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Assessment Reports - a tool for reliance
Frequently Asked Questions[1]

What is an 'assessment report' and why are they important for regulatory reliance?

1. What are assessment reports?

Assessment reports detail and explain how the reviewing national regulatory authority (NRA) assessed the safety, efficacy and quality data within a submission dossier to inform its final decision on a regulatory action.

Each NRA review should be well–documented: "A good review provides a well-written and thorough report of the evidence-based findings and conclusions provided by the applicant in the dossier, and the reviewers' assessment of the conclusions and rationale for reaching a decision. It contains clear, succinct recommendations that can stand up to scrutiny by all the parties involved and could be leveraged by others."[2]

These reports outline areas of concern and questions which the NRA had and how these were addressed by the applicant. Assessment reports are produced by many NRAs and some publish their reports on the NRA's website in support of public accountability and transparency.

2. What types of reports are issued by NRAs?

There are product focused assessment reports either for the initial registration of new products or major post-approval changes such as new indications or dosage forms. In addition to product-focused assessment reports, there are manufacturing site focused inspection reports related to the adherence to good manufacturing practice (GMP) verified via inspection of the manufacturing site either physically or via desk-based assessment. These inspection reports are usually issued by the national inspectorate within the NRA that has performed the inspection or occasionally by a regional/district inspectorate within a country (e.g. within China).

The format, nomenclature and presentation of assessment reports varies between NRAs, and there is no commonly accepted international standard. Therefore, NRAs wishing to receive and rely on these reports should avoid requesting a specific type of report which may only be available from a specific NRA.

Public assessment reports are produced following the approval of a medicine to provide transparency on the review and demonstrate how NRAs are fulfilling their responsibilities to

[1] For more information on Assessment Reports, please refer to IFPMA's Position paper on Assessment Reports.
[2] WHO Annex 9 - Good review practices

safeguard public health. Assessment reports contain data on the product generated by the pharmaceutical industry applicant.

Public assessment reports are produced by the majority of mature NRAs but are not widely produced by NRAs in emerging economies. Lack of public assessment reports is likely to become an impediment in the future as more NRAs seek to rely on one another's approvals and the World Health Organization (WHO) seeks to expand the pool of NRAs who may be relied upon. Several other public bodies also provide public assessment reports, e.g. WHO.

In Europe, for example, an important role of the European Public Assessment Report (EPAR) is to reflect the scientific conclusions of the relevant European Medicines Agency (EMA) committee at the end of the assessment process, thereby providing the grounds for the committee's opinion on whether or not to approve an application[3]. EPARs are redacted for commercially sensitive information. All EPARs are published on the EMA website and can be viewed under human medicines.

3. What is the World Health Organization's position on assessment reports?

To support regulatory reliance and collaborative reviews, WHO believes member states should share unredacted reports, where possible, which is important to build trust and to optimize reliance on outcomes from other regulators[4]. WHO recognizes that there are legal, technical and practical issues associated with the sharing of assessment reports that need to be overcome. Member States are further encouraged to collaborate; to use existing resources in more efficient manner; and to improve transparency by making public assessment reports (PARs) detailed enough, particularly on comparability, and publishing, for example, PARs for both approved and rejected medicines.

4. Does WHO issue any kind of assessment reports?

The WHO Public Assessment Report (WHOPAR) is prepared for prequalified products. When a full assessment for a health product is carried out, the assessment report summarizes the review of the product data and information that was submitted in the product dossier and provides relevant information on the product's quality, safety and efficacy. In the case of abbreviated assessments, the assessment report provides the relevant product information as approved by the reference NRA and discusses supplemental data and information reviewed by WHO. The structure and format of the WHOPAR are adapted from the European Public Assessment Report, as published by the EMA, to serve the requirements of WHO medicines prequalification.

[3] https://www.ema.europa.eu/en/medicines/what-we-publish-when/european-public-assessment-reports-background-context

[4] According to 2018 18th ICDRA recommendations

Who issues an assessment report and what is a redaction?

5. Who produces assessment reports?

Product focused and manufacturing site focused reports are typically produced to summarize the conclusions of the review. Both reports are issued by the party that has produced these reports, this means either by the NRA or the Inspectorate that conducted the physical inspection of a manufacturing site.

6. What is a redacted Assessment Report and how are the scope and extent of redactions decided?

According the Cambridge English dictionary, redaction is *"the process of removing words or information from a text before it is printed or made available to the public or the text itself after this has been done"*. The need to redact information is governed by legal processes, and it is not something which is instigated by the biopharmaceutical industry. Laws vary per country but, for example in the European Union, the following applies:

Regulation (EC) No 726/2004:

Article 13(3): "The Agency shall immediately publish the assessment report on the medicinal product for human use drawn up by the Committee for Medicinal Products for Human Use and the reasons for its opinion in favour of granting authorisation, after deletion of any information of a commercially confidential nature."

