responses (strongly agree, agree) are displayed to the right of the centre, while negative responses (disagree, strongly disagree) are displayed to the left of the centre. In addition, a number of survey questions were open ended allowing survey respondents to provide more information in their responses.

Sixteen (16) survey questionnaires were completed and returned by inspectors who participated in the three (3) CHIP inspections (**Table 4**).

Survey responses represented the full range of participants. There were 3 industry responses, representing responses from 2 manufacturers and 1 sponsor, there were 6 responses from participating authorities (consisting of 2 responses from inspectors from the lead inspectorate and 4 responses from inspectors from the supporting inspectorate), and 7 responses from observing inspectors. Surveys were returned by inspectors from the same authority who participated in the same inspection and surveys were returned by more than one authority depending on their role in the inspection, i.e. participating authority or observer.

Although the majority of survey questions were identical, some questions were specific to authority participants or to industry participants.

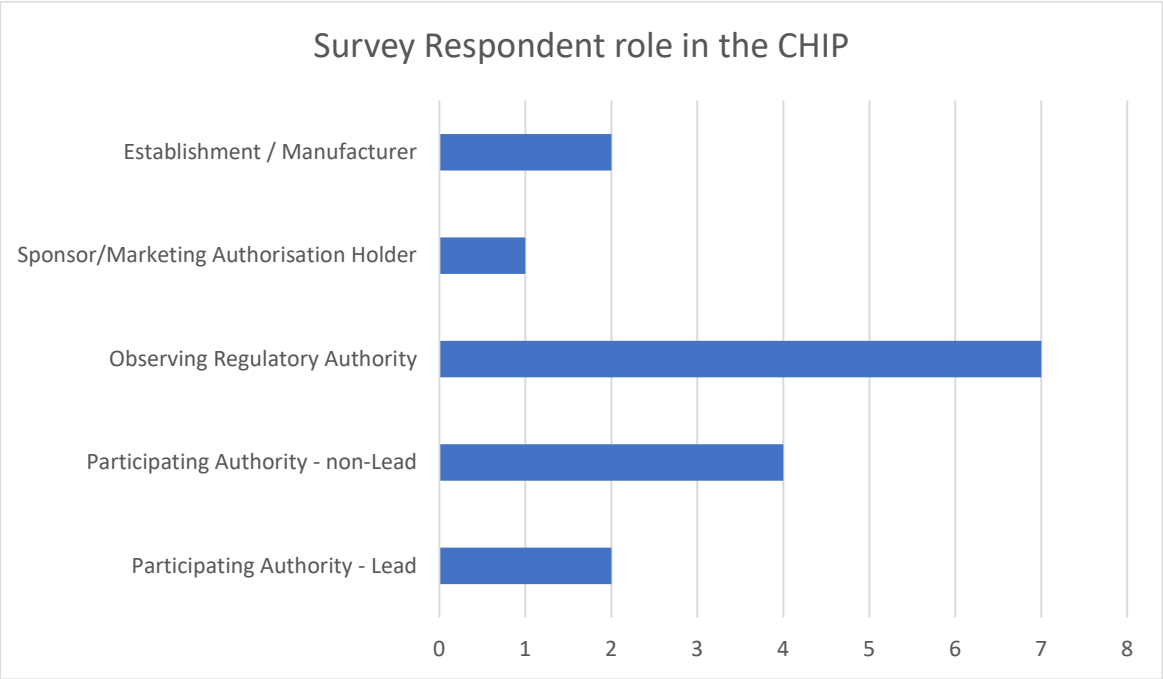
The distribution of completed surveys is summarised as follows;

Table 4 Distribution of Completed Surveys

	Number of surveys returned				
CHIP Inspection	Sponsor / marketing authorisation (MA) holder	Manufacturer	Lead Inspectorate	Participating Inspectorates	Observers
1			1	1	4
2	0	1	1	3	3
3*	1	1	0	1	~~0~~

* Only one completed survey provided by MA holder/sponsor and manufacturer for inspection 1 and 3.

Figure 2 Summary of Completed Questionnaires

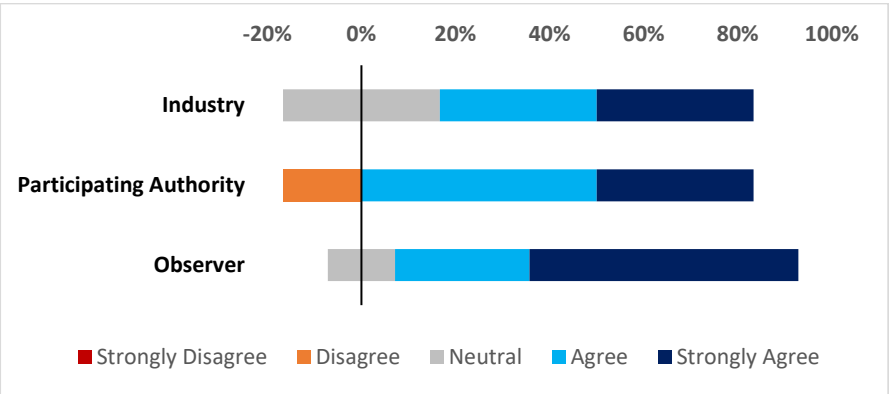


The survey questions addressed five general categories (1) overall pilot satisfaction, (2) operational outcomes, (3) resource requirements, (4) clarity and communication, and (5) regulatory interaction, and are discussed in turn below.

