CHAPTER 12A **INTERNATIONAL QUALITY MEDICINES – GENERIC AND BIOSIMILAR**

PART 1: **GENERIC**

OVERVIEW

The International Quality Medicines – Generic and Biosimilar is a pharmaceutical Sector Committee established under the EuroCham Healthcare Forum[1] in August 2016. The IQMED - Generic and Biosimilar Sector Committee includes FDI or foreign pharmaceutical companies with head offices based in ICH[2] countries and Representative Offices in Vietnam. Our companies all have products marketed in a minimum of 10 countries in Asia Pacific (APAC), the EU and North America and have 50 per cent of their portfolio revenue categorised in Originator, Generic Group 1, Group 2 as current tender regulation or with Bio-Equivalence/Bio-Availability (BE/BA) from the EU.

All the IQMED - Generic and Biosimilar members are strongly committed to the common mission of delivering affordable, high-quality, sustainable and trusted off-patent medicines and services to Vietnamese people. Key activities of the IQMED - Generic and Biosimilar Sector Committee focus on policy advocacy and collaboration with key healthcare stakeholders such as the Government, providers and payers in Vietnam in order to build efficient legal frameworks and implementation platforms.

I. OFF-PATENT PHARMACEUTICAL DIFFERENTIATION THROUGH HEALTH TECHNOLOGY ASSESSMENT (HTA) METHODOLOGY

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

Issue description

Universal coverage is the most critical healthcare priority in Vietnam today. The Government aims to reach 90 per cent of the population with access to public healthcare insurance by 2020.[3] Transforming healthcare to provide universal coverage highlights the need for high-quality generic pharmaceuticals and efficient management of Government funds.

The majority of patients in Vietnam are treated with Off-Patent Pharmaceuticals (OPP) which include off-patent originators, branded and unbranded generics. OPP currently holds 87 per cent volume and 73 per cent value of the total pharma market, according to the latest Total Vietnam Pharma Audit published by IQVIA in February 2018.[4]

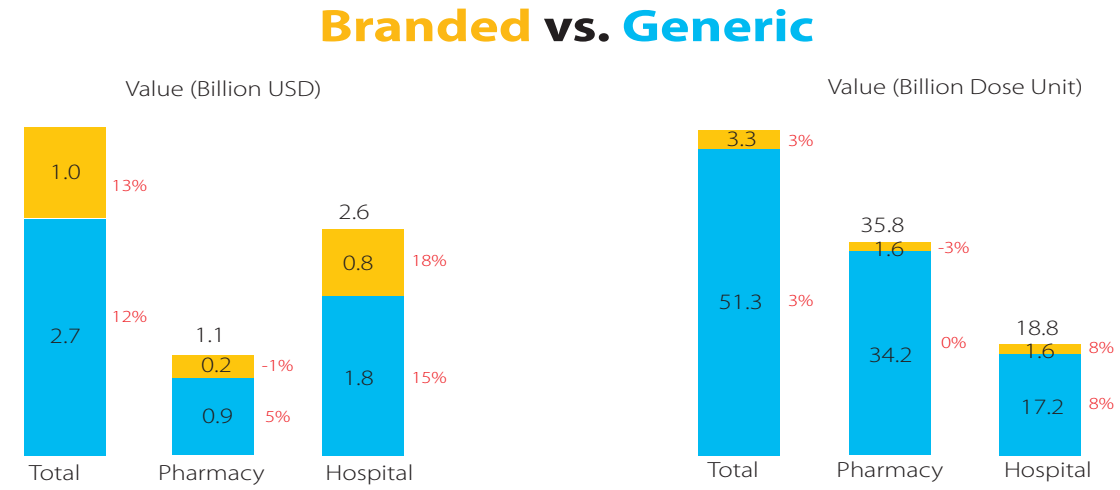
1 EuroCham's Healthcare Forum is a coordination platform for Sector Committees operating in the Healthcare industry– at present International Quality Medicines - Generic and Biosimilar (IQMED - Generic & Biosimilar), Medical Devices and Diagnostics (MDD SC) and Pharmaceuticals (Pharma Group). The Healthcare Forum enables industry representatives to discuss, share and advocate on common interests and topics. Given its inherently diverse nature, it also covers different interests of those industry representatives. All Sector Committees are equally supported by EuroCham

2 ICH: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. More information available at: <http://www.ich.org/home.html> last accessed on 22 December 2018.

