ASEAN PHARMACEUTICAL REGULATORY POLICY

Draft - Version of August 31 2021

(Document reflecting consensus of PPWG and AHC 3)

ASEAN Pharmaceutical Regulatory Policy

Version of August 31

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Abbreviations

ACCSQ	ASEAN Consultative Committee for Standards and Quality
ACTD	ASEAN Common Technical Dossier
ACTR	ASEAN Common Technical Requirements
AHC 3	ASEAN Health Cluster 3
APRF	ASEAN Pharmaceutical Regulatory Framework
APRP	ASEAN Pharmaceutical Regulatory Policy
BE MRA	ASEAN Mutual Recognition Arrangement (MRA) for Bioequivalence (BE) Study Reports of Generic Medicinal Products
GMP MRA	The ASEAN Sectoral MRA for Good Manufacturing Practice Inspection of the Manufacturers of Medicinal Products
PPWG	ASEAN Pharmaceutical Product Working Group
PMAS	Post Market Alert System

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Introduction

ASEAN leaders have agreed on the establishment of a single market and production base across ASEAN. This vision is articulated in ASEAN Chapter and ASEAN Economic Community Blueprint documents. Pharmaceuticals, due to their socio-economic implications represent an important element in this vision. Aside from that, the ASEAN leaders stressed the importance of rapid access to essential pharmaceutical products in order to manage public health emergencies and agreed to initiate ASEAN cooperation on Drugs and Vaccine Security and Self-Reliance.

Aiming to remove technical barriers to trade, the ASEAN Economic Ministers have adopted the ASEAN Trade in Goods Agreement in 2009 and delegated the ASEAN Consultative Committee for Standards and Quality (ACCSQ) to oversee the implementation of initiatives for a single pharmaceutical market and production base for the deeper economic integration. The ACCSQ has a key coordinating role in shaping ASEAN market integration for trade of goods and collaborates with Member States' regulatory bodies in this effort.

To facilitate the development of strategies and integration initiatives eliminating technical barriers in trade of pharmaceuticals, ACCSQ established the ASEAN Pharmaceutical Product Working Group (PPWG), comprising representatives from all ASEAN Member States' regulatory authorities for pharmaceuticals.

The PPWG has been established:

- to support a reduction of technical barriers to trade in the pharmaceutical products; and
- to provide improved access to pharmaceutical products, without compromising the safety, efficacy and quality of pharmaceutical products placed in the ASEAN market.

Since its establishment, PPWG has pursued harmonization and recognition in several important areas of pharmaceutical regulation. The results of these initiatives include the development of:

- ASEAN Sectoral MRA on GMP Inspection for Manufacturers of Medicinal Products (GMP MRA),
- Post Market Alert System (PMAS),
- ASEAN Common Technical Dossier (ACTD),
- ASEAN Common Technical Requirements (ACTR),
- ASEAN MRA for Bioequivalence of Study Reports of Generic Medicinal Products (BE MRA)

These initiatives are in differing stages of implementation and comprise a combination of voluntary measures as in the ACTD, ACTRs and PMAS and obligatory requirements in the GMP MRA and the BE MRA. To achieve the final objective – ASEAN free market of pharmaceutical products - the PPWG has recognised a need to enhance and expand these initiatives, enabling systematic coordination, implementation and monitoring.

The ASEAN Health Ministers have established Health Cluster 3 (AHC 3): *Strengthening health system and access to Care.* This group of experts focus on the developmental aspects of healthcare with the objectives of ensuring that the ASEAN Community has universal access to essential health care, safe and good quality medical products including traditional and complementary medicines.

Noting current needs for ensuring a timely access of pharmaceutical products to ASEAN citizens, to address management of emergency situations and concerns on substandard and falsified pharmaceuticals, the ASEAN Health Ministers have adopted several initiatives to integrate supply chain of pharmaceuticals and to ensure ASEAN secure access to drugs and vaccines. The alignment of regulatory pathways, promotion of regional collaboration and institutional strengthening aiming at implementation of International/WHO regulatory standards are seen crucial to achieve the objectives of these initiatives. It has been recognised, that in order to provide a structure and instruments to realise the free flow of safe, efficacious and quality pharmaceuticals in the region, to facilitate access to needed pharmaceuticals and eliminate substandard and falsified products, it is important to adopt first a common ASEAN Pharmaceutical Regulatory Policy (APRP). The APRP will include the principles and other key features serving as a common basis for coordination and development of the ASEAN Pharmaceutical Regulatory Framework (APRF) and will be followed by the development of legal instruments when required to implement such policy. The APRP will provide guidance for the development of additional initiatives to support the integration of the market in the pharmaceutical sector.

The basis and the vision of the proposed ASEAN Pharmaceutical Regulatory Framework is the close cooperation and collaboration of *National Regulatory Authorities*[1], which operate using common standards and procedures, eventually recognise each other's regulatory outcomes or come jointly to a common regulatory position.

Creation and deployment of the APRP requires consultation with and collaboration of stakeholders having roles within pharmaceutical regulatory framework, especially those involved in production and distribution chain of pharmaceuticals, regulators, healthcare professionals and the public.

The ASEAN Pharmaceutical Policy will be reviewed periodically and updated as required to reflect new developments in ASEAN health policies and in global pharmaceutical regulatory environment.

Objectives

- To provide a basis, direction and a policy framework to ASEAN Member States and ASEAN National Regulatory Authorities to facilitate the development of harmonised strategies that facilitate enhancement of national regulatory systems and market integration initiatives;
- To support the measures adopted for removal and reduction of technical barriers to intra ASEAN trade in the pharmaceutical products[2] in order to develop an integrated ASEAN Market and to enhance ASEAN pharmaceuticals security and self-reliance;

[1] *For the purpose of the APRP the National Regulatory Authority means the National Regulatory Authority responsible for regulation of pharmaceuticals in ASEAN Member States. There may be a single National Pharmaceutical Regulatory Authority in an ASEAN Member state or there may be additional institutions responsible for specific sectors of pharmaceutical regulation or certain prescribed regulatory functions. In such case each of the authorities is considered to be included in the term "National Regulatory Authority".*

[2] *Pharmaceutical product*

a. Any substance or combination of substances presented for treating or preventing diseases in human beings or

- To ensure timely access to high quality, safe and efficacious pharmaceutical products and their availability through transparent and accountable procedures in order to support healthcare systems in ASEAN and protect public health;
- To enhance efficiency and effectiveness of regulatory practices in ASEAN by strengthened cooperation among ASEAN National Regulatory Authorities in regulation of pharmaceutical products, including vaccines, antidotes and other critical or life-saving pharmaceuticals, entering the market in ASEAN Member States, based on regulatory and technical standards, practices and guidelines jointly agreed by ASEAN National Regulatory Authorities; and
- To strengthen cooperation among ASEAN National Regulatory Authorities in combating pharmaceutical products and pharmaceutical operators[3] non-compliant with relevant legislation and regulatory requirements.

Scope

The APRP addresses sectors concerned with quality, safety, efficacy and availability of pharmaceuticals from the health and economic aspects. The scope encompasses the development of the policies, approval and recognition arrangements, harmonised regulatory requirements and practices by governmental institutions and associated supporting mechanisms of ASEAN Member States for human pharmaceutical products placed on the market in ASEAN Member States, including vaccines, antidotes and other critical or life-saving pharmaceuticals. The scope additionally includes all activities related to the development, testing, manufacture and distribution of pharmaceutical products.

Apart of marketed pharmaceuticals, the APRP deals with special categories of non-marketed pharmaceutical products especially medicines used in emergency situations, including vaccines, antidotes and other critical or life-saving pharmaceuticals, or medicines for a special access use[4].

The APRP does not apply to veterinary pharmaceuticals and to other categories of health products such as medical devices, traditional medicines, health supplements and cosmetics, which are subject to other ASEAN Agreements.

The APRP does not apply to regulation of pricing of pharmaceutical products. The APRP does not prevent an individual ASEAN Member State and its health authority to adopt specific measures in emergency and special situations identified by and relevant to such Member State.

Principles

These principles establish common grounds for construction of a collaborative arrangement of ASEAN National Regulatory Authorities. Actions undertaken for the planning, implementation and monitoring would be guided by these principles through a close and structured cooperation arrangements.

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b. Any substance or combination of substances which may be administered to human beings with a view to making a medical diagnosis or to restoring, correcting or modifying physiological function in human beings.

Pharmaceutical products include, for example, chemical medicinal products, biological medicinal products (e. g. vaccines, /anti/toxins), including medicinal products derived from human blood or human plasma, advance therapy medicinal products (e. g. gene therapy medicinal products, cell therapy medicinal products), herbal medicinal products and radiopharmaceuticals.

[3] *Pharmaceutical operators—government and non-governmental entities involved in development, pre-clinical and clinical testing, manufacture, laboratory testing or distribution of pharmaceutical products.*

4 Special access use – regulatory pathway for making an unapproved, mostly new pharmaceutical product available to treat a seriously ill patient when no other treatments are available.

I. Integrated "Life-Cycle" Approach

To ensure the quality, safety and efficacy of pharmaceuticals in ASEAN, it is necessary to consider all relevant aspects of development (including preclinical and clinical testing), sourcing of materials, production, placement on the market and market withdrawals, distribution, product-related information, post-marketing oversight (including market surveillance and pharmacovigilance), use and disposal.

Guidance for Implementation

Regulatory and control systems in ASEAN Member States should supervise and evaluate these activities according to regulatory requirements, harmonized standards and good practices and to enable necessary action to be taken whenever necessary.

II. Harmonized standards and good practices

Harmonisation of technical regulatory requirements, standards, practices and guidelines should cover all elements related to regulation of quality, safety and efficacy of pharmaceuticals throughout the life-cycle. The harmonized technical requirements, standards, practices and guidelines should be based on international standards, practices and guidelines for pharmaceutical products, including those developed by WHO[5], OECD[6], ICH[7] and PIC/S[8], unless there are substantiated reasons based on scientific or technical information.

Guidance for Implementation

All ASEAN Member States shall participate in the development of ASEAN harmonized technical regulatory requirements, standards, practices and guidelines and should implement them according to jointly agreed timetable.

ASEAN Member States are encouraged actively participate in the development of international technical regulatory standards, practices and guidelines for pharmaceutical products to ensure that the concerns of the region are considered.

III. Legislation for pharmaceutical regulation

ASEAN Member States shall ensure, to the furthest extent possible, that national pharmaceutical legislation is comprehensive, up to date, covers all necessary elements, is aligned with international and ASEAN Agreements whenever applicable and supportive to implementation of the ASEAN Pharmaceutical Regulatory Policy.

The regulatory actions, cooperation and mutual recognition agreements among ASEAN Member States should be supported by appropriate legal arrangements whenever necessary.

Guidance for Implementation

Each Member State shall subject a finished pharmaceutical product to marketing authorisation before its placement on the market. Legislation should define responsibilities of marketing authorization holders, pharmaceutical operators and regulators for all stages of the life-cycle, referencing ASEAN harmonized regulatory requirements, international standards, practices and guidelines whenever these are available and appropriate. Legislation should also deal with public health emergencies and

[5] *World Health Organization*
[6] *Organization for Economic Co-operation and Development*
[7] *International Conference on Harmonization*
[8] *Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme for Pharmaceutical Products*

special situations in which pharmaceutical products may be authorized for use by other than conventional marketing authorization procedures.

Regulatory bodies should be adequately empowered to enforce the regulatory requirements and legislation.

IV. Regulatory assessments, inspections and testing

Member States should undertake all necessary measures to ensure that only pharmaceutical products which conform to the available harmonized ASEAN technical regulatory requirements, international standards, practices and guidelines are granted marketing authorisation. Member States should not refuse, prohibit or restrict the granting of marketing authorisation to any such pharmaceutical products which comply with the harmonized ASEAN technical regulatory requirements, standards, practices and guidelines unless there is a justifiable health risk or other concern as defined in national legislation or there is a contradiction to the national health policy.

The regulatory assessments, inspections and testing should reflect the risk-based assessment of individual pharmaceutical products and activities of pharmaceutical operators and should respect risk benefit-consideration especially in public health emergency and special situations as identified by and relevant to the ASEAN Member State.

Guidance for Implementation

Regulatory evaluations and controls should be carried out in an independent, objective, and transparent manner, using relevant contemporary scientific information and data. Harmonised technical regulatory requirements, standards, practices and guidelines should all be respected. Regulatory decisions should be appropriately justified, documented and communicated to the parties concerned.

Appropriate preventive and/or corrective measures should be taken whenever there is a risk to public health.

During the transition to the implementation of the APRP, pharmaceutical products which have yet to comply with the harmonized ASEAN technical regulatory requirements, standards, practices and guidelines may continue to be placed in Members States' markets–through existing national arrangements. Such products will only enjoy benefits of the ASEAN integrated pharmaceutical market after compliance with harmonized ASEAN technical regulatory requirements, standards, practices and guidelines is achieved].

V. Collaboration to increase effectiveness and efficiency, to reduce duplication of resources and enable mutual recognition of regulatory decisions.

Effectiveness, efficiency, risk-based proportionality and minimization of duplication through collaboration, work-sharing, reliance and mutual recognition should guide the organization of regulatory work in ASEAN. The regulatory outcomes and decisions accomplished via active participation of all ASEAN Member States by harmonised procedures should be recognized by all ASEAN Member States, if applicable. An arbitration or reconciliation procedure should be defined to resolve non-acceptance situations.

In order to avoid unnecessary duplication of effort, assessments and controls of pharmaceutical products and pharmaceutical operators performed by other countries, regions or relevant international bodies in line with international or equivalent standards should be considered by ASEAN National Regulatory Authorities. International consultations should be held, when necessary.

Guidance for Implementation

To increase effectiveness and efficiency by reducing duplication, regulatory expenditures and wastage of invested resources, the National Regulatory Authorities *of ASEAN Member States should establish an effective arrangement, by which the* National Regulatory Authorities of Member States *will be able to closely collaborate, harmonize their regulatory requirements, share evaluations for market authorisation of pharmaceuticals, share outcomes of inspections, testing results, pharmacovigilance assessments and other regulatory outcomes.*

The scope of contribution to the development and participation in the collaborative arrangement of ASEAN pharmaceutical regulatory bodies may vary according to expertise and resources available in ASEAN Member States. Continual strengthening, development and harmonization of regional regulatory requirements should be undertaken to respond to the local regulatory challenges and changes in the global regulatory environment.

The structured cooperative arrangement will enable collaboration in all phases of the life cycle, from product development to final use and include collaboration on assessments of pharmaceutical products of common interest–providing scientific opinion on emerging issues. The cooperative arrangement of ASEAN pharmaceutical regulators will serve as a platform for collaboration in all regulatory operations, especially including inspections, marketing authorisations, pharmacovigilance, laboratory testing and market surveillance. This cooperative arrangement should facilitate regulatory actions against substandard and falsified products and pharmaceutical operators non-compliant with relevant legislation, regulatory standards and regulatory decisions. It would comprise the National Regulatory Authorities*, committees, task forces and other bodies functioning under the direction of a committee of senior representatives of Member States* National Regulatory Authorities*.*

VI. Strengthening and Harmonisation of Regional and National Pharmaceutical Regulatory Systems

ASEAN Member States shall ensure that national plans or roadmap be available to define and monitor the implementation of ASEAN harmonised requirements, standards, practices and guidelines.

ASEAN Member States shall ensure that adequate resources are allocated where needed to ensure that all elements of the ASEAN Pharmaceutical Framework function effectively, including National Regulatory Authorities and all other bodies within the collaborative arrangement ASEAN Pharmaceutical Regulatory bodies established to implement the APRF.

Guidance for Implementation

ASEAN Member States should ensure that their national pharmaceutical regulatory systems function effectively, are at a level of performance, efficiency and effectiveness that supports the implementation of the ASEAN Pharmaceutical Regulatory Policy, and that National Regulatory Authorities*–in their territories fully participate in the development of structured cooperative arrangement of ASEAN Pharmaceutical Regulatory bodies including its operating procedures. The Member States will foster the compatibility of regulatory approval processes and adoption and implementation of harmonized requirements, standards, practices and guidelines, wherever possible.*

ASEAN Member States should seek to ensure that unnecessary regulatory and administrative barriers to intra -ASEAN trade are eliminated. There should be established cooperation and information exchange between regulatory authorities and relevant stakeholders to combat the move of substandard and falsified pharmaceutical products.

Particular attention should be given to assist ASEAN Member States with less advanced pharmaceutical regulatory system in their effort to bring their system to the desired level. In this

regard, ASEAN Member states with advanced pharmaceutical regulatory systems, where applicable and possible, should provide technical assistance on a bilateral or multilateral level.

VII. Transparency and information sharing

ASEAN Member States shall ensure the development and implementation of policies, plans and regulatory requirements for pharmaceuticals is undertaken in a transparent manner. ASEAN Member States shall make every effort to ensure effective communication of policies, plans and regulations with all stakeholders, including pharmaceutical operators, healthcare professionals, general public and other stakeholders at national and regional levels.

Pharmaceutical operators, healthcare professionals, and general public should be informed of the objectives and rationale for introducing regulatory measures and be invited to contribute to the decision-making process when applicable. Views of affected parties should be taken into account.

Transparency and public availability of information on institutional arrangements and regulatory measures in ASEAN Member States lead to clarity of requirements, facilitate implementation, compliance and communications between all parties involved in pharmaceutical regulation. For this purpose, the ASEAN Member States will make measures of general application relating to pharmaceutical products readily available to interested persons together with an implementation timetable. Reasonable time between the information release and entry into force of such measures should be provided, except where not possible on grounds of urgency.

Transparency in regulatory requirements and the information sharing among Members States' National Regulatory Authorities would support ASEAN initiatives on recognition and cooperation between the Member States. The sharing of information shall be in a manner that respects the confidentiality of proprietary information and appropriate arrangements should be adopted that ensure to enable the sharing of such information possible when needed.

ASEAN Member States should undertake education of relevant parties to enhance awareness on regulation.