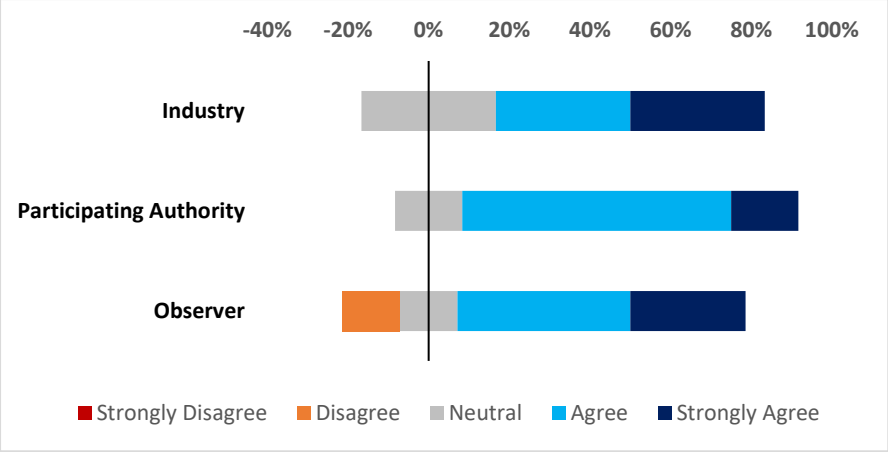
6.1 Overall pilot satisfaction

In order to objectively evaluate the success of the CHIP, a number of success metrics were proposed (**Table 6**). These success metrics reflect the key outcomes that signify the effectiveness and efficiency of the collaborative assessment processes. These metrics were used to guide the survey sent to participating companies and regulatory authorities.

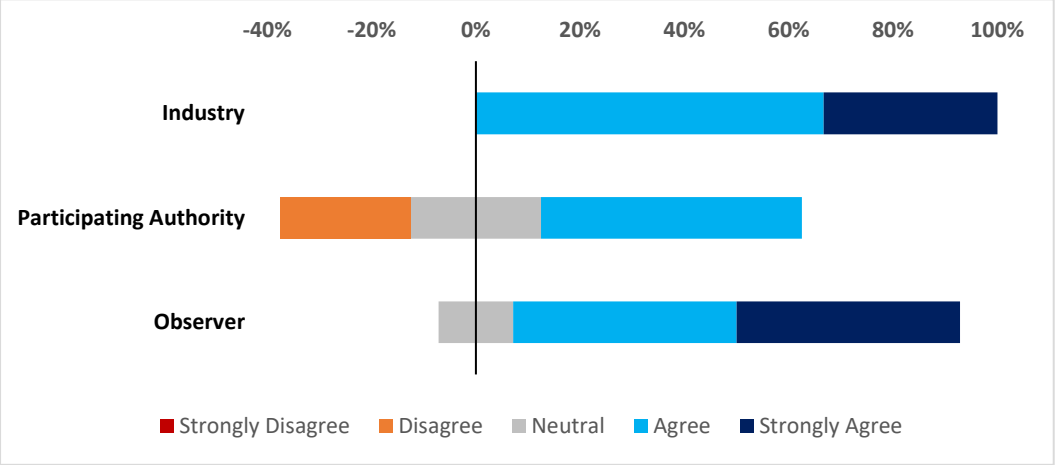
Question 1. The overall experience of the participation to the pilot is considered positive



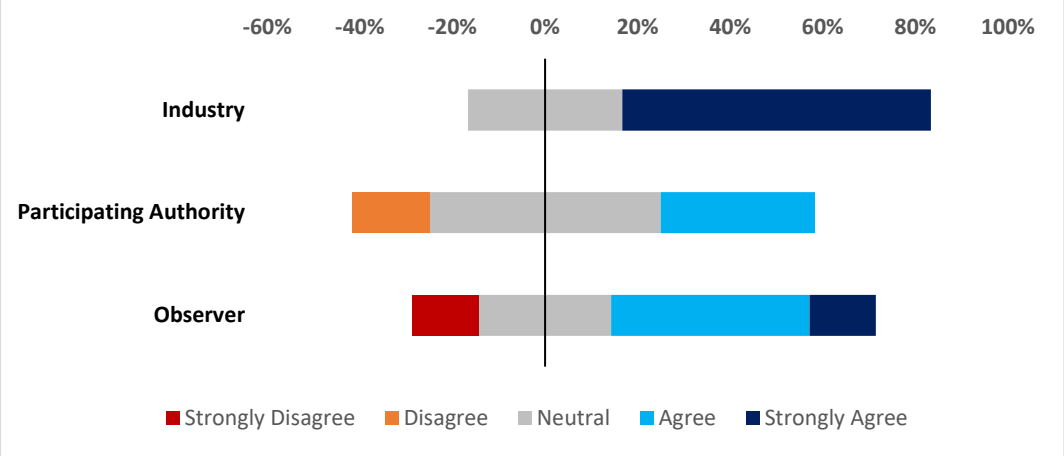
Question 2. Would you consider participation in the future?



Question 3. Do you feel the collaborative hybrid inspection process could develop into an operationalized tool that can be deployed in the future? If not, why?



Question 4. Overall, do you feel participation in the pilot had an observable impact on assisting Regulators and industry develop a hybrid collaborative approach to inspection that can benefit patients and industry?



Industry respondents reported a overall satisfaction with the pilot with the three responses ranging from neutral to strong agreement(Q1). Authority responses confirmed that the interaction among the inspectors was very positive and that a common approach by the inspection team was easily identified, resulting in a common list of deficiencies, a common inspection report and a common closing letter. Similarly, industry participants noted that the CHIP was operated in a constructive atmosphere and inspection by multiple agencies at the same time is advantageous. It was noted that contact time with the agencies during the process was enhanced during the pilot as compared to the standard process. Any issues that were identified could be discussed openly and transparently by both industry and regulators. A consolidated list of observations at the close out meeting and a joint inspection report and having consolidated timelines for inspection response was highly appreciated, with suggestions for development of harmonised templates for inspection observations and inspection report formats. Conversely, it was reported by a participating inspector that they needed more time to clarify expectations, procedures, and timeline harmonization with their domestic regulations. Similarly, for an industry participant they indicated that procedural timing misalignments caused delays in approval of the post approval change and required a second inspection. However, this may be a misunderstanding as the delay in approval and the requirement for a second inspection were due to the non-compliance of the facility at the first inspection and not due to misalignment of timings.

