



# Comparative Regulatory Requirements and Strategic Decisions for Asean Markets for Topical and Nasal Route Dosage Forms

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## KEYWORDS

Strategic  
Decisions, Asean  
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## ABSTRACT:

**Introduction:** Regulatory frameworks for topical and nasal dosage forms in ASEAN (Association Southeast Asian Nations) countries remain fragmented, creating challenges for pharmaceutical companies pursuing multi-country approvals.

**Objectives:** To evaluate and compare the regulatory requirements for topical and nasal dosage forms across ASEAN markets, and to propose strategic approaches for effective regulatory submissions.

**Methods** Regulatory documents and market-specific guidelines were reviewed for all ten ASEAN member states, supported by insights from practical submissions and case examples.

**Results:** Distinct differences were identified in dossier format adherence, reference product criteria, bioequivalence expectations, and country-specific documentation and testing norms.

**Conclusions:** Country-specific regulatory strategies, supported by harmonization tools such as ACTD and Mutual Recognition Arrangements (MRAs-In the ASEAN region, MRAs are part of efforts to promote regulatory convergence, reduce duplication, and expedite product approvals across member states), are essential for accelerating approvals across ASEAN.

## 1. Introduction

The ASEAN pharmaceutical landscape is complex due to varying country-specific regulations despite regional harmonization efforts. This complexity becomes more prominent for topical and nasal dosage forms, where local requirements such as reference product obligations, stability conditions, and in vitro studies vary significantly.

Pharmaceutical companies must understand and comply with both ASEAN-wide guidelines such as the ACTD and ACTR and individual national requirements to achieve timely product approvals and ensure patient access to quality medicines<sup>1,2</sup>.

This article compares regulatory requirements across ASEAN nations and provides strategic insights to help Marketing Authorization Holders (MAHs) develop effective and compliant regulatory pathways for topical and nasal dosage forms.

## 2. Objectives

The primary objective of this study is to evaluate and compare the regulatory requirements applicable to topical and nasal dosage forms across ASEAN member countries. In doing so, the study aims to identify regional divergences and convergence points and recommend tailored strategies that optimize regulatory submissions and approvals.



**Export Sales Trend Analysis for Topical and Nasal Dosage Forms (2019–2023):** In addition to regulatory comparisons, export sales data of topical and nasal dosage forms in ASEAN markets provide insight into demand trends and strategic focus areas for manufacturers. Over the last five years, topical formulations have consistently held a higher market share compared to nasal formulations, although both categories have shown upward trajectories.

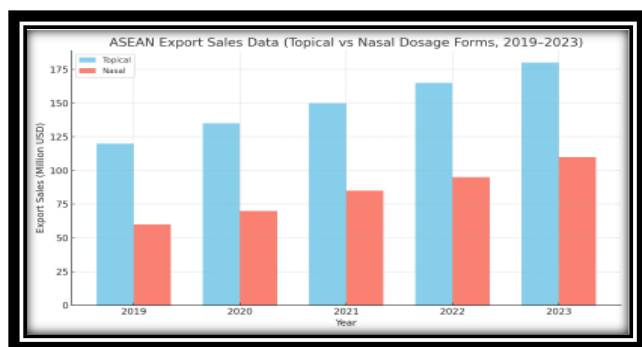


Figure 1: ASEAN Export Sales Data for Topical vs Nasal Dosage Forms (2019–2023)  
(Values in Million USD)

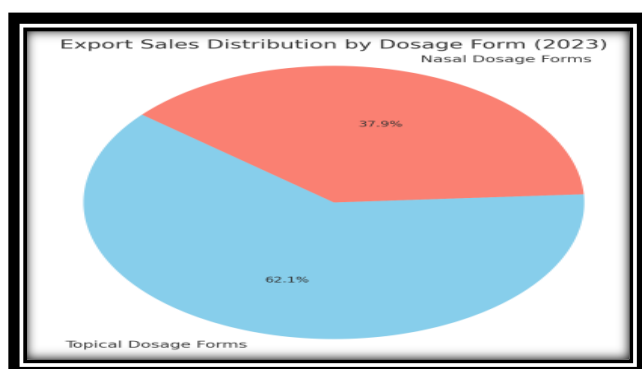


Figure 2: Export Sales Distribution by Dosage Form in ASEAN – Year 2023

As shown in Figure 1, export sales of topical dosage forms rose from USD 120 million in 2019 to USD 180 million in 2023, while nasal formulations increased from USD 60 million to USD 110 million during the same period. This indicates sustained growth across both categories. The 2023 distribution (Figure 2) highlights that topical products constituted approximately 62% of total exports, reinforcing their dominant position in ASEAN trade dynamics.

For a pharmaceutical product to gain approval across the ASEAN markets, it must meet the varied and unique requirements of each country. Understanding these regulatory differences and harmonizing them during product development is crucial for timely market access and ensuring patient safety<sup>1,2</sup>.

This research provides a detailed examination of the regulatory nuances within ASEAN, offering strategies that can help pharmaceutical companies overcome barriers to approval. The impact of factors such as query timelines, approval timelines, and dosage form-specific technical expectations are discussed to support Marketing Authorization Holders (MAHs) in developing an ASEAN-wide registration strategy. It aims to inform stakeholders on the key differences between ASEAN member states, promoting efficient regulatory strategies for the approval of topical and nasal route dosage forms in the region.

