

Comments and suggestions from reviewer

Title: WHO Questions and Answers: Similar Biotherapeutic Products (WHO/SBP_Q&A/DRAFT/DEC 2017)

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General/Overall comment				
	For the following considerations, the above-mentioned reviewers are confident that the new WHO administration reverses the document “ WHO Questions and Answers: Similar Biotherapeutic Products (WHO/SBP_Q&A/DRAFT/DEC 2017) ” and duly attends the request of WHA67.21 to the Director General “to convene WHO’s Expert Committee on Biological Standardization to update the 2009 guidelines, taking into account the technological advances for the characterization			

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	<p>of biotherapeutic products and considering national regulatory needs and capacities and to report on the update to the Executive Board”.</p> <p>1. The Colombian debate</p> <p>IFARMA, <i>Misión Salud</i>, the Drugs Information Centre of the National University of Colombia, the Colombian Bishop Conference, the Colombian Medical Federation, OBSERVAMED and the Committee of Oversight and Cooperation in Health have been participating on regulation discussions of biologic products since 2008, mainly in Colombia, but also in regional discussions including the Pan American Network for Drug Regulatory Harmonization (PANDRH) and the International Conference of Drug Regulatory Authorities (ICDRA) of 2014. The process in Colombia, and certainly in Latin America (notably Brazil, Ecuador, Peru and Argentina), was very conflictive moving from polarized positions.</p> <p>In the Colombian case we had, on one hand, a position leaded by NGOs (like IFARMA, <i>Misión Salud</i>, the Drugs Information Centre of the National University of Colombia, the Colombian Medical Federation, OBSERVAMED and the Committee of Oversight and Cooperation in Health), faith-based organizations (like the Colombian Bishop Conference) and some generic producers and their representatives, which made emphasis on the importance of having a biologic medicines’ regulation that promotes both quality and access to these drugs¹. In the opposite hand, the position leaded by multinational pharmaceutical companies, some academical representatives and some patients’ organizations was focused on promoting a regulation that should focus on unnecessarily restrictive standards, with the subsequent and potential negative effect on access to biologic medicines.</p> <p>The evolution of the debate in Colombia showed this clear polarization from a regulatory perspective. The first group defended that biological products could and must be managed in the same way of chemical synthetized products, and therefore, that it was possible to work with the same regulation making the respective specifications for each group. The other group sustained that biological products were so different that a different regulation was imperative.</p> <p>Recognizing this debate, and specially the need of ensuring access to quality biologic medicines, the Ministry of Health of Colombia issued the Decree 1782 of 2014, “that regulates health registration,</p>			

¹ <http://www.mision-salud.org/documentos-y-libros/medicamentos-biologicos-sin-barreras/>

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	<p>ensuring the safety and efficacy of this type of medication and allowing patients to have therapeutic alternatives available of equal quality and lower price.”² With this decree, “the biotechs requesting health registration must meet a package of 9 types of tests that will ensure drug quality and patient safety”. Due to the impact that this regulation would have on increasing access to medicines, as a consequence of a higher competition in the market, it has been sued by the association of multinational pharmaceutical companies in Colombia, Afidro, before the Council of State of Colombia, the supreme tribunal with jurisdiction over administrative issues in the country. This process is still on going³.</p> <p>2. Debates at PANDRH</p> <p>This polarization happened with high similarity in the above-mentioned countries and was part of strong debates into the PANDRH. Around 2010, NGOs, whom were always part of the meetings, were not invited anymore⁴, and discussions converted in a permanent confronting between national generic industries and multinationals before representatives from Regulatory Agencies⁵. This confrontation evolved in favour of the proposals of multinational industries, which are one of the financial sources of PANDRH⁶, despite a lot of protests, technical discussions, documents and communications for the record, in an unpeaceful process.</p> <p>3. International debates</p> <p>In the global scenario, we noted very fast that there was an agenda, fuelled by multinationals, to promote this kind of restrictive regulations. The main reason is that patents for biological products are weak and in some developing countries, especially middle-income ones, are prohibited. So, by means to magnify differences with chemical products, they decided to push regulations to obtain the exclusivity not available by patents. It included the need to create a new language proposing the term</p>			

² <https://www.minsalud.gov.co/English/Paginas/Decree-on-biotech-access-to-safe,-effective-and-good-quality-medicine.aspx>

³ <http://www.consejodeestado.gov.co/actuaciones.asp?numero=11001032400020170002500>

⁴ For unknown reasons, the minutes of the meeting where this decision was made are not available anymore at PAHO website:

http://www.paho.org/hq/index.php?option=com_content&view=article&id=4446%3A2010-grupo-trabajo-productos-biotecnologicos-gt-bio&catid=8607%3Ared-parf-grupos-de-trabajo&Itemid=41776&lang=fr

⁵ The permanent membership of this Working Groups on Biotechnology products was composed by delegates from: Mercosur, Andean Community, SICA, CARICOM, NAFTA, FIFARMA, ALIFAR, and others. Available at: <http://slideplayer.com/slide/10440852/>

⁶ See article 5.1. of PANDRH statutes <file:///C:/Users/franc/AppData/Local/Temp/pandrh-statutes-dec2015.pdf>

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	<p>“Biosimilars” to avoid the use of the term “generics”. Certainly, biological products are chemical products.</p> <p>But in the case of biologics, some characteristics like micro-variability, high molecular weight, complexity, glycosylation, could be exaggerated and exacerbated to obtain a specific-restrictive regulation. Each one of them could be solved by specifications with the same traditional regulation applied to a very wide range of products with a lot of differential characteristics. Applying the same approach, one could propose to create a new regulation, new nomenclature, for any category of medicines, antibiotics for example.</p> <p>We are afraid that, for large historical reasons, especially related to the financing of WHO, there was a process into the organization to get closer to Pharma agenda, as it happened with Avian Flu, the Oseltamivir case, some cancer medicines and the blood pressure normal levels, just to mention the most well-known and sound cases. The participation as observer, at the ICH, a big pharma-oriented conference, shows the subordinated character of the top level international organization on health.</p> <p>3.1. Resolution WHA67.21</p> <p>After the WHO guidelines on evaluation of similar biotherapeutic products was adopted by the WHO Expert Committee on Biologics standardization in 2009, the higher decision-making body of WHO, the World Health Assembly, adopted in 2014 the “Resolution on Access to biotherapeutic products, including similar biotherapeutic products, and ensuring their quality, safety and efficacy”⁷ (WHA67.21). The scope and approach of this resolution timely brought into the discussion the necessary consideration of biologic medicines to be affordable and of quality. Considering that quality is the only important focus for the regulation of biologic medicines misses the point of need that quality medicines are affordable to countries and people. This is the reason why the resolution urges Member States:</p> <p>“1) to develop or strengthen, as appropriate, national regulatory assessment and authorization frameworks, with a view to meeting the public health needs for biotherapeutic products, including similar biotherapeutic products;</p>			

⁷ http://apps.who.int/gb/ebwha/pdf_files/WHA67-REC1/A67_2014_REC1-en.pdf#page=25

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	<p>(2) to develop the necessary scientific expertise to facilitate development of solid, scientifically-based regulatory frameworks that promote access to products that are affordable, safe, efficacious and of quality, taking note of the relevant WHO guidelines that may be adapted to the national context and capacity;</p> <p>(3) to work to ensure that the introduction of new national regulations, where appropriate, does not constitute a barrier to access to quality, safe, efficacious and affordable biotherapeutic products, including similar biotherapeutic products;”</p> <p>The same resolution requested the Director General:</p> <p>“(1) to support Member States in strengthening their capacity in the area of the health regulation of biotherapeutic products, including similar biotherapeutic products;</p> <p>(2) to support, as appropriate, the development of national regulatory frameworks that promote access to quality, safe, efficacious and affordable biotherapeutic products, including similar biotherapeutic products;</p> <p>(3) to encourage and promote cooperation and exchange of information, as appropriate, among Member States in relation to biotherapeutic products, including similar biotherapeutic products;</p> <p>(4) to convene WHO’s Expert Committee on Biological Standardization to update the 2009 guidelines, taking into account the technological advances for the characterization of biotherapeutic products and considering national regulatory needs and capacities and to report on the update to the Executive Board;</p> <p>(5) to report to the Sixty-ninth World Health Assembly on progress in the implementation of this resolution.”</p> <p>Not recognizing the spirit of this resolution, the document under this consultation (WHO/SBP_Q&A/DRAFT/DEC 2017) is moving back the process of awareness on the importance that biologic medicines be affordable and accessible and of how continuous technological advances can favour the task of licensing biocompetitors and, therefore, increase access to these medicines.</p> <p>“Currently, most high-cost medications are biotechnological The exponential increase in health spending associated with their high prices represents a factor of the first order in the crisis of the</p>			

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	<p>systems of health, characterized by the difficulty of providing people with services and products that meet your needs.”⁸</p> <p>Although the document mentions, in relation to the WHA67.21 resolution, “In April 2015, an informal consultation on the possible amendment of the Guidelines was organized. All participants from national regulatory authorities (NRAs) from both developing and developed countries, as well as industry recognized and agreed that the evaluation principles described in the WHO Guidelines were still valid, valuable and applicable in facilitating the harmonization of SBP requirements globally.”, it is difficult to understand and accept how “an informal consultation” could change what was decided by the World Health Assembly. Therefore, the development of the “Questions and Answers” of the document doesn’t take into account the need of having regulatory frameworks that promote access to quality, safe, efficacious and affordable biotherapeutic products and the urgent need of considering the technological advances for the characterization of biotherapeutic products, national regulatory needs and capacities. Instead, from our perspective the document under consultation follows and attends the concerns of pharmaceutical multinationals corporations.</p> <p>4. The key argument of anticompetitive biologics regulation⁹</p> <p>The fundamental argument with which the anti-competitive registration regulation has been pressed is that it is not possible to obtain generics of these products because of their complexity, their large size and the difficulty of reproducing the production process in an identical manner. Consequently, clinical studies would be required to ensure the efficacy and safety of generics of these products. A "decrease" of these standards for registration would result in deficiencies in the quality of products with serious risks to the health of patients.</p> <p>Although it is true that biotechnological medicines make use of new knowledge and technologies from different areas, they are still medicines. Its matrix are the living beings, from which they are produced, extracted, purified and use active substances, that is, they are biological.</p> <p>The scientific and technical advances and the advanced state of the art of the analytical procedures, make of them the fundamental thing in the characterization of the biological medicines. In other</p>			

⁸ <http://www.mision-salud.org/wp-content/uploads/2015/06/Medicamentos-Biol%C3%B3gicos-sin-Barreras.pdf>

⁹ Ibid.

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	<p>words, the argument of the complexity of biotechnological drugs as an impediment to their characterization is false, to the extent that science and technology have been developing highly specific analytical processes that have resolved the complexity of these drugs.</p> <p>Therefore, the possibility of using an abbreviated route for the registration of drugs whose characterization by analytical methods is possible, as is the case of some monoclonal antibodies, is valid, as well as their approach as generics.</p> <p>5. Final consideration</p> <p>The importance of achieving Universal Health Coverage, which is considered within the Sustainable Development Agenda 2030, is free of doubt. In order to make it possible, governments must have regulatory frameworks that ensure both sustainability and access to biologic medicines. In this vein, it would be necessary that the new technical team under the direction of Dr. Tedros Adhanom Ghebreyesus reverses this process and duly develops the aim of WHA67.21, which fully recognizes the needs of sustainability of national health systems and the people need to access to quality biologic.</p>			