The majority of authority respondents agreed that their experience was positive and expressed willingness to participate in future pilots (Q2). Similarly, all industry respondents agreed that the pilot has the potential to evolve into a global regulatory pathway or programme for future collaborative inspections. This strong positive feedback highlights the industry participants' endorsement of the collaborative inspection process and their recognition of the positive outcomes from the pilot. While it is acknowledged that this data represents the viewpoint of only three industry participants, (one applicant/sponsor and two manufacturing facilities) considering the industry's strong emphasis on global regulatory reliance on inspection outcomes, it is reasonable to anticipate that this positive sentiment would extend more broadly within the industry. The feedback from regulators, especially from participating authorities was very similar to industry feedback. Specifically, the majority of participating inspector respondents either agreed or strongly agreed that the overall experience was positive. Additionally, there was a stronger agreement regarding their potential participation in future pilots. Observer regulatory authorities also provided a positive response to this question.

There was a positive opinion expressed on the future use collaborative hybrid inspections (Q3). However, participating authorities highlighted that future use could be limited to special situations e.g., when there is an urgent need for several competent authorities to get an inspection result of the same manufacturing facility, or if travelling may not be possible or would like to be avoided. Future work could focus on more alignment with the criteria to use a collaborative hybrid inspection, procedural harmonization and making additional resources available. However, there appears to be a substantial additional administrative burden on the participating authorities.

Industry comments indicated support for the CHIP as a future operational tool, noting the potential for reduced number of inspections, operational efficiencies for the manufacturing facility and the Marketing Authorization Holder (MAH). However, a lot of effort was needed to host the pilots and so further work is needed to harmonise regulations, and more clarity around how ICMRA members (which require PAI inspections) can benefit from the CHIP (e.g. as observers) or leveraging the inspection report for their approval decisions.

Observer authority responses were also optimistic, highlighting that the pilot has shown that collaboration is possible, and the hybrid approach may in some circumstances offer an advantage over remote inspections.

The majority of respondents agreed that participation in the pilot had an observable impact on assisting regulators and industry to develop a hybrid collaborative approach to inspection that can benefit patients and industry (Q4). Participating authorities commented that the hybrid inspection process would be more effective if either used only for routine surveillance inspections. More flexibility and better alignment between the dossier assessment processes and timelines is needed. Observers noted that the CHIP approach shows some potential but would be expected to be a tool in the toolkit rather than become the standard approach for inspections and that a future major benefit from this approach could be to apply the model for inspections in non-MRA/non-PICS countries.

Industry responses indicated that centralized approach will ultimately reduce resources and time to get medicines to patients that need them. Patients would benefit if the final approval of the post-approval change is done collaboratively by all the participating authorities with aligned timelines.

6.2 Operational outcomes

Question 5. Do you feel the CHIP inspection team provided you with the information needed to be ready for the first day of the hybrid inspection? If not, please explain.

These industry survey responses indicate that very good pre-inspection interactions took place with the inspection team; email and phone conversations occurred multiple times leading up to the inspection. Communication with the team was open and transparent and the overall preparation and information given by the CHIP Team was good, although one response indicates that at the beginning it was not quite clear how the active or remote inspectors would pose their questions, (directly, indirectly via CHIP Coordination Officer etc.).

There was frequent and close contact with the team leading up to the inspection. Discussions included IT requirements, with in site testing of the technical set up and ensuring cybersecurity requirements could be met. One area identified for further improvement was making more advance document requests for the remote team, as manufacturers may find it difficult to support information requests covering different review areas during the inspection.

All industry participants agreed that the role of the CHIP Coordinating Officer was clear and beneficial in facilitating communication with the inspection team (onsite and remote) and in providing logistical support.

The influence of time zones on the inspection were noted in the survey responses form industry where accommodation for the inspection team was needed in one inspection.

Question 6. What was your experience with the IT platform(s) used to interact with the remote inspection team?

A key element of the hybrid inspection was the need for an IT platform that could serve as the interface between the manufacturer and the inspection team. Two of the industry participants agreed that it was possible to use a single IT platform for seamless information sharing with all participating and observing authorities. SharePoint worked very well for sharing of documents and for the hybrid facility tour an iPhone camera with stabilising stick (Gimbal) and microphone/speaker (Jabra) worked very well. One inspector reported some problems with their authority security requirements prevented access to some files on SharePoint.

A participating inspector noted that the biggest challenge they had was to observe aseptic processing via remote video to assess if activities were being conducted adequately.

Preparatory activities undertaken by the manufacturer prior to the inspection included;

- Identify available IT resources (Software, Hardware etc.)
- Set up multiple camera phones and different locations to provide proper viewing and also have a laptop using a speakerphone to allow audio and conversations to be heard.
- Testing of Wi-Fi coverage in the production areas.
- Purchasing hardware (I-Phone sticks, microphones etc.)

Audio quality for virtual tours was noted in the survey response as an area that is difficult to control. Using an iPhone for filming and an external microphone worked well for the hybrid facility tour.

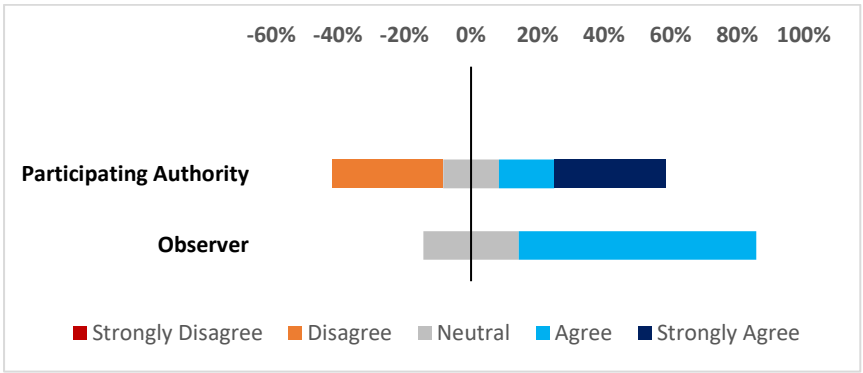
Industry participants identified possible resources and/or technology that can be deployed to maximise benefits of a hybrid approach such as;

- Having a harmonized technology approach published for file sharing but also live streaming video could reduce effort in the future.
- Including remote inspectors in tours of cleanroom is complex due to devices needed to stream and restrictions for maintaining the aseptic core. Limits ability for streaming video but also audio conversations for remote team to participate in.
- A standardized set of technologies including cloud-based system to upload relevant documents for inspection review, remote interactions and collaboration between manufacturer and various inspecting agencies.
- Detailed expectations, for the hybrid facility tour (tools, coverage, quality) could be useful for the future.

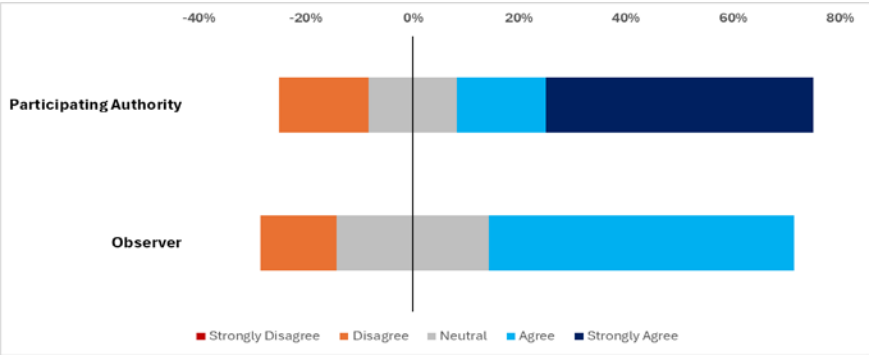
Question 7. What are possible areas of identified resources and/or technology that can be deployed to maximise benefits of a hybrid approach?

- It was noted that a hybrid inspection requires substantial IT requirements/support.
- Authority participants indicated that a co-ordinator and/or assistant resources to assist the inspection team is of great benefit.
- Implementation of a common information sharing platform among the main competent authorities. The manufacturer is best placed to co-ordinate the logistics on site and between the team and the site.

Question 8. All participating authorities were able to agree on a single list of deficiencies, including region specific, and on a final decision.



Question 9. All participating authorities actively engaged in communication (on-site and remote) to find consensus when misalignments were identified.



Question 10. From your perspective, were there any significant discrepancies between on-site and remote inspectors apparent during the inspection that affected your inspection response?

The survey responses (Q8 and Q9) above indicate some disagreement amongst regulators that each inspection team was able to agree amongst themselves on a single set of deficiencies observed and their significance, so that a final decision could be taken. This may reflect that for one inspection, there were two reports that while they were aligned on the main deficiencies from GMP requirements, there were regional specific requirements also identified during the inspection (refer to Section 5.3).

Responses in the industry survey agreed that for the opening and closing meeting, and daily meetings/interactions with the inspection team, expectations were clearly communicated.

Despite this good agreement, industry survey responses (Q10) also reflected the experience of the first pilot where there were deficiencies from regional specific GMP requirements. , Nevertheless, the respondent confirmed in their responses that while they would prefer a single report, they understood that authorities operate under different legal systems.

For industry participants there was not sufficient clarity regarding next steps and expectations regarding how CAPA responses should be provided. Respondents indicated that there was a mismatch between expectation (a single CAPA response/timelines) versus reality (two CAPA responses / different timelines). It was also unclear how the respective authorities would assess the CAPA's for product approval decisions. These differences exist due to regional differences in inspection and how the inspection fits with the national assessment timetable. Further work to explain in advance to manufacturers the regional differences that may exist between the participating authorities in the inspection team could address this issue.

Industry survey responses confirmed that they were able to agree with any objectionable issues identified by the inspection team during the hybrid inspection and they were able to address them through the proper regulatory mechanism.

Question 11. The final decisions were transparent and there was a clear and documented rationale behind the regulatory decision made.

The three industry responses disagreed with this statement in the survey, however no additional comments were provided to illustrate the point of disagreement.

Question 12. Participation in the pilot did not have a negative impact on standard or expected action dates.

Only one industry response was received neither agreeing nor disagreeing with the statement. However, data collected by the CHIP team indicate that participation in the pilot did not have a negative impact on standard or expected assessment times and as can be seen in Table 5, the parallel submission and joint inspection allowed earlier access and approval in the involved countries based on one single inspection.

Table 5 Duration of the pilot applications

CHIP	Application Submission date (dd/mm/yyyy)	Decision Date (dd/mm/yyyy)	CHIP Inspection Dates (dd/mm/yyyy)	Overall duration (days)
Pilot 1	16/06/2023	13/10/2023	17 – 27/09/2023	118
Pilot 2	18/01/2024	17/05/2024	12-16/02/2024	119
Pilot 3	01/03/2024	20/06/2024	21-24/05/2024	110

