FIFARMA
Federación Latinoamericana de la Industria Farmacéutica

Position Paper - Transparency in Regulatory Decision Making on the Approval for Biosimilar Products

FIFARMA members are involved in the research and development of innovative healthcare products, and provide state of the art healthcare solutions through a variety of products and services aimed to improve and save patients' lives across the globe, placing safety as one of our primary objectives. We are aware of the important role that the research-based pharmaceutical industry has to play as a stakeholder in the health care system and willing to support and engage in the increasing push that the society is demanding to make health industry transparent, with the ultimate goal of improving patient care and open up new opportunities.

A. The FIFARMA Position Transparency in Regulatory Decision Making on the Approval for Biosimilar Products

- It is in the general interests of patients, physicians, healthcare workers, producers and providers that there is a high level of public trust and confidence in the approved medical products.
- Developing and maintaining trust with stakeholders in approved medical products depends, amongst other factors, on transparently developed regulations and on their product specific application.
- Making transparent in a timely manner what regulation applied, what data basis used for the assessment and what rational is behind a medical product's approval or rejection will also allow better informed decision-making at the physician and payer level.
- The recently launched initiative from the International Pharmaceutical Regulators Forum (IPRF) on the publication of Public Assessment Summary Information for Biosimilar (PASIB) is highly valuable and if properly implemented by regulatory agencies will significantly contribute to transparency and ultimately trust with all stakeholders.
- As a good regulatory practice the availability of public assessment summary information should not be limited to Biosimilars, but should be available to any type of medical product e.g. novel biotherapeutics, vaccines or pharmaceutical products manufactured by chemical synthesis .

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B. Introduction and Problem Statement

Transparency is an important principle of good regulatory practice and as such any regulatory agency should be as open and transparent as possible about it's working processes and how it comes to decisions – generally and ideally also product specific.

In accordance with the WHO guidance Regulatory Assessment of Approved rDNA-Derived Biotherapeutics: "The sharing of information between NRAs regarding the basis for regulatory decisions on biotherapeutic products, including SBPs and the availability of publicly available evaluation reports are considered an important support for regulatory authorities that are less experienced in dealing with these highly complex products and may accelerate the assessment of the products. Communicating details of what information was reviewed and how it was incorporated into decision-making is also important for prescribers, patients and other stakeholders and can help them gain confidence in biotherapeutic products. The summary basis of decision documents of Health Canada, the European Medicines Agency and the United States Food and Drug Administration are examples of informative documents."[1]

Also regulatory agencies in Latin America are aware of this demand and are more actively involved in efforts how to increase transparency in the regulatory decision-making processes. Some of them like ANVISA or INVIMA publish already "Summary of Decision Documents" when approving and/or rejecting biosimilar/pharmaceutical products.

C. The International Pharmaceutical Regulators Forum (IPRF) proposal for "Public Assessment Summary Information for Biosimilar (PASIB)"

The IPRF has amongst other goals the intention to enable all participating regulatory agencies to identify and recommend new approaches and best practices dealing with the challenges of a rapidly evolving globalized pharmaceutical industry and as such providing the members an opportunity to leverage the expert scientific knowledge, regulatory and operational experience, on-going technical harmonization work, and information access of other participating regulators.

In March 2016, IPRF published the Template for Public Assessment Summary Information for Biosimilar (PASIB), and was open for comments from the stakeholders.

[1] Regulatory Assessment of Approved rDNA-Derived Biotherapeutics, WHO, Geneva Oct 12 to 16th 2015 http://www.who.int/biologicals/RA_for_BTP_for_WHO_web_editor_2_Nov_2015(2).pdf?ua=1

The proposed Public Assessment Summary Information for Biosimilar (PASIB) is intended to increase transparency and to facilitate the transition from a local assessment report to one prepared in the English language. The proposed template is divided in three parts: Part A-Administrative Information, Part B-Submitted Data and Reviewer Summary and Part C-Reviewer Conclusions.

In the part A-Administrative Information, the regulator and the marketing authorization holder will include information such as: product name, license number, API manufacturing facilities and batch release site, pharmaceutical form, quantitative composition, packaging material, package size, route of administration, local legal basis, approval date and information regarding the Reference Biotherapeutic Product.