3 Prime Minister Nguyen Xuan Phuc's speech at the National Health Insurance Teleconference on 3 June 2016.

4 "Total Vietnam Pharma Audit", IQVIA, February 2018. Available at: <https://www.quintilesims.com>, last accessed on 27 January 2019.

Figure 10: Vietnam's total pharma market split by branded and OPP[5]



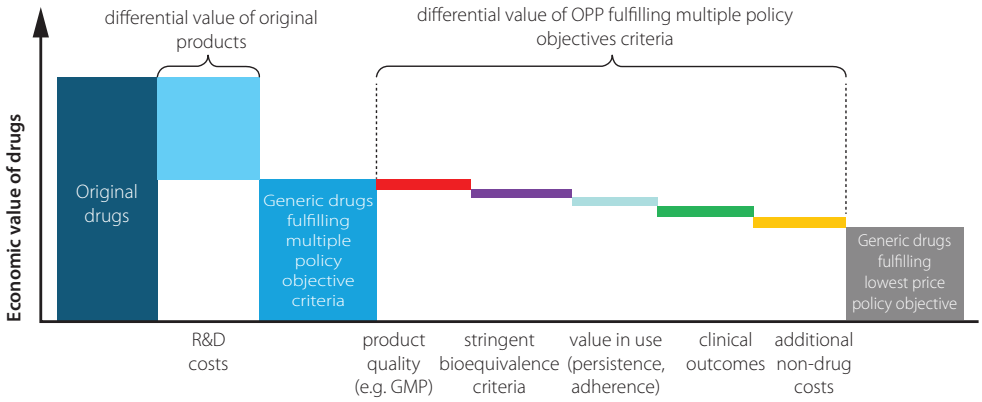
Source: IQVIA Sales Audit Q4/2017

However, there are value differences within OPP. These include Manufacturing Certification (EU or PIC/S Good Manufacturing Practice (GMP) and WHO GMP)[6], Stringent Bio-Equivalence Criteria, Value in Use (Persistence and Adherence), Clinical Outcome and Additional Drug Cost.

For example, there are regulatory-based differences when comparing sub-quality generics. Active Pharmaceutical Ingredients (APIs) used in high-quality OPP products should come from sources with either Drug Master File (DMF) or a Certification of Sustainability to the monographs of the European Pharmacopoeia Procedure (CEP). Facilities are regularly audited by the European Directorate for the Quality of Medicine and Healthcare (EDQM)[7] as well as local authorities of related EU countries, and the United States Food & Drug Administration (USFDA). There are OPP manufacturers who do run international pharmacoviligence systems, including in Vietnam, to continuously monitor the safety of their marketed products. All finished formulations of those OPP are considered as original or as having BA/BE studies with the reference product in the related countries. This means that the quality of those OPP is always measured to the reference/original product and cannot be inferior. These manufacturers have production sites in the EU, U.S. or other PIC/S countries and their products are marketed in these markets as well. Generics manufacturers who cannot fulfil the above-mentioned criteria are considered as manufacturers of sub-quality generics.

5 *Ibid.*
6 European Union (EU) Pharmaceutical Inspection Co-operation Scheme (PICS/S), Good Manufacturing Practice (GMP) and World Health Organisation (WHO).
7 Further information on EDQM is available at: <https://www.edqm.eu/> last accessed on 11December 2018.

Figure 11: Value differentiation between Off-Patent Pharmaceuticals[8]



Unfortunately, there is limited OPP differentiation in Vietnamese healthcare decision making, specifically in the areas of registration, reimbursement, formulary listing, and pricing. Therefore, the IQMED-Generic and Biosimilar Sector Committee initiated the evidence-based Health Technology Assessment (HTA) for OPP to sustain the accessibility of affordable and good quality medicine for the Vietnamese population.

Potential gains/concerns for Vietnam

The proper approach to OPP differentiation in Vietnam's healthcare decision making will not only achieve early patient access to high-quality OPP products but also ensure efficient public spending on healthcare management. Key positives for Vietnam's healthcare industry could be derived from adopting best practice in other markets. These include:

1. Ensuring comprehensive patient outcome and safety;
2. Sustaining high-quality OPP for Vietnamese patients with reliable pricing;
3. Ensuring efficiency in Government spending;
4. Increasing quality standards within OPP manufacturers;
5. Ensuring the reliability of manufacturers for Vietnamese patients.

Recommendations:

Evaluating current infrastructure conditions, the IQMED - Generic and Biosimilar Sector Committee proposes that the Government implement 3 important activities which will support the initiative of universal healthcare coverage:

- Upgrade differentiated category mechanisms in hospital tenders, taking into consideration the real-life patient outcome benefit factor. Differentiated categories will ensure medicine with the same quality level is reimbursed and evaluated in the same lot. This will sustain access to quality medicine in hospital tenders.
- Implement the Multi-Criteria Decision Analysis (MCDA) evaluation in drug decision making, i.e. the National Reimbursement Drug List (NRL), as this will ensure a comprehensive and transparent mechanism. Given the importance of the NRL and the comprehensive dossier required in its evaluation, MCDA would be the best-fit solution for an evaluation mechanism. The implementation should be based on the outcome of the workshop that took place in Hanoi on the 13th of July, 2017.[9] Participants in this workshop included 19 key stakeholders from the Ministry of Health (MOH) such as Drug Administration of Vietnam (DAV), Health

8 Kaló Z et al., Value in Health, 2015. Available at: <http://www.valueinhealthjournal.com> last accessed on 22 December 2018.
9 "IQGx Workshop on Multi-Criteria Decision Analysis (MCDA) Methodology and Applications in Decision-Makings for Off-Patent Pharmaceuticals (OPP)" *EuroCham Advocacy Update*. Available at: <https://www.eurochamvn.org/node/16779> last accessed on 22 December 2018.

Economics Association, National Centralised Drug Procurement Center, Finance and Planning Department, Medical Service Administration Department, Health Insurance Department and Vietnam Social Security.

- Following discussion during the Conference, adopting the MCDA framework is strongly recommended in order to support drug decision making in Vietnam, especially in the Drug Procurement (tender) process of OPPs. The next steps should include committee member finalisation and criteria selection, weighting and scoring for tender decisions. This should be followed by a customised framework for manufacturers to present their products for consideration.

Table 3: Initial MCDA, Definition and Performance Categories (Outcome)[10]

Name of criterion	Intended definition	Performance categories
Equivalence with the reference (original) product	To capture evidence on health outcomes from pharmaceutical, bioequivalence and clinical trials (efficacy data from controlled clinical settings)	› No data on pharmaceutical equivalence › Pharmaceutical equivalence › Interchangeability defined based on local criteria › Bioequivalence proven based on local criteria › Bioequivalence proven based on European EMA or U.S. FDA criteria › Therapeutic equivalence proven in clinical trial › Improvement in efficacy and/or safety based on clinical trial data
Real world clinical or economic outcomes such as adherence or non-drug costs	To capture evidence on health outcomes (effectiveness) and costs from real-world data	› No real-world data on equal a) tolerability, b) adherence and persistence, c) non-drug cost › International real world data on either equal a) tolerability, b) adherence and persistence, c) non-drug cost › Local real-world data on either equal a) tolerability, b) adherence and persistence, c) non-drug cost › International real-world data on improvement in a) tolerability, b) adherence and persistence, c) non-drug cost › Local real-world data on improvement in a) tolerability, b) adherence and persistence, c) non-drug cost
Product stability and drug formulation	To capture evidence on stability and drug formulation	› No data on product expiry or stability › Data on non-inferior product expiry or stability in the local environment › Data on improved product expiry › Data on improved product stability in the local environment › Data on improved product expiry and stability in the local environment
Quality assurance	To capture evidence on manufacturing, product quality and standardisation	› Limited information on quality assurance › Local/non-GMP quality assurance only for active product ingredient › Local/non-GMP quality assurance for the entire manufacturing process › WHO GMP certification › EU or PIC/s GMP

10 P.L. Tuan, P.H.T. Kiet, D. Brixner and V. H. Ngo (2017) *Development of multiple criteria decision making analysis framework for off-patent pharmaceuticals decision making in Vietnam*. Available at: <https://www.eurochamvn.org/sites/default/files/uploads/20171002%20_VN_MCDA_Whitepaper_ENG_FINAL_sent.pdf> accessed on 22 December 2018.