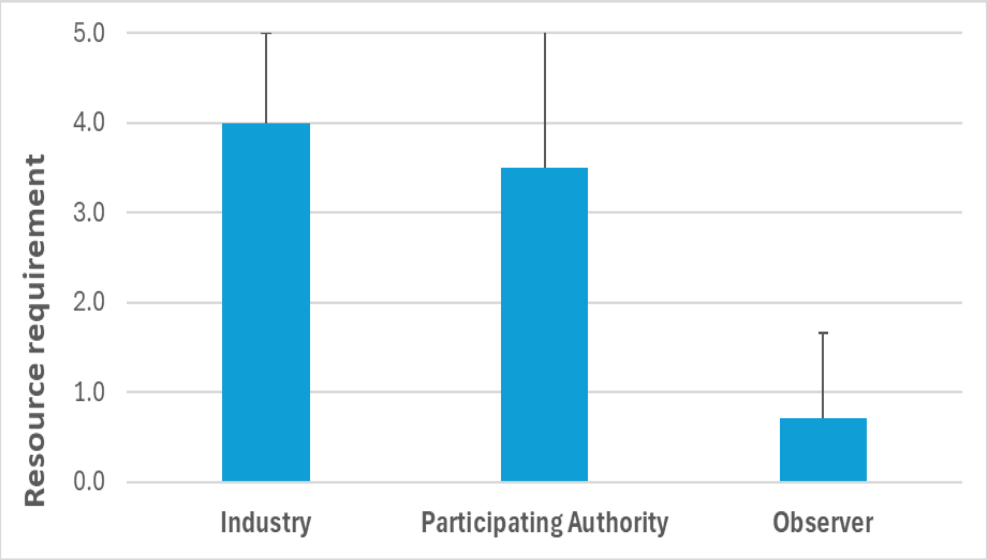
Question 13. Participation in the pilot did not lead to an overall increase in regulatory expectations for Sponsors, compared to standard requirements.

There was one response received to this question neither agreeing nor disagreeing with the statement.

Overall, industry responses are at best ambivalent towards the pilot impact in terms of authority decision making, timelines and regulatory expectations. Further work for future pilots could focus on explaining the inspection report and CAPA review and the related decision-making process more clearly.

6.3 Resource requirements

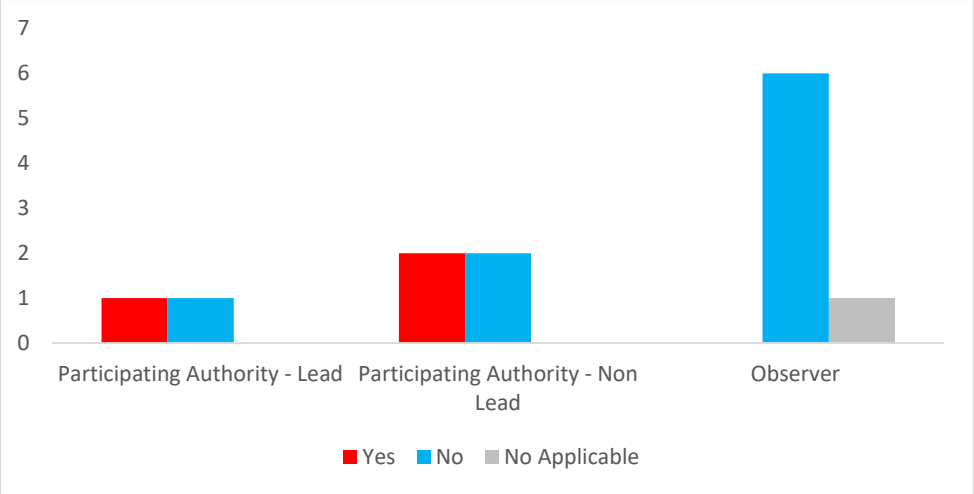
Question 14. What was the resource requirement needed to participate on the collaborative hybrid inspection? Rate on a scale from 0 to 5, with 0 = no additional resources and 5 = Significantly more additional resources.



All parties involved with the CHIP confirmed that extra resources were needed to participate in the pilot. Participating authorities confirmed that extra resources were needed for each phase of the inspection. These extra resources were needed as more extensive co-ordination was needed to support the inspection. For example, coordinating different international agency review timetables, coordinating the joint written report, coordinating review of the responses and any additional information needed to make a final recommendation, coordinating file sharing pre-inspection, during inspection, and after inspection.

Observing authorities reported that, participating in the collaborative hybrid inspection required more resources, although the level of resource requirement was much lower than that reported by the participating authorities.

Question 15. Were additional resources needed to prepare the inspection report?



Responses from participating authorities revealed an even split in terms of responses, indicating that extra resources may be needed on a case-by-case basis for inspection report preparation, depending on the demand for extra co-ordination and communication in file sharing and response review to finalise the report. Observers had no need of additional resources in inspection report preparation.

Question 16. Having participated in the pilot, do you feel more resources were needed to host the inspection when compared to a standard inspection? Why or why not?

Industry responses were very definite in their comments that more resources were needed to manage a hybrid collaborative inspection, submitting comments that up to double the resources were needed to host a routine inspection (Q17). The CHIP approach is undoubtedly complex involving on site inspectors and remote inspectors, each of which are from different authorities and time zone differences adding to the complexity. Industry responses noted that supporting the offline paper review/questions in parallel and the high amount of pre-inspection requests and translations of documents was an important increased workload. During the inspection the manufacturer had to provide extra rooms to handle the workstreams and conversations which in turn affected the availability of subject matter experts to support each stream.

Question 17. Do you feel the benefits derived from participation in the collaborative hybrid inspection outweighed the resource requirement?

Industry responses to this question were divided. Two responses (1 manufacturer / 1 sponsor) agreed that the benefits outweighed the resource requirement needed. The manufacturers response noted that the harmonized approach and parallel inspection was a benefit but being inspected to multiple regulations simultaneously was difficult to navigate as a host. Constantly switching between US, EU, PIC/s and Health Canada regs. when responding to inspector inquiries was very difficult. Having harmonized regulations would make the CHIP more straightforward.

Similarly, the CHIP allowed for inspections by multiple authorities at the same time. This was a big benefit (In future if the Chip is expanded to include more observers especially from LATAM, Africa, Asian markets and they understand the mechanism this would be more beneficial, leading to greater efficiency. This will also allow the observing Agencies to establish trust with each other and

in the process). Lack of harmonization in regulations and process with different agencies did cause challenges during the CHIP.

