IPRP
International Pharmaceutical Regulators Programme

7 May 2024

Outcome of the IPRP Quality Working Group (QWG) pilot project for information sharing via an ASMF/DMF database

The IPRP Quality Working Group (QWG) focuses on collaboration, information sharing and regulatory convergence for Quality information contained in applications for medicines. As part of its work programme, the QWG launched a pilot project to explore the feasibility and requirements for information sharing for drug substance information via the establishment of a database of selected Active Substance Master File (ASMF)/Drug Master File (DMF) received by members' organisations, with the overarching goal of facilitating efficient use of resources, timely authorisation, and availability of safe, effective, and high-quality drug products. This document is a summary of the project and its outcome.

1. Background

Many drug substances (APIs) manufacturers supply their material globally. A single drug substance manufacturer may be supplying multiple drug product manufacturers with the same drug substance obtained from the same manufacturing process, supported by the same or similar documentation via an ASMF/DMF. Information sharing for assessment of API quality information (e.g. assessment reports for ASMF/DMF) was considered by the IPRP QWG as a great opportunity for regulatory cooperation and convergence, in line with its mandate.

To enable information sharing, a prerequisite was to identify in which regulatory authorities/organisations of the QWG a same or similar ASMF/DMF was submitted. The QWG developed tools, such as the definition of common submission forms for ASMF/DMF, a Quality Assessment Report template, Guidance for Quality Assessors – Drug Substance, which are available on the IPRP website (www.iprp.global). To complete the kit of tools it was decided to build a database containing key elements for identification of these ASMF/DMFs, to:

- Determine the frequency of potentially similar ASMF/DMFs held by regulatory authorities/organisations.
- Determine the extent of similarity and the nature of differences between potentially similar ASMF/DMFs held by regulatory authorities/organisations.
- Develop within regulatory authorities processes for the receipt of ASMF/DMFs that include steps for checking the availability of assessment reports from other organisations.
- Develop routine lines of communication for assessment reports sharing between organisations.

2. Project key elements and milestones

The project involved several QWG regulatory authorities/organisations, which participated in the pilot on a voluntary basis, in line with the Standard Operating Procedures of IPRP. The project included the following steps:

a) Initial project scoping
b) Definition of basic database requirements
c) Listing APIs of interest
d) Engagement with Industry and communication via the IPRP website
e) Setup of the initial pilot database
f) Pilot use of the database
g) Review of the pilot.

a) Initial project scoping:

The following authorities/organisations volunteered to participate in the pilot project: ANVISA, Brazil; EDQM; Health Canada, Canada; HSA, Singapore; MHLW/PMDA, Japan; SAHPRA, South Africa; Swissmedic, Switzerland; TFDA, Chinese Taipei; TGA, Australia and WHO.

For the purposes of the pilot project, the IPRP QWG agreed that information to be stored in the database would have a limited scope and would also be limited to metadata information enabling to identify which ASMF/DMF was submitted where. Participants in the project would only upload information they were permitted to share, getting, if necessary, the ASMF/DMF holder's consent. The participating regulatory authorities/organisations committed to treat information contained in the database fully confidentially and to gather prior consent from the ASMF/DMF holder for each report they wished to exchange.

b) Definition of basic database requirements:

The IPRP QWG determined the general requirements and attributes of an IT solution that could be used to support the pilot project to share ASMF/DMF information between members. From the beginning, a distinction was made on the needs for a pilot project compared to that of a (future) live database, the needs for the pilot being more basic to facilitate the achievement of the project's goals.

The IPRP QWG agreed that the database would contain only administrative information associated with selected ASMF/DMFs and would not contain any confidential business information such as the ASMF/DMFs themselves or their assessment reports. It was also agreed not to enter any lifecycle information (e.g. post approval changes) at the start, as this required further detailed discussion.

A list of key elements that the database should contain was developed, to enable the identification of common ASMF/DMF submitted to different authorities/organisations. They were largely based on the ASMF/DMF common submission form established by the QWG.

c) List of active substances of interest:

The IPRP QWG decided to start the pilot project with a limited scope and therefore established a short list of about 20 APIs of common and highest interest, while keeping the possibility for a regulatory authority/organisation to enter any other API of interest into the database.

d) Engagement with Industry and communication:

The IPRP QWG understood that the success of information sharing for ASMF/DMF assessment depended widely on the buy-in of API manufacturers, and therefore communicated actively with Industry stakeholders to promote the project and attract volunteers.

Expression of interest:
A proactive approach was taken by calling for Expression of Interest from API Industry associations as well as API manufacturers working on global markets, inviting them to take part in the pilot and to provide feedback concerning the project and its goals.

A letter was sent to 19 identified stakeholders, which contained 3 questions:

- What benefits and concerns are identified if regulatory authorities share ASMF/DMF administrative details in the mentioned secure database.
- What benefits and concerns are identified if regulatory authorities share assessment reports in a secure way to support the assessment of an application for a medicinal product.
- Given the stated goal of sharing assessment reports, are there any potential issues if the request to share reports is made at the same time as the request to participate in the pilot project, or should the regulatory authorities consider a 2-step approach (initial request to participate in the pilot project, followed by requests to share assessment reports each time it has been identified that the same ASMF/DMF was submitted in more than one jurisdiction.

Limited feedback was received on the letter. In parallel, meetings with Industry stakeholders which mainly took place in the margin of QWG meetings were used to communicate about the pilot project and to gather Industry's views.

It should be noted that Industry stakeholders expressed some reservations about the project. They highlighted potential issues regarding confidentiality and on the fact that the API documentation submitted to different authorities was often not the same, as regulatory standards and expectations were different.

Eventually, the participation of API manufacturers in the pilot was not up to the expectations.

ASMF/DMF holder's consent to enter data into the database:

From the discussions amongst the QWG participating regulatory authorities/organisations, it became obvious that there were different legal frameworks allowing or not the sharing of administrative information associated to ASMF/DMFs. Therefore, it was considered necessary to either inform or obtained consent from individual API manufacturers before entering their data into the pilot database.

e) Setup of the initial pilot database:

For the pilot project, the database was established in the form of a spreadsheet, hosted by the EDQM in a non-public, secure IT environment, with restricted access for identified users from the IPRP QWG.

A process to identify ASMF/DMF candidates and to enter data into the database was established for agencies participating in the pilot and written operating procedures were prepared to support the participating organisations in the exercise.

f) Pilot use of the database:

The pilot was initially scheduled for a period of 18 months and was extended to 24 months. The Covid-19 pandemic had a significant impact on the work of regulatory authorities/organisations and affected this pilot as well.

Although 10 regulatory authorities/organisation initialled planned to take an active part in the project, 7 authorities entered data into the database (ANVISA, Brazil; EDQM; HSA, Singapore; Swissmedic, Switzerland; TFDA, Chinese Taipei; TGA, Australia and WHO).

At the end of the pilot phase the database contained 108 entries, associated with 50 ASMF/DMF holders located in 15 countries.

From these entries, there were less than 10 "matches": same substance from same ASMF holder submitted to at least 2 participating agencies, so less than 10%. On these matches, it was not verified whether the documentation submitted by the ASMF/DMF holder to the agencies was identical/similar, however it could be observed that in a number of cases the standard claimed was not the same (e.g. API documentation submitted as Ph. Eur compliant or as USP compliant).

g) Review of the pilot phase:

At the end of the pilot, as the number of entries and the number of matches were not high, a survey was performed within the organisations which participated in the pilot, to gather feedback on the use of the database and to understand why it was not used as much as initially foreseen. The following reasons were given:

- The process to enter data into it was time consuming, in particular because of the need to gather ASMF holder's permission or because several departments within the agency were involved in the process, making the use of the database difficult
- There was limited information in the database, i.e. few APIs and only administrative information.
- The priorities of the agency changed.
- It became clear that companies do not submit the same documentation to different regulatory authorities which does not facilitate reports sharing.

3. Conclusion

This project included various aspects beyond the setup of a pilot database containing information for ASMF/DMFs.

It allowed defining the key requirements to identify ASMF/DMF submitted by companies and establishing processes for the recording of API quality data within agencies/organisations.

The results obtained highlighted the limitations of the project. They showed that for the same API different regulatory standards are used and different documentation is submitted to the different regulatory authorities/organisations.

Further work would be needed to enhance information sharing in the area of ASMF/DMF submission, such as:

- Understanding better the differences in documentation submitted by API manufacturers to different agencies and the claimed regulatory divergences.
- Industry stakeholders should be encouraged to help for the submission and identification of a same ASMF/DMF.
- Confidentiality of information. Different agencies have different legal frameworks and ways to consider the data associated with an ASMF/DMF, which limits the processes which can be put in place.
- Strengthening inter-agency sharing practices, confidence, and experience in the use of other agencies' reports, as well as promoting the use of reports from other agencies.

The pilot project was closed and the QWG agreed to focus on improving regulatory convergence and on finding ways to exchange assessment reports manually via bilateral agreements.