Regulation (EC) No 1049/2001:

"Article 4

1. The institutions shall refuse access to a document where disclosure would undermine the protection of:

[…] (b) privacy and the integrity of the individual, in particular in accordance with Community legislation regarding the protection of personal data.

2. The institutions shall refuse access to a document where disclosure would undermine the protection of:

- commercial interests of a natural or legal person, including intellectual property, […]"

To fulfil these legal requirements, the EMA has a standardized redaction process in place when it produces its EPARs. The EMA uses the final assessment report and sends it to the applicant for justified comments. Then the EMA decides which proposed redactions to accept and publishes the EPAR.[5]

Similarly, the US FDA is constrained in law in what it can make publicly available and is not authorized to disclose trade secrets, confidential information or financial information or other material listed *in section 552(b) of title 5*.

[5] https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/principles-be-applied-deletion-commercially-confidential-information-disclosure-emea-documents_en.pdf

While the US FDA does make much information public (Action Package and Summary Basis of Regulatory Action), redaction of confidential information would be undertaken.[6]

"FDA will also publish an Action Package upon approval of a new drug application (NDA) or BLA. An "Action Package" includes documents generated by FDA related to review of the application, summary documents with conclusions from all reviewing disciplines about the drug that note any critical issues or disagreements between the applicant and the review team, and more. Specifically excluded from disclosure in the Action Package are trade secret and confidential commercial or financial information." [7]

"FDA further publishes a Summary Basis of Regulatory Action on its website within 48 hours after the date of approval, except where redaction is required." [8]

The US FDA requires a confidentiality commitment to be in place to provide non-public information with a counterpart NRA.

"A Confidentiality Commitment (CC) is a document that sets up the legal framework for FDA to share certain kinds of non-public information with FDA counterparts in foreign countries and international organizations as part of cooperative law enforcement or regulatory activities. A CC must be in place in order for FDA to share non-public information with a counterpart, but a CC never requires FDA (or its counterpart) to share information." [9]

What types of assessment information are available?

7. What is *interim assessment information* and individual questions and answers (Q&As)?

We consider *interim* assessment information to be any piece of information submitted to a NRA at a point in time during assessment, including the information originally submitted by the applicant and any formal exchanges between the applicant and the NRA (usually in the form of individual Q&As). *Interim* assessment information may be produced when the review is ongoing to summarize a point of view from one reviewer to inform other reviewers involved in the process. Interim assessment information may also be sent to the applicant directly to address queries and understand the perspective of the NRAs at that particular point in time. Viewpoints expressed within interim assessment information may change as the review proceeds, especially if the applicant is able to resolve the NRA's initial concerns.

In the final assessment report, the information is curated, and it can be rearranged so it is clear and adequate for interpretation in the process of regulatory decision-making. Unlike *interim* information, this final aggregate of information (the so called 'unredacted assessment report') is conclusive, while at the same time being reflective of the exchanges between NRAs and the applicant.

[6] https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=report.page
[7] [See 21 U.S.C. §355(l)(2) https://www.law.cornell.edu/uscode/text/21/355]
[8] [21 U.S.C. §355(l)(2)(E) https://www.law.cornell.edu/uscode/text/21/355]
[9] https://www.fda.gov/international-programs/international-arrangements/confidentiality-commitments

8. Can this type of information be useful for reliance purposes?

Responses to questions posed during assessment are generally based on national scientific requirements, and serve to clarify specific issues. This information is of an *interim* nature and reflective of local requirements and focus areas. Furthermore, the full assessment history, including any relevant findings coming from *interim* assessment information (such as individual Q&As), is reflected in the final unredacted assessment report – this document provides conclusive evidence that is far more suitable to support regulatory reliance procedures than any type of *interim* information. A public version of this aggregate information is the ideal tool for this purpose as it overcomes the confidentiality issues governed by national laws.

Exceptionally, *interim* information can be provided when assessment reports don't exist or when the NRA needs further details. However, this requires an appropriate legal framework to be in place to ensure there are proper controls to protect the confidentiality of this information.

What are best practices for sharing assessment reports?

9. Under which circumstances can unredacted assessment reports be shared between NRAs?

It is IFPMA's position that unredacted assessment reports should not be released into the public domain. These reports may be shared between NRAs when one NRA is relying in part or in whole on another NRA's assessment as part of a reliance procedure for the same product and from the same applicant. However, this exchange requires that the NRAs have established a confidentiality agreement, sometimes connected with a Memorandum of Understanding or Mutual Recognition Agreement, in order to safeguard the confidential nature of the document exchange, i.e. patient confidentiality & commercially confidential information.