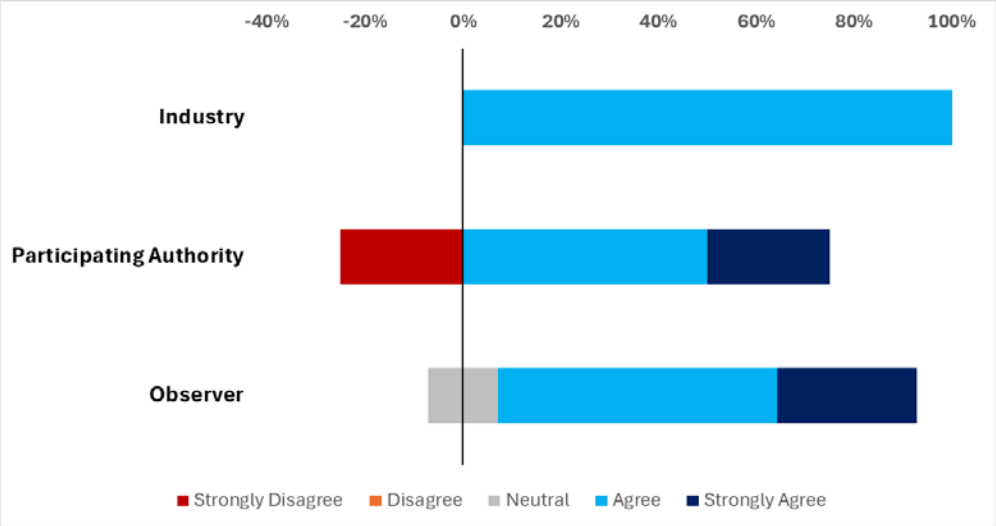
The remaining manufacturers response was that they would see a fully positive resource/benefit balance once other Health Authorities (ICMRA members) which require pre-approval inspections will leverage the CHIP inspection for their regulatory approval decisions and not conduct their own pre-approval inspection.

One observer noted that the additional resource was offset as no travelling was required for the inspection team and the hybrid approached permitted a more focused and shorter inspection. The opportunity to collaborate with international regulators was also identified as a benefit.

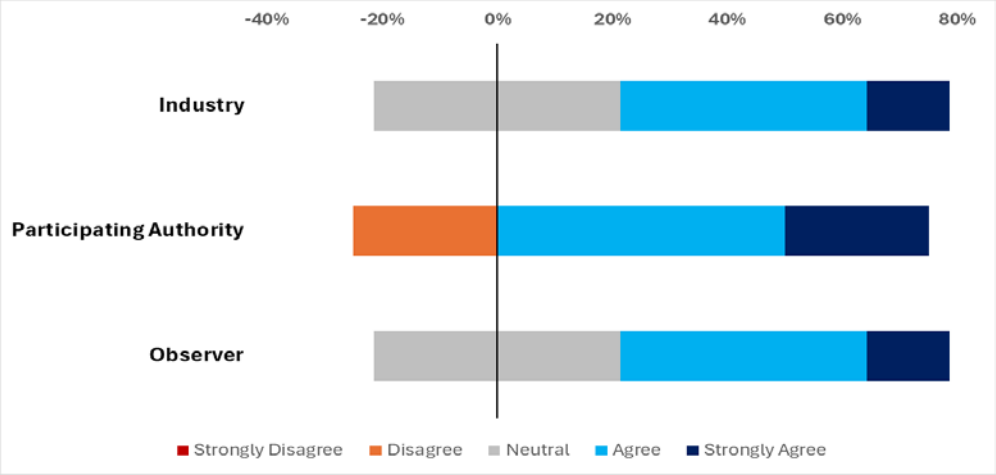
On the other hand, inspectors like being on-site to conduct an inspection and participating as a remote inspector may not overcome this preference.

6.4 Clarity and communication

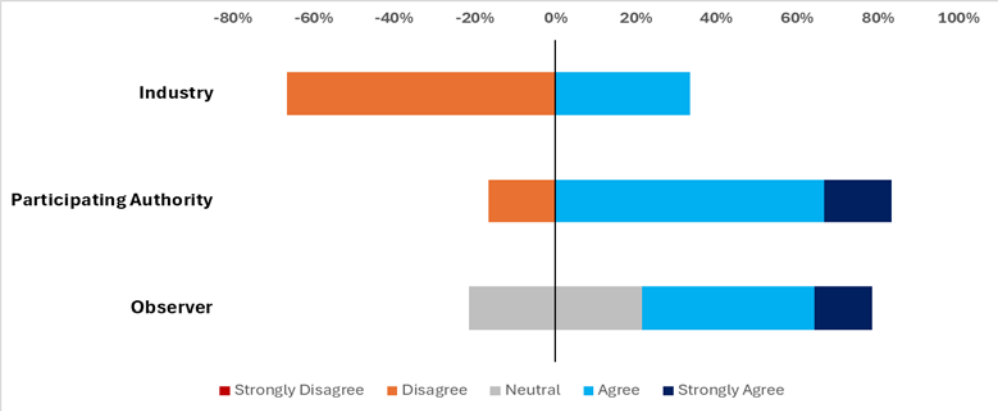
Question 18. Sufficient guidance was provided in the preparation of the hybrid inspection (e.g., regarding procedural and practical aspects of how the hybrid inspection would be conducted).



Question 19. During your preparations, did you and your team find available material on the ICMRA website regarding CHIP to be a helpful resource?



Question 20. Communication and information sharing from the establishment or from the participating authorities was timely and efficient. There were no significant delays in communication which impacted on inspection activities or agreed timelines.



The responses to these survey questions confirmed that the guidance material prepared in advance of the pilot was sufficient for preparation of the inspections and the information provided was a helpful resource to all participants once the applications to the pilot were received and inspections commenced. Participants noted in comments that the material on the ICMRA web site and the availability of the CHIP Pilot team was very helpful to their planning and completion of the inspection. Responses from industry participants provide some helpful indicators to how the materials could be improved for a second pilot.