Macroeconomic benefit	To capture wider economic benefits of selecting the medicine (e.g. tax, investment, employment etc.)	› The manufacturer has no local investment in the country › The manufacturer has minor local investment in the country › The manufacturer has moderate local investment in the country › The manufacturer has significant local investment in the country
Reliability of drug supply	To capture the stability and reliability of drug supply (history and future guarantee)	› Major and multiple problems in the last 5 years › Minor and fairly frequent problems in the last 5 years › Single precedence of supply problems in the last 5 years › No precedence of supply problems in the last 5 years › Manufacturer is financially capable and willing to guarantee supply
Pharmacovigilance	To capture data collection and assessment on adverse events of pharmaceuticals	› No pharmacovigilance system › Qualified person for pharmacovigilance › Qualified person and sophisticated system to collect pharmacovigilance data
Added value service related to the product	To capture extra services provided alongside the drug with quantifiable and demonstrated outcomes/benefits	› No program or service › Availability of value-added service › Major value-added service with demonstrated outcomes
Price	Acquisition cost of the pharmaceutical product compared to the lowest price available	N/A

› Introduce a faster registration timeline for high-quality OPP and an effective product introduction and visa approval process to ensure such products are being introduced in a timely manner.

The IQMED - Generic and Biosimilar Sector Committee is strongly committed to further collaborating with the Government to bring global expertise, best-practice sharing, models and tools in planning and implementing these activities.

II. AFFORDABLE TREATMENT OPTIONS FOR VIETNAMESE PATIENTS

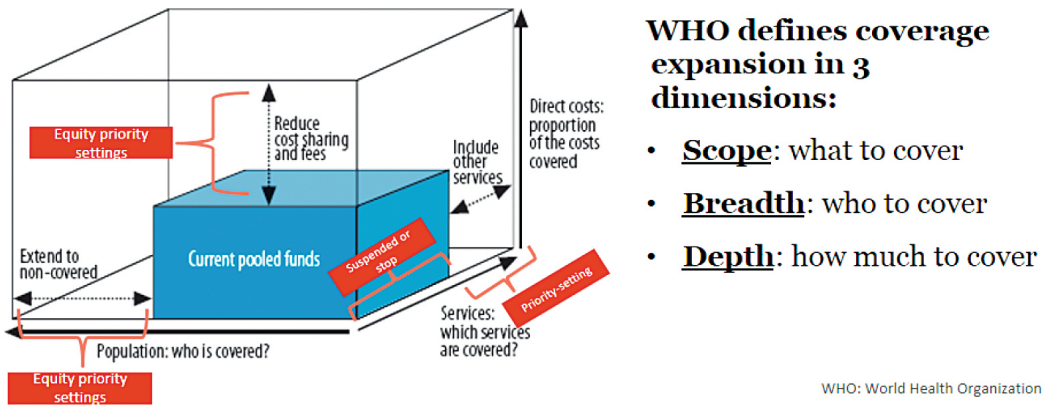
Relevant Government authorities: Ministry of Health (MOH), Vietnam Social Security (VSS), National Assembly (NA) – Committee on Social Affairs.

Issue description

One of the key healthcare objectives of the Vietnamese Government is universal coverage. According to Vietnam Social Security (VSS), by the end of July 2018, 87.2 per cent of the Vietnamese population has been enrolled and given access to the healthcare reimbursement system.[11] The coverage expansion not only enrolls more patients but also provides better benefits and reduces patients' self-pay if it is clearly defined with 3 dimensions aligning with WHO guidance.

11 87.2 per cent of the Vietnamese population has been covered by Health insurance, *Vneconomy*, available at < http://vneconomy.vn/ty-le-bao-phu-bao-hiem-y-te-dat-872-dan-so-2018080100563933.htm> last accessed on 23 January 2019.