10. Unredacted assessment reports will provide NRAs with a greater insight into the approval decision - why can't industry supply these reports?

As mentioned earlier, the need to redact and the scope of redactions is frequently pre-determined by national legislation. A common mis-conception is that Industry controls the content of redactions, but this is not the case. It should be noted that in practice very little information is redacted by NRAs, and therefore it is misleading to assume that unredacted assessment reports will provide further insights into the review. In most cases, the term "unredacted" is being used rather loosely beyond its true legal definition and is intended to refer to interim assessment information. Please refer to the response to question #7 on interim assessments.

11. What are the current considerations for sharing unredacted assessment reports between NRAs?

The current considerations to share unredacted assessment reports are mostly legal, technical or practical in nature.

Legal: To safeguard the appropriate exchange of confidential information between NRAs, a bilateral confidentiality agreement or Memorandum of Understanding (MoU) should be in place. When these agreements are not in place, pharmaceutical companies may be requested to supply the reports but this does not solve the existing concerns on maintenance of confidentiality and safeguarding of intellectual property to ensure that the information does not inadvertently get into the public domain.

Technical: If utilized, appropriate and secure IT platforms and electronic delivery systems need to be in place to support the exchange of information. Such safeguards require significant investment into a global or regionally secure IT platform technology that can facilitate interagency exchange.

Practical: The reference NRA providing the assessment report might not have additional resources to support the assessment report sharing with third-party NRAs. This process is usually beyond their legal remit to protect public health in their territory. Because the medicine is already available to their patients, the NRA may not be able to justify these resources to help another NRA. Appropriate funding mechanisms for these additional activities would need to be established.

Since there might be different outcomes in the assessment reports of different health authorities (e.g. different specifications, labels), NRAs are encouraged to select one reference country from which they receive the assessment report for the initial marketing applications and maintain this reference also for the post-approval setting. This would be similar to the EU Mutual recognition system, where one reference member state is identified to lead all assessments and makes the final recommendations.

Is there a role for industry?

12. How can Industry help?

The ideal exchange of assessment report information is between NRAs who have the appropriate confidentiality agreements in place. The assessment reports are authored by NRAs and contain their views on the applicant's data. When questions or clarifications arise, these are clearly best resolved by the authors of the report rather than the applicants trying to say what they think the NRAs meant.

However, on a case by case basis, individual companies may elect to share assessment information where NRAs are not able to do this provided that the necessary safeguards for protecting patient confidentiality and commercially confidential information can be provided.

13. Oftentimes assessment reports provided to an NRA via a reliance procedure contain more details than were filed in the original regulatory submission. Why don't pharmaceutical companies provide the same information to all NRAs?

There are typically two common reasons why the regulatory applications are not identical:

1) if the applications are not filed at the same point in time, routine updates may have been made to the second filing due to new data that has been generated, e.g. updated clinical safety information or updates to product stability information; and

2) the national requirements globally still differ despite progress made in regulatory harmonization. Pharmaceutical companies must comply with the national requirements in a given country.

The question arises as to whether individual companies could elect to provide additional details beyond national requirements for a given country. Such an approach would lead to sharing large amounts of data/analyses to NRAs that could add complexity to the review process (e.g. large amounts of data, difficult to identify specific information) and could delay approval of registration.

Furthermore, there are often concerns with the provision of more detailed information on Chemistry Manufacturing and Controls (CMC), as more data registered can lead to an increased need to report post approval changes in all the countries. In practice, this leads to a range of approval dates for a given change that could span several years. This can contribute to product shortages as global production has switched to a new process and the pharmaceutical companies can't supply compliant product to the NRAs that didn't approve the change.

14. How can the biopharmaceutical industry help encourage trust building between NRAs?

The IFPMA is supportive of strengthening regulatory systems and increasing their efficiency through the implementation of regulatory reliance. We are confident that the effective implementation of regulatory reliance will benefit patients, healthcare providers, NRAs and the biopharmaceutical industry.

Therefore, we would like to recommend and support education and training workshops to discuss good regulatory and reliance practices. These workshops would help to provide more clarity and practical insights into regulatory practice, including insights from assessors working at different NRAs. These workshops could be facilitated by academia or third parties.

We also encourage policy makers to consider these aspects when discussing state aid or technical support for emerging economies. We can provide best practice examples from countries that have established additional funding mechanisms. For example, the Swiss Development Agency has provided funding to Swissmedic for supporting their program on marketing authorisations for global health products. This allows a close working relation and support between Swissmedic assessors and defined African NRAs.