- Reflect in Pilot material what could be main regional differences between inspectorates
- Include more detail in terms of procedures and timelines. For example, clarify whether there would be a single report and consolidated observations and response to observations.
- A harmonized process/template for Confidentiality Agreements.
- A commonly (pre-)approved platform for document sharing could in future reduce the efforts.
- Detailed expectations for the hybrid facility tour (tools, coverage, quality)
- A standard set of pre-requested documents could be helpful otherwise transparency about the increased set of potential pre-requested documents could be helpful.

The survey responses indicate that the logistical aspects of the inspection planning were handled in an efficient manner. The material prepared in advance of the pilot and provided on the ICMRA web site ensured that all participants were aware of their roles and responsibilities prior to the start of the inspection.

The responses to Q20 revealed differences between authority participants and industry participant perception of communication between the inspection teams and the inspected facility. Industry responses, especially for the first Pilot were not in agreement that communication was timely and efficient. Authorities on the other hand did find that communication with the manufacturer was timely and efficient.

The industry survey asked if the final decisions were transparent and there was a clear and documented rationale behind the regulatory decision made. Two of the three industry responses disagreed with this statement. Unfortunately, no extra information was provided in the questionnaires for this question but reviewing other responses it may be that this disagreement may relate to the post inspectional steps. For one Pilot survey responses indicated that the timing of the inspection and the post approval submission in one jurisdiction were not aligned and so the respondent considered that they were not afforded time for their inspectional responses to be considered and that this that ultimately delayed overall approval dates.

6.5 Regulatory interaction

Confidentiality agreements were required before the start of each inspection. This included the requirement for existing confidentiality agreements between regulatory agencies, as well as dedicated Sponsor authorisation letters granting permission for each participating and observing regulatory authority to discuss the inspection amongst each other. The majority of participating and observer authorities agreed that the confidentiality agreements were in place prior to the start of the collaborative assessment.

From the outset of the pilot programme, the role of observers was considered important to the overall impact of the pilot. By joining as an observer, even if a post approval change was not formally filed in their jurisdiction, observers still had the opportunity to be part of the collaborative inspection process to get a greater insight a remote hybrid inspection could be carried out and to provide feedback from the experience as an observer on the CHIP.

Question 21. Observing authorities why did you volunteer to observe the hybrid inspection?

Observers noted that the ICMRA CHIP was a great opportunity to observe inspectors from different jurisdictions working together, and it was also an opportunity to see manufacturing facilities located outside their own jurisdictions. Observers noted that it was a great opportunity to learn more about challenges faced during hybrid inspections and to compare experiences. Furthermore observers indicated that it was important to understand the implementation of hybrid inspection process to be in a better position to input and provide feedback on the next stages of the project.

Question 22. Observing authorities what did you hope to gain from participating on the hybrid inspection?

Observers noted that they hoped to identify potential gaps, challenges, benefits, and areas for improvement when implementing and conducting hybrid inspection, especially applying it to third country inspections. To evaluate the effectiveness of collaborative hybrid inspections.

From a technical point of view, observers wished to evaluate whether online participation allows for sufficient involvement and whether sufficient depth of detail can be achieved (in particular regarding the on-site tour).

Question 23. Observing authorities what benefit(s) did you gain from participating as an observing authority? Please specify.

Observers noted that they had gained a greater appreciation of collaborative work between inspectorates, including harmonization in the inspection approaches, a practical insight into how such a collaborative hybrid inspection is conducted, and the effectiveness of collaborative hybrid inspections. The process was useful as an exercise in co-inspection and confidence building, and allowed identification of opportunities within domestic frameworks.

7. Evaluation of the pilot success based on agreed Key Performance Indicators

To objectively evaluate the success of the collaborative assessment pilots, a number of key performance indicators (KPIs) were developed prior to the start of the pilot, considering the objectives of the pilot stated in Section 3. These KPIs reflect the key outcomes that signify the effectiveness and efficiency of the collaborative assessment processes. The evaluation of the KPIs outlined in **Table 6** show that 13 out of 16 KPIs were fully achieved, whereas three KPIs were only partially achieved. The successful completion of 81% of all KPIs points to the overall success of the pilot.

Table 6 Evaluation of pilot success based on agreed KPIs

No.	Metric	Outcome	KPI achieved Yes/No/ Unclear?	Basis for answer
1.	**Quality of collaboration**	There was effective collaboration between the on-site and virtual inspection teams.	Yes	The survey responses confirmed that there was effective collaboration between the on-site and virtual inspection teams.
2.	**Project management and role clarity**	The logistical aspects of the inspection planning were handled in an efficient manner. All participants were aware of their roles and responsibilities prior to the start of the inspection.	Yes	The survey responses confirmed that the material prepared in advance of the pilot and provided on the ICMRA web site ensured that all participants were aware of their roles and responsibilities prior to the start of the inspection.
3.	**Quality of remote participation**	The virtual/remote inspection teams were able to engage seamlessly with the on-site team. There was efficient information exchange to facilitate smooth and productive interactions. Authorities joining remotely were able to obtain the information they needed in a timely manner.	Yes	The survey responses confirmed that it was possible to use a single IT platform for seamless information sharing with all participating and observing authorities. Authorities joining remotely were able to obtain the information they needed in a timely manner.
4.	**IT infrastructure**	The IT infrastructure was of sufficient quality to allow effective interactions in any work included in GMP inspection, such as facility tours and document inspections between inspection teams, and between the virtual inspection team and the site.	Partial	The survey responses confirmed that document exchange was easy to achieve. Audio quality for the facility tour was noted as an area for improvement. One response indicated that it was difficult to observe aseptic processing via remote video.