Figure 12: Universal Healthcare Coverage 3-Dimensional Expansion



Source: World Health Organisation[12]

In practice, patients in Vietnam are currently overburdened with high out-of-pocket payments due to a shortage of quality healthcare facilities and long waiting times. Therefore, affordable treatment options are required. However, affordable treatment should not be at the cost of quality. MOH is considering alternative treatment options for the largest number of Vietnamese patients, whilst containing cost. Formulating policies for complex affordability issues requires strong collaboration between the Government and the industry.

The affordability of treatment is managed at multiple levels: First, at a product/drug level through the Government selection and assessment process; and second, at a service level through patient out-of-pocket costs during a hospital visit.

Affordability is not limited to price. It requires a proper assessment of the real cost of delivering the service in its entirety. The cost of using low-quality therapeutic solutions and the consequences of a medical error or infection has to be taken into consideration. Frequent hospital visits by a patient not only increases the pressure on hospital resources, but also exposes the patient to additional service fees, especially for those who have a chronic disease.

Potential gains/concerns for Vietnam

Vietnam is considered to have a high share of out-of-pocket payments, which means that a high proportion of households face severe difficulties managing their income and subsequently their health. Empowering patients to manage their health at home and developing home-care services will reduce the pressure on already crowded hospitals and reduce the out-of-pocket payments incurred by patients during hospital visits.

Opportunities exist to develop a process that assesses the merits of drugs or products using criteria over and above pricing. This will result in the establishment of a sustainable model of care, based on affordability.

Locally produced drugs or products do not automatically mean lower prices, and an equally branded/innovative product does not always mean value for money. That is why it is necessary to assess each product on its own merits, regardless of its origin, provided that quality standards are met.

Recommendations:

In our view, the Government should review product categorisation, such as branded or generics, in light of experience and data collected in recent years. The process should be revised to ensure that it is delivering the desired objectives, whilst ensuring continuous improvement in cost containment. The introduction of

12 "Health financing for universal coverage", *World Health Organisation*. Available at: <https://www.who.int/health_financing/strategy/dimensions/en/> last accessed on 28 January 2019.

pharmaco-economy-based assessment will ensure that the cost/effect relationship of products and drugs has been taken into consideration and this, in turn, is more likely to deliver a better distribution of funds.

We also believe that MOH should further facilitate the home treatment concept (out-patients) through favourable reimbursement schemes in order to reduce the number of hospital visits, especially by patients with chronic diseases. This will limit out-of-pocket payment for patients.

III. SUSTAINABLE SUPPLY SOURCE FOR LOCAL DEMAND

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

Issue description

The Government aims to have 80 per cent of domestic demand met by local producers by 2020, as specified in Decision 68.[13] The current ratio of domestic demand is 50 per cent, therefore, in order to achieve this objective, it is clear that a strong focus on investment in local 'quality' manufacturing from foreign organisations is needed.

Another critical aspect to accomplish this objective is to put in place a transparent and robust tender process, ensuring the Government achieves value for money. However, there are two key issues with the current tender process as it stands. First, the tender result for each category only includes one choice of supplier. It does not include alternative suppliers or a commitment on tender quantities, which can result in critical shortages. Moreover, based on current product categorisation for the procurement process, products in the same or different categories may not necessarily reflect the true overall value of each product.

Potential gains/concerns for Vietnam

The IQMED - Generic and Biosimilar members could offer long-term, affordable medical solutions with guaranteed quality standards for the Vietnamese healthcare market. However, local regulations, policies and guarantees should be put in place to ensure local long-term investment. Meanwhile, long-term commitments for marketing authorisations should be curtailed to supply the market with more choice in terms of price and quality. Both are important factors contributing to the improvement and efficiency of spending on State budgets and health insurance funds. Not only will this secure stable supplies, but it will also increase the number of Vietnamese working in the production sector, thus creating employment opportunities for the Vietnamese population.

Recommendations:

- The Government should have clear policies and guarantees to strongly support the long-term presence and investment of foreign investors in the Vietnamese market, ensuring 80 per cent of domestic demand can be met by local qualified producers in the coming years;
- Continue an advanced categorisation of the procurement process in Vietnam that will present opportunities for improvement, deliver benefits to the Government and control the budget. Both relevant authorities and key stakeholders have now obtained adequate experience of and insight into the current process of procurement, including the categorisation of drugs. The IQMED - Generic and Biosimilar member companies recommend further detailed discussions about the identified gaps in the process and opportunities for improvement;
- The relevant authorities shall have measurements for the actual volume which suppliers must strictly commit to deliver; and
- A mechanism should be set up to allow hospitals to buy a 2nd choice, and for the insurance to reimburse the same value as the winning tender – in cases of limited supplies or unavailability.

13 Decision 68/QD-TTg dated 10 January 2014 of the Prime Minister approving the National Strategy for development of the pharmaceutical industry in the period to the year 2020 and vision to 2030.

PART 2: **BIOSIMILAR**

OVERVIEW

Biological medicines, also known as first-generation biopharmaceuticals, have been produced for the last 30 years and are in clinical use for a number of diseases. Recently, the expiry of many of these product patents led to the development of other similar biologics at lower costs, with the same safety, purity and potency as their original (reference) medicines. These similar biologics are generally referred to as biosimilars.

Biosimilar medicines are not the same as generic medicines (a medicine which contains exactly the same molecule as an existing chemical medicine, such as aspirin). This is because, unlike chemical medicines, biological medicines cannot be exactly copied. Biosimilar medicines also have nothing to do with complementary or natural medicines nor with herbal medicines. However, biological medicines (including biosimilar medicines) come from living organisms, such as living cells that have been modified using biotechnology. This allows these living organisms or cells to produce the active substance of the biological medicine. This active substance is then harvested from the cells. These active substances (e.g. proteins) are usually larger and more complex than those of chemical medicines.

BIOSIMILAR: INCREASING PATIENT ACCESS TO STATE-OF-THE-ART THERAPIES

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

Issue description

The development of biosimilars is an attempt to improve access challenges faced by patients, generate cost savings for healthcare systems and increase treatment options for healthcare professionals.

Potential gains/concerns for Vietnam

Benefit for patients:

The introduction of affordable, high-quality biosimilars improves access to life-changing medicines for patients worldwide. The EU saw a 100 per cent increase in the use of biologic treatments after the introduction of biosimilars in the EU.[14]

Benefit for HCPs:

Introduction of biosimilars drives competition, resulting in increased treatment options and value-added services to support patient care and the healthcare community. Between 2016 and 2020, 225 new active substances are set to come to market worldwide, with 30 per cent expected to be biologics.

Benefit to Payors

Biosimilars introduce competition, increasing the affordability of biologics which delivers savings for healthcare systems, helping to liberate resources that can be used to improve care and fund next-generation medicines. Cumulative savings over the next five years (2016-2021) in the EU5 and the U.S. combined could range from 49 billion EUR to 98 billion EUR.

14 "Biosimilars", *US FDA*. Available at: <https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/> last accessed on 28 January 2019.

Health economic benefit from biosimilar medicines (in the EU)

Aging is accelerating in the EU. In supporting the growing elderly population, EU countries will be obliged to spend an increasing proportion of their GDP to provide the required level of healthcare coverage. New and innovative therapies offering irrefutable advances, will continue to escalate costs and increase patient expectations. Healthcare expenditure is high on the agenda of every Member State in the EU, with all governments being tasked to deliver the best and most-up-to-date patient care, while at the same time trying to limit the potentially huge increases in associated costs. Over the past 10 years, the introduction of high-quality biosimilar medicines has made a significant impact in reducing healthcare expenditure across EU. This reduction has helped to manage the budgets and have allowed better access to important medicines for a greater number of patients.[15]

Recommendations:

Based on EU experience, the IQMED - Generic and Biosimilar recommends the Government to consider and facilitate the introduction of high-quality biosimilar medicines to reduce the health expenditure and balance the healthcare expectations.

ACKNOWLEDGEMENTS

EuroCham International Quality Medicines – Generic and Biosimilar Sector Committee

15 "Delivering on the Potential of Biosimilar Medicines", *IMS Institute for Healthcare Informatics (2016).*