In the final part of section A, the summary of outcomes will be provided including the following:

- Comparability exercise to demonstrate similarity
- Availability of full assessment report/link
- Indications applied for
- Authorized indications for the Biosimilar

In the part B-Submitted Data and Reviewer Summary, quality data such as product composition, analytical methods, data assessment outcomes are included and also a description of the mechanism of action, non clinical data and data from clinical studies with particular relevance to demonstrate biosimilarity:

- Pharmacokinetic, PK
- Pharmacodynamics, PD
- Efficacy
- Safety
- Immunogenicity
- Post authorization risk measures: Risk Management Plan (or equivalent)

In case the jurisdiction has specific regulations regarding interchangeability additional data that have been generated to justify that claim will be provided here as well.

In the part C-Reviewer Conclusions, the NRA will provide with appropriate level of detail the final conclusions regarding

- Quality
- Nonclinical
- Clinical Studies
- Risk Management
- Overall Conclusions

D. FIFARMA Considerations on the PASIB document

Fifarma is fully supportive of this initiative and would like to take the opportunity to congratulate the IPRF for bringing this forward. Transparency on which and how information was reviewed and incorporated into decision-making is a key component of good regulatory practice. It is also considered a key factor driving regulatory convergence and ultimately building confidence and trust in agencies capabilities approving safe and efficacious medicines.

Different agencies are already disclosing information as outlined in the PASIB template or part of it. The initiative proposed by IPRF promotes a common template enhancing alignment in communication and a harmonized approach on how to present the information and should encourage NRAs[2] who do not currently publish their reviews to engage in this initiative.[3] The proposed template by IPRF should be completed with an appropriate level of product specific details and in accordance with the local requirements. It should be published by the NRA in a timely manner when they approve a biosimilar.

Taking into account resource constraints in many agencies we agree with IPRF that the publicly available summary report could be short, but we think it also should be meaningful to allow stakeholders to follow the thinking of the agency that lead to the approval decision e.g. a convincing story addressing the evaluation and justification of the similarities and differences comparing the reference product with the biosimilar product should be provided.

We also consider it as an excellent approach from IPRF accompanying the template with product specific examples from different regulatory agencies on how the PASIB could be implemented[3]. It is great to see all the examples pointing towards a similarity that according to

[2] NRA National Regulatory Authorities
[3] http://www.i-p-r-f.org/index.php/en/new/template-review-biosimilar/applications/consultation/process/

the respective agencies would allow the extrapolation of all indications also approved for the reference product In addition it would be highly beneficial to provide examples where the totality of evidence provided by the sponsor did not convince the regulatory agency to approve all but only a limited number of indications approved for the reference product.This will open additional perspectives and learnings.

E. Further suggestions on information to be included in the PASIB

- NRA should clearly indicate which guideline/regulatory pathway has been used to approve the product because in some countries there are several pathways indicated under the Biosimilars regulations.
- It will be important to provide the appropriate level of detail regarding the information submitted by the sponsor, such as the number of RBP and SBP batches that have been analyzed as this would indicate the depth of product understanding.
- The high level data summaries should also include discussions on:
    - why the physicochemical characteristics and biological activities compared are the ones that have relevance for safety and efficacy of the product
    - why differences observed between the biosimilar and the reference product were considered not to affect the quality, safety or efficacy of the product.
- For the Clinical Studies, it will be important to provide details on the study design e.g. number of patients/healthy volunteers, equivalence/comparability margins, to provide clarity to physicians and alignment with the regulatory decision.
- The decision on extrapolation of indications should be accompanied by a scientific discussion elaborating why or why not indications could be extrapolated making reference to the underlying evidence.

F. Conclusion

It is in the general interests of patients, physicians, healthcare workers, producers and providers that there is a high level of public trust and confidence in the approved medical products. This will build confidence in the prescription of biosimilars and thus leading to an increase in uptake. Developing and maintaining trust in approved medical products depends amongst other factors, on transparently developed regulations and on their product specific application. Making transparent what regulation applied, what data basis used for the

assessment and what rational is behind a medical product's approval or rejection will also allow better informed decision-making at the physician and payer level. FIFARMA members strongly believe that the initiative from IPRF is highly valuable and if propery implemented may significantly contribute to achieving transparency, drive regulatory convergence and ultimately trust with all stakeholders. We think that this initiative should not be limited to Biosimilars, but application of the same concepts to other type of products such as biotherapeutics, vaccines as well as pharmaceutical products manufactured by chemical synthesis etc. should be considered by regulatory agencies.