### 3. Methods

This research is based on a comprehensive review of publicly available regulatory documents, country-specific submission guidelines, and regional harmonization protocols (e.g., ACTD, ACTR). The review encompassed all ten ASEAN member states—Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, the Philippines, Singapore, Thailand, and Vietnam. In addition to official documentation, the study incorporated insights from real-world submission experiences and case studies involving topical and nasal formulations.

#### Registration Procedure in ASEAN:

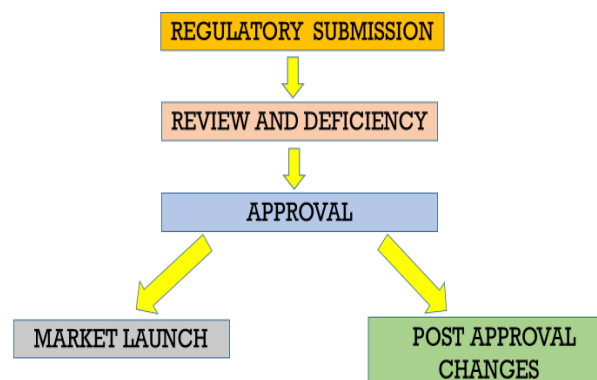


Figure 3 Regulatory Procedure for ASEAN Markets



### • Regulatory Submission:

ASEAN, comprising ten Southeast Asian countries, follows a harmonized regulatory approach under the ASEAN Common Technical Dossier (ACTD) and ASEAN Common Technical Requirements (ACTR). However, practical implementation and timelines vary by country. The article focuses on both topical and nasal dosage forms, which often present regulatory challenges due to their formulation complexity and local testing requirements.

In the ASEAN region, regulatory submission requires the preparation of a comprehensive dossier following the ASEAN Common Technical Dossier (ACTD) format. This dossier must be tailored to meet the specific submission requirements of each country's regulatory authority (e.g., National Pharmaceutical Regulatory Agency in Malaysia, FDA Philippines). Submission also needs to consider ASEAN Mutual Recognition Arrangements (MRAs) to facilitate approval across multiple countries. The following are the member states.



Figure: 2 Regulatory Regions for ASEAN Markets

Submissions must align with the ACTD format and may require country-specific adaptations based on the regulatory authority (e.g., NPRA in Malaysia, BPOM in Indonesia, FDA in the Philippines). Local representation and pre-submission consultations are recommended to ensure alignment with expectations.

### • Review and Deficiency Identification:

Upon submission, regulatory bodies in ASEAN countries review the dossier for compliance with both regional and national guidelines. The review process may differ between countries. Nasal sprays often require detailed data on device performance, droplet/particle size distribution, and in-use stability. Topical formulations may trigger in vitro testing requirements, especially

when reference products differ in formulation (e.g., creams vs. ointments). MAHs should anticipate longer timelines for nasal formulations due to complexity. The timelines and query response expectations vary across countries. Hence, preparing a regulatory roadmap with clear query handling SOPs and early alignment with local regulatory partners is critical. Regulatory reviews focus on the completeness and quality of submitted data. For topical and nasal forms, authorities may request device performance data, container integrity tests, particle size distribution, or in vitro permeation studies, depending on dosage type<sup>5,6</sup>. Timely and structured responses to queries are essential for avoiding delays.

### • Approval:

Following successful deficiency resolution, approval is granted by the respective national authorities. ASEAN's Pharmaceutical Product Working Group (PPWG) and harmonization initiatives such as MRAs and reliance on reference country reviews aim to streamline this phase<sup>2,5</sup>.

### • Market Launch:

After approval, launch readiness involves compliance with labeling, distribution licensing, and pharmacovigilance norms. Any post-approval changes such as site transfer or formula updates must be resubmitted for evaluation<sup>4,6</sup>.

## 4. Results: Comparative Analysis

The regulatory requirements for pharmaceutical products, especially topical and nasal dosage forms, are varied across ASEAN countries.

The comparative analysis revealed significant differences in regulatory expectations across member countries. Variability was observed in multiple dimensions, including:

- The mandatory use of country-specific reference products
- Requirements for bioequivalence or comparative in vitro studies
- Stability data conditions based on climatic zones
- Country-specific labeling, image submissions, and site-specific documentation
- Acceptance criteria for solvents and excipients



Regulatory Requirement	ASEAN Markets
<b>Submission/ Process Validation</b>	Typically, three consecutive batches
<b>Stability Condition and Duration: Three batches</b>	- Accelerated (6 Months): 40°C ± 2°C / 75% ± 5% RH. - Long-Term (Min 12 Months): 30°C ± 2°C / 75% ± 5% RH (Zone-IVB)
<b>Bioequivalence (BE) Study</b>	- US/EU BE study for reference products acceptable. Comparative Dissolution profile required for stringent authorities within ASEAN.
<b>Labelling</b>	Must be country-specific, adhering to language, legal, and cultural requirements.

Table 1: Common Regulatory Requirements across ASEAN<sup>1,4,2,5</sup>

Regulatory Requirement	Topical	Nasal
Reference Product (PE)	✓	✓
Product Image Submission	✓	✓
Solvent Restrictions	✓	✓
Requirement for NCE/MR Products	✓	✓
COA & Analytical Raw Data	✓	✓
Site-Specific API/DMF Requirements	✓	✓
Wet ink signed and stamped documents	✓	✓

Table 2: ACTD Specific Regulatory Requirements in ASEAN Markets<sup>1,6</sup>

Regulatory Requirement	Topