CHAPTER 15 INTERNATIONAL QUALITY MEDICINES (IQMED) – GENERIC AND BIOSIMILAR

OVERVIEW

Vietnam is ranked as the 16th most populous country in the World, with a population of approximately 99 million people as of 2023.[1] The percentage of the population aged 65 and above currently accounts for 9% and is expected to increase significantly from this level.[2] Meanwhile, Vietnam has reached middle-income economic status, has made significant progress over the past two decades on Universal Healthcare (UHC) coverage, and seeks a national coverage rate of at least 93.2% by 2023 and 95.15% by 2025.[3] Growing disposable income will likely boost consumer spending on overall healthcare services and pave the way for innovative healthcare solutions. Given the above key economic factors, Vietnam requires pharmaceutical progress that can meet the ambitions of the government and the people's needs. Meeting these needs requires collaboration between policymakers and industry toward effective patient outcomes and strong sector development.

PART 1: GENERICS

I. ACCELERATE THE AMENDMENT OF LAW ON PHARMACEUTICALS AND RELATED LAWS AND REGULATIONS

Relevant authorities: Ministry of Health (MOH), Government (GOV), National Assembly (NA)

Issue description

Seven years have passed since Pharma Law 2016[4] was passed by the National Assembly Session XIII. With the purpose of creating an important legal corridor to strengthen and improve the efficiency of state management, ensuring favourable conditions for Vietnam's pharmaceutical industry to develop and integrate internationally, and securing an adequate supply of quality drugs to the people, this paved the way for necessary changes.

Regardless, there is still work to be done to ensure that regulations are coherent and consistent with international best practices, reflect societal changes in the wake of the pandemic, and boost international integration.

Specifically, in the newly revised Pharma Law, two topics require amendments and supplements.

1. Extension of Marketing Authorisations (MAs)

Under the current regulations[5], even if technical details of a drug remain unchanged during its extension, its MA applications must be evaluated and submitted to the Council for Granting Certificates of Marketing Authorisation. For years, numerous well-known, tried-and-true drugs have been distributed throughout Vietnam and around the world without any quality concerns. However, the current Pharma Law 2016 mandates a thorough registration process for these drugs, akin to that for new drug registrations. This step is unwarranted and excessive. Such procedures burden the responsible authorities, causing delays in appraisal and subsequently impacting the manufacture, distribution and accessibility of medicines.

1 "Vietnam population", *Worldometer*, 31 October 2023. Accessed at: Vietnam Population (2023) - Worldometer (worldometers.info), last accessed on 31 October 2023.
2 Population ages 65 and above (% of total population)-Viet Nam, *World Bank data*. Accessed at: https://data.worldbank.org/indicator/SP.POP.65UP.TO.ZS?locations=VN&most_recent_year_desc=true, last accessed on 31 October 2023.
3 Value of Innovation, *KPMG*, 2022. Accessed at: VOI-Refreshment_11082022_twopageview-Edited-reduced-size.pdf, last accessed on 31 October 2023.
4 Law 105/2016/QH13 dated 6 April 2016 of the National Assembly on Pharmacy (Pharma Law).
5 Circular 08/2022/TT-BYT dated 5 September 2022 regulating the registration of drugs, drug raw materials (Circular 08).

In line with international best practices, the validity period of a certificate of MA of drugs and medicinal ingredients is 5 years from the date of first issuance or extension; and an indefinite validity period in the second extension unless the drug needs to be continuously monitored for safety and effectiveness on the basis of the advice of the Advisory Council. Furthermore, the license extension period for MA certificates should be strictly adhered to according to the one-step lifetime extension process. This would enable companies to send an extension application to the relevant bodies, ensuring approval by a set deadline. If authorities are unable to meet this deadline for any reason, the ending or already expired MA, together with the extension request, will stay valid until a fresh MA is provided. Such an approach resonates with the essence of the Prime Minister's Decision 1661.[6]

2. New drugs registration process

To facilitate, accelerate and broaden Vietnamese patients' access to new therapies and drug technologies, it is necessary to apply a rapid fast-track registration process for new drugs, especially those with new active ingredients, or new combinations of old active ingredients, drugs with old active ingredients but new strength, new dosage forms, new indications. Even though the active ingredients are old, but when developing new properties, it is necessary to apply high-tech processes, and carry out full studies depending on each product such as clinical studies, bio-equivalence studies, and stability at different temperature conditions. The research and development of these drugs is often faster and more economical because they are based on active ingredients that are available, have been on the market for many years, and have been proven to be safe and effective when used, thus meeting more and more diverse treatment needs for each individual patient.

The suggested approach is to follow the registration schedule outlined in Article 33.1 of Circular 08 for expedited appraisal, and Article 33.2 of Circular 08 for accelerated appraisal of drugs that have already been approved in at least one State Regulatory Authority (SRA) country. In terms of clinical data requirements, applications can be made in alignment with the clinical development guidelines established by U.S. Food and Drug Administration (FDA), World Health Organization (WHO), European Medicines Agency (EMA) or the regulatory authority of the respective SRA country.

For drugs containing new combinations of previously approved active ingredients, the proposal is to streamline the process by mandating only one pharmaceutical certificate (CPP) from any single SRA country. This requirement applies irrespective of whether the country in question is the manufacturing country responsible for MA, thus replacing the previous requirement of two CPPs (one from the manufacturing country and one from the SRA) as stipulated in Article 22.4.c of Circular 08.

Shortening registration times would benefit everyone, including:

- **Patients -** Would witness improved treatment outcomes from a broader array of affordable drugs and therapies.
- **Businesses -** Would see growth with the ability to register and market more products.
- **Vietnam's economy -** Would enjoy augmented investments, a growing cadre of pharmaceutical professionals, and a state-of-the-art domestic healthcare infrastructure ensuring patient safety.
- **Authorities -** Would experience workload reduction and fewer redundant tasks.

Potential gains/concerns for Vietnam

Prime Minister's Decision 1661 on streamlining administrative procedures under the Ministry of Health's purview paves the way for potential amendments to the Pharma Law 2016, specifically to endorse simplified lifetime MA extensions.

In recent years, significant collaborative efforts by the National Assembly, the Government, and the Ministry of Health have been made to prevent drug shortage for patients' treatment and prevention. The Drug Administration of the Ministry of Health has extended the validity of MAs for 10.243 drugs until the end of the year 2022, as

6 Decision 1661/QD-TTg dated 4 October 2021 of the Prime Minister on approval of simplification and deduction of administrative procedures of business operations under management scope of Ministry of Health (Decision 1661).

per Resolution 12[7] of the Standing Committee of the National Assembly. However, these extensions expired on 31 December 2022. By the end of July 2023, another 11.291 drugs received extensions until the end of 2024, in accordance to Resolution 80 of the National Assembly.[8] It is important to note that these extensions are only temporary measures due to the ongoing impact of the COVID-19 epidemic. There is still looming concern that the MAs extended under Resolution 80 will expire at the close of 2024 unless comprehensive and long-term solutions are put in place.

Incorporating a sustainable, long-term solution into the Pharm Law 2016 and related regulations is imperative. Such a solution should include a simplified process for lifetime MA extension and establish a mechanism to hold authorities accountable if extensions are not processed in timely manner. Furthermore, there is a need to revise the procedure for the initial registration of drugs to fully unlock the potential of the healthcare sector.

Recommendations

In the interest of the patients' wellbeing and as part of our mission, we recommend the following:

- Revise and redraft the Pharma Law 2016 with consideration for the comments and suggestions of the industry;
- Prepare clear guidelines regarding the introduction of a simplified MA extension process, along with clear transitional steps and implementation milestones;
- Amend first-time drug registration processes with a feasible timeline, transitional steps and milestones;
- Introduce the responsibility of authorities in the case of delays;
- Submit the new draft Pharma Law for National Assembly approval in October 2024;
- Implement regulatory coherence and adjust related regulations by January 2025; and
- A number of regulations, including the extension of MA, need to take effect immediately after the Pharma Law takes effect, to avoid drug shortages for patients' treatment and prevention.

II. EXPAND THE SCOPE OF FIE'S OPERATIONS

Relevant authorities: Ministry of Health (MOH), Government (GOV), National Assembly (NA); Ministry of Planning and Investment (MPI); Ministry of Industry and Trade (MOIT)

Issue description

According to Article 91.10 of Decree 54[9], foreign-invested enterprises (FIEs) operating in the pharmaceutical industry are not allowed to engage in drug and medicinal ingredient distribution activities in Vietnam, except for those drugs and medicinal ingredients they manufacture within the country.

Under the current regulation, in the case of Contract Manufacturing (CMO) or toll manufacturing/technology transfer, FIEs acting as contract acceptors (manufacturers) are permitted to sell CMO or toll manufacturing/technology transfer products they produce. However, FIEs acting contract givers can only sell CMO products through registered wholesalers, typically local pharmaceutical companies, who subsequently distribute them to hospitals and pharmacies. Alternatively, FIEs must perform on-spot export and import procedures if they wish to sell their localized products directly. Both of these mechanisms result in a negative impact on patients, who end up paying higher prices to cover unnecessary additional costs, in order to access high-quality, safe and effective medicines.

7 Resolution 12/2021/NQ-UBTVQH15 dated 30 December 2021 of the Standing Committee of the National Assembly on permission to implement certain mechanisms and policies in the health sector in service of COVID-19 prevention and control practices (Resolution 12).

8 Resolution 80/2023/QH15 dated 9 January 2023 on regarding continuation in implementation of certain COVID-19 management policies and use of marketing authorization licenses of medicines or pharmaceutical materials expired from 1 January 2023 to 31 December 2024 (Resolution 80).

9 Decree 54/2017/ND-CP dated 8 May 2017 providing guidelines for implementation of the Law on Pharmacy (Decree 54).

In essence, foreign investors, despite going through costly technology transfer, manufacturing and registration procedures, are limited in their activities within the sector. This limitation makes investment in CMO, tolling, and pharmaceutical technology transfer for the production of patented drugs, specialised drugs, innovative generic drugs, vaccines, and biological products less appealing for foreign investors. More importantly, these regulations are not aligned with the spirit of Prime Minister's Decision 376[10], which outlines strategies for developing the domestic pharmaceutical industry to reach level IV on the WHO classification scale. The goal is to have market value ranking among the top three ASEAN regions and enable the provision of affordable, high-quality, safe, and effective medicines.

Potential gains/concerns for Vietnam

With the expected development of diverse localized products, local manufacturers can obtain know-how technologies and apply them to produce their own products. On the other hand, FIEs' extensive expertise in drug development, sales, and marketing can be used to expand their business in Vietnam, domesticate high-quality drug manufacturing, and expand treatments for patients.

Recommendations

To incentivize CMO, toll manufacturing and technology transfer in Vietnam, we ask the government to consider the following recommendations:

- Expand the scope of the rights of FIEs'. Specifically, FIEs which are the contract giver or contract acceptor performing the CMO/technology transfer should be allowed to perform activities related to distribution of the localized products in Vietnam by themselves. This is a-must-have-regulation to boost the local manufacturing of high-quality, affordable, safe, and effective medicines in Vietnam;
- Revise Tender regulation for Tolling and Tech Transfer products following the classification of Marketing Authorization Approval. Tolling and Tech Transfer products should be classified as local products not foreign products; and
- Provide Tender & Procurement incentives for localized high-quality products that will attract more foreign investment in the Pharma industry in the coming time.

PART 2: BIOSIMILARS

I. INCREASING PATIENT ACCESS TO STATE-OF-THE-ART THERAPIES

Relevant authorities: Ministry of Health (MOH), Vietnam Social Security (VSS), National Assembly (NA) – Committee on Social Affairs.

Issue description

Biosimilars[11] serve as an innovative solution to enhance the accessibility challenges faced by patients in obtaining biologics, which are advanced treatment therapies. They not only generate healthcare system saving but also diversify treatment options for healthcare professionals.

10 Decision 376/QD-TTg dated 17 May 2021 on approving Development program for pharmaceuticals industry and domestically produced herbal ingredient until 2030 and vision to 2045 (Decision 376).

11 "Biosimilars", US FDA, 03/01/2023, Available at: <www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/>; last accessed on 7 September 2023
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Anita Krishnan et al. Biosimilars 2015:5 19–32. Kumar, J. et al., Pharmacovigilance 2015, S3; Richard Markus et al. BioDrugs (2017) 31:175–187; Jun Wang et al. Pharmaceuticals 2012, 5, 353-368;
The Biosimilars Council 2017: Biosimilars in the U.S. – Providing more patients greater access to lifesaving medicines. Available at: <http://pr.euractiv.com/pr/biosimilar-medicines-opportunity-dramatic-increase-patient-access-across-europe-153876>, <www.medicinesforeurope.com/biosimilar-medicines/our-5-pillars/>, </www.karger.com/Book/Toc/279159>, last accessed on 18 February 2021.

Potential gains/concerns for Vietnam

Benefit for Patients

With the global population on the rise and simultaneously aging, multiple chronic conditions (MCCs) are becoming increasingly prevalent, with nearly one in every three adults living with an MCC. Biologics are being used for a myriad of these MCCs, and with their prices surging, biosimilars present a more cost-effective yet equally efficacious alternative. By offering similar treatment outcomes as reference biologics in terms of quality, safety and efficacy, biosimilars amplify patient access to potentially life-changing medicines. Groups such as women, the elderly, and those in lower-income brackets stand to benefit immensely from biosimilars. At least 400 million people worldwide cannot access essential health services and more than two billion cannot afford to buy the medicines they need. The EU saw a 100 percent increase in the use of biologic treatments after the introduction of biosimilars. In the US, biosimilars have been used in 364 million days of patient therapy and supported 150 million incremental days of therapy that patients would otherwise not have received without biosimilar competition. An estimated 1.2 million US patients could gain access to biologics by 2025 because of increasing biosimilar availability.[12]

Benefit for Healthcare Practitioners

The introduction of biosimilars drives competition, resulting in increased treatment options and value-added services for patient care and the healthcare community, thereby allowing healthcare practitioners (HCPs) to administer top-tier biologics to a larger patient base while reducing costs. By 2029, with around 120 biologic medicines expected to lose their exclusivity, the potential for biosimilars grows.[13] However, the true potential of biosimilars can only be unleashed with better educational endeavours around their safety and efficacy, and a clearer understanding among HCPs of their significance.

Benefits for Healthcare System

With increasing healthcare expenditures, particularly for MCCs, financial constraints on healthcare systems are tightening. The global spending on healthcare is expected to reach USD24.24 trillion by 2040 with the cost of biologic medicines accounting for a substantial proportion of this expenditure. There's growing evidence that biosimilars relieve the healthcare budget pressure and support more sustainable healthcare systems. The substantial savings realised can improve patient access by allowing more patients to be treated from the same budget. Thus, biosimilars will enable stakeholders – including payers, clinicians, and patients – to benefit from a greater choice of treatment options, and more patients will have access to these treatments. By introducing competition with biosimilars, the savings generated could reach between USD44 billion and USD250 billion over a ten-year period in the U.S., with the value dependent upon the policy adopted in the coming years. Globally, the cumulative savings opportunity for biosimilars from 2021 to 2026 is estimated at USD285 billion.[14] Access to cost-effective treatment is paramount for the short-, medium-, and long-term sustainability of healthcare systems. Biosimilar medicines represent a cost-effective alternative which give healthcare systems a way either to save money or divert that money to solve other pressing healthcare problems, however more actions are required for the continued adoption of biosimilars, including ensuring long-term market sustainability for biosimilars and better educating healthcare professionals.

Recommendations

We would like to make the following recommendations:

- Consider the early issuance of guidance for biosimilar dossier technical appraisals;
- Include a specific definition for biologics that are not approved as a biosimilar, such as bioscopies and noncomparable biologics, in the Pharma Law to help healthcare professionals have accurate and complete understandings about circulating biologics;

12 "Biosimilars and Access to Treatment", *Sandoz*. Available at <https://www.us.sandoz.com/our-work/biosimilars/biosimilars-and-access-treatment>, last accessed on 09 October 2023.
13 "Value of Biosimilars", *Sandoz* available at < https://www.sandoz.com/node/34211/printable/pdf>, last accessed on 09 October 2023.
14 Global Medicine Spending and Usage Trends – Outlook to 2025", IQIVIA Institute for Human Data Science. Available at <https://www.fdanews.com/ext/resources/files/2021/04-30-21-IQVIA.pdf?1619810914>, last accessed 09 October 2023.

- Consider the early issuance of healthcare professional guidance for using biosimilars in clinical practise to improve patient treatment efficacy and safety; and
- Increase biosimilar's medical educational and training activities to healthcare professionals and healthcare authorities for improving knowledge.

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