No.	Metric	Outcome	KPI achieved Yes/No/ Unclear?	Basis for answer
5.	**Quality of communication**	There was effective and timely communication between the inspection teams and the manufacturing site. The site staff and Sponsor were aware of who to communicate with during the inspection. There were no significant delays in communication which impacted on inspection activities or agreed timelines.	Yes	The survey responses confirmed that there was effective and timely communication between the inspection teams and the manufacturing site. Data collected by the CHIP team confirmed that inspection activities took place within agreed timelines.
6.	**Consistency in decision making**	Consensus was reached on inspection findings and communicated to the company on a predetermined date. Consensus was reached regarding the sites' proposals for addressing inspection findings.	Partial	The survey responses confirmed that consensus was reached on main inspection findings but in one Pilot there were additional regional specific requirements that also had to be addressed and communicated to the company. Consensus was reached regarding the sites' proposals for addressing inspection findings.
7.	**Confidentiality Arrangements**	The required confidentiality agreements were place prior to the start of the CHIP. Confidentiality-related issues did not hinder any aspect of the inspection.	Yes	The CHIP team ensured that all confidentiality arrangements were in place prior to the start of the inspections. There was no confidentiality-related issues arising from any of the inspections in the CHIP.
8.	**Impact on workload and inspection efficiency**	The inspection workload was appropriately distributed among the participating inspection teams. Any increases in regulatory authority resource requirements were offset by the benefits derived from a multi-agency inspection approach. Participation in the CHIP did not result in a significant increase in workload for the	Partial	Workload distribution appears to be evenly distributed. The survey responses confirmed that participation in the CHIP did result in a significant increase in workload for the manufacturing site and/or Sponsor compared with a standard single agency inspection. Increases in regulatory authority resource requirements were offset by the benefits derived from a multi-agency inspection approach.

No.	Metric	Outcome	KPI achieved Yes/No/ Unclear?	Basis for answer
		manufacturing site and/or Sponsor compared with a standard single agency inspection		
9.	**Inspection completion time**	Participation in the CHIP did not have a negative impact on standard inspection times.	Yes	Survey responses were favourable towards inspection times and all inspections took place within the overall assessment timeline.
10.	**Final Decisions issued within a similar timeframe**	It was possible for all participating authorities to issue their final inspection decision within a similar timeframe.	Yes	Survey results indicate that It was possible for all participating authorities to issue their final inspection decision within a similar timeframe.
11.	**Identification of Focus Areas**	It was possible to identify resources and/or technology that can be deployed to maximise benefits of a hybrid approach	Yes	The survey has confirmed that it was possible to identify resources and/or technology that can be deployed to maximise benefits of a hybrid approach.
12.	**Training and Knowledge Sharing**	There was effective sharing of knowledge and best practices among the inspection teams.	Yes	The survey has confirmed that here was effective sharing of knowledge and best practices among the inspection teams.
13.	**Transparency and Accountability**	The final inspection findings were transparent and there was a clear and documented rationale behind the decisions made.	No	Industry survey responses disagreed with this statement. although no extra information is available in the questionnaires for this question, it seems from other responses that the main issue relates to the post-inspection steps and specifically with respect to the submission of the post-approval change in one jurisdiction.
14.	**Pilot Extension Feasibility**	The pilot cases provided sufficient data to inform the decision whether or not to develop the CHIP into a tool that can be deployed in a future crisis situation.	Yes	There was a positive opinion expressed in the survey on the use of collaborative hybrid inspections in the future.

No.	Metric	Outcome	KPI achieved Yes/No/ Unclear?	Basis for answer
15	**Stakeholder Satisfaction**	Industry and regulatory authority participants were satisfied with how the process was managed.	Yes	There was a positive opinion expressed in the survey on how the process was managed.
16.	**Impact on Public Health**	Participation in the CHIP had an observable impact on public health and/or availability of medicines on the market.	Yes	There was a positive opinion expressed in the survey that participation in the pilot had an observable impact on assisting regulators and industry develop a hybrid collaborative approach to inspection that can benefit patients and industry.

8. Conclusion

The ICMRA collaborative hybrid inspection pilot successfully completed three inspections supporting a range of products and post-approval changes. Multiple participating and observer regulatory authorities were involved throughout the course of the pilot. For the first time, the following resources were developed:

a) A protocol for inspectors to collaborate on joint inspections
b) Guidance for manufacturers on what to expect during a collaborative inspection
c) A standardised inspection timetable that considered regional requirements

These three tools facilitated the collaboration among the global inspection teams and provided clear milestones for applicants and manufacturers, while also adhering to current regional requirements and procedures. These tools may also be used to support collaborative inspections outside the ICMRA pilots.

Consensus on inspection findings and compliance outcomes was achieved for all three pilot inspections. Participating authorities successfully agreed on the manufacturers CAPA plan and any post-inspection information requests. This process required several discussions between the inspection teams. Due to regional-specific requirement, additional minor observations were cited in one case.

Participation in the pilot did not add regulatory burden to industry participants. Each inspection was completed within the agreed timetable and meant a reduction in the number of separate regulatory authority inspections for the individual manufacturers in order to support the approval of the requested change.

Despite the limited number of cases, the pilot has demonstrated that it is possible for global regulators to cooperate and to reach harmonised compliance verification for manufacturing facilities within the existing regulatory and legal frameworks. Such timely verification can have a positive impact on medicines supply and availability, as it reduces the number of inspections at manufacturing facilities, allows manufacturers to implement faster manufacturing changes to increase capacity and thus respond with more agility to increased market demands or disruptions of global supply chains.

When considering applications to the CHIP, the CHIP participating authorities have to pay close attention to mutual recognition agreements (MRAs) that are in place between participating authorities. All the sites that were selected for this pilot were located on the territory of MRA partners, but were nonetheless included in order to test the CHIP procedure. Future pilots should look to include sites that are located outside the territory of MRA partners to allow broader participation of Regulatory Authorities in the process.

Despite the positive experience of the CHIP, increased resources, especially for Regulatory authorities, were required to support a hybrid inspection, compared to a conventional on-site inspection. Further pilots should include criteria to select only products and sites that justify the extra resource, or identify methods to reduce the overall resource burden in preparation for and carrying out and reporting the inspection. However, industry feedback early in the CHIP process indicated that regulator focus on admitting only products with higher medical need discouraged industry participation in the CHIP.