ASEAN Pharmaceutical Regulatory Policy

one vision
one identity
one community

ASEAN Pharmaceutical Regulatory Policy

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ASEAN: A Community of Opportunities for All

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Foreword

The adoption of the ASEAN Pharmaceutical Regulatory Policy (APRP) by the ASEAN Economic Ministers and ASEAN Health Ministers, in 2022, marks a significant milestone in ASEAN's ambitious goals of integrating the market for pharmaceutical products and for ensuring timely access to high quality, safe and efficacious pharmaceutical products and ultimately protect the health of the ASEAN people. The APRP sets the foundation for enhanced harmonisation of regulatory requirements, deepening the collaboration between ASEAN's national regulators, and creating an enabling environment for innovation, investment, and trade in the pharmaceutical sector.

DATO LIM JOCK HOI
Secretary-General of ASEAN

Pharmaceutical priorities are shared responsibilities of different stakeholders and national line agencies. For many years, the Economic and Health Sectors have made significant progress in integrating the ASEAN pharmaceutical sector through initiatives to improve access to medicines, harmonise technical requirements and promote mutual recognition of inspections and reports for pharmaceuticals. Nevertheless, there is a wide spectrum of areas where further collaboration would be desirable from both the economic and healthcare perspectives.

I am glad to note that the APRP has been developed in an efficient manner through close collaboration of officials from ASEAN Member States' Economic and Health Sectors. The concurrent adoption of the APRP demonstrated a paradigm shift in ASEAN's policy towards a holistic approach to cross-sectoral collaboration in the pharmaceutical sector. This will ultimately lead to further development, convergence, and harmonisation of the structure of the national regulatory systems across ASEAN. The adoption of the APRP sets in motion a new plan for development of the ASEAN Pharmaceutical Regulatory Framework Agreement. which will link the existing and future initiatives and instruments developed by Economic and Health Sectoral Bodies in ASEAN and provides a pathway for an extension of cooperation and collaboration through the entire life-cycle of pharmaceutical products.

DATO LIM JOCK HOI
Secretary-General of ASEAN

Introduction

ASEAN leaders have agreed on the establishment of a single market and the production base across ASEAN. This vision is articulated in the ASEAN Charter and ASEAN Economic Community Blueprint 2025 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 harmonisation 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 for pharmaceutical products - 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 secure access to drugs and vaccines in ASEAN. 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 a comprehensive set of 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 recognising 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 the production and distribution chain of pharmaceuticals, regulators, the healthcare professionals and the public.

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

[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". In order to ensure that all aspects of the product life-cycle are considered in the regulatory function of Member States, inter-agency coordination would be appropriate when different authorities are responsible in specific stages and aspects of the life cycle.*

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;
- 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.

[2] *Pharmaceutical product:*

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

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/biopharmaceuticals), 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. Each AMS may define the scope of pharmaceutical products subject to its laws and regulations for pharmaceutical products in its territory respecting common principles.

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

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, for example, 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 from 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]. 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.

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.

[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.

Principles

These principles establish common grounds for the 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 arrangement.

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[5], use and disposal.

Guidance for Implementation

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

II. Harmonised 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 harmonised technical requirements, standards, practices and guidelines should be aligned with the international standards, practices and guidelines for pharmaceutical products, including those developed by WHO[6], OECD[7], ICH[8] and PIC/S[9], unless there are substantiated reasons based on scientific or technical information.

[5] *Post-marketing oversight – a set of regulatory measures overseeing post-approval commitments and reporting of marketing authorization holders and post-approval development and changes of pharmaceutical products. It includes renewals and withdrawals of marketing-authorizations, regulatory post-approval inspections, pharmacovigilance and market surveillance.*
[6] *World Health Organization*
[7] *Organization for Economic Co-operation and Development*
[8] *International Council for Harmonisation*
[9] *Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme for Pharmaceutical Products*

Guidance for Implementation

All ASEAN Member States shall participate in the development of ASEAN harmonised technical regulatory requirements, standards, practices, and guidelines and should implement them in their national regulatory requirements according to jointly agreed timetable. Additional specific national requirements should not be maintained unless there are substantiated reasons based on scientific or technical information.

ASEAN Member States are encouraged to 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, and 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 arrangements 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 for marketing authorisation before its placement on the market. Legislation should define responsibilities of marketing authorisation holders, pharmaceutical operators and regulators for all stages of the life-cycle, referencing ASEAN harmonised regulatory requirements, international standards, practices and guidelines whenever these are available and appropriate. Legislation should also deal with public health emergencies and special situations as identified by and relevant to Member States in which pharmaceutical products may be authorised for use by other than conventional marketing authorisation 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 ASEAN harmonised 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 ASEAN harmonised technical regulatory requirements, standards, practices, and guidelines unless there is a justifiable health risk or other concerns as defined in the 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 considerations 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. The efficiency in the regulatory processes and reduction of the regulatory burden of Members States could be facilitated through the adoption of a risk-based approach in regulation. 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 ASEAN harmonised technical regulatory requirements, standards, practices and guidelines may continue to be placed in ASEAN Members States' markets through existing national arrangements, to ensure to the farthest extent possible, uninterrupted patient access to those products. Such products will enjoy benefits of the ASEAN integrated pharmaceutical market after compliance with ASEAN harmonised technical regulatory requirements, standards, practices and guidelines applicable for these products is achieved, as appropriately determined by ASEAN Member States.

V. Collaboration to Increase Effectiveness and Efficiency, to Reduce Duplication of Resources and Enable Mutual Recognition or Adoption of Jointly Developed Regulatory Decisions.

Effectiveness, efficiency, risk-based proportionality and minimisation of duplication through collaboration, work-sharing, reliance, and mutual recognition should guide the organisation of regulatory work in ASEAN. The regulatory outcomes and decisions accomplished via active participation of all ASEAN Member States where possible, through harmonised procedures should be recognised 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. Bilateral or multilateral consultations should be held, when necessary.

The concepts of reliance and recognition supported by robust reliance processes, including the listing of stringent Reference Regulatory Authorities and adoption of these concepts in daily practice are critical to minimise duplication of work and improve efficiency and effectiveness in regulatory decision making.

Guidance for Implementation

To increase effectiveness and efficiency by reducing duplication, regulatory expenditures and wastage of invested resources, the ASEAN National Regulatory Authorities should establish an effective arrangement, by which the National Regulatory Authorities of Member States will be able to closely collaborate, harmonise 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 National Regulatory Authorities may vary according to expertise and resources available in ASEAN Member States. Continual strengthening, development and harmonisation 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, including but not limited to inspections, clinical trials, assessments

of pharmaceutical products submitted for marketing authorisation and post-approval changes, pharmacovigilance, laboratory testing, market surveillance and providing scientific opinion on pharmaceutical products of common interest and emerging issues. This arrangement should also 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.

Member States should develop and implement specific initiatives for recognition and reliance in a stepwise approach, based on the level of regulatory confidence and developments in the ASEAN Member States.

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

ASEAN Member States shall ensure that national plans or roadmaps will 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 of 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 harmonised 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 movement of substandard and falsified pharmaceutical products within the ASEAN region.

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.

Guidance for Implementation

Transparency and public availability of information on institutional arrangements and regulatory measures in ASEAN Member States will 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 conducted 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 and regulatory arrangements at both national and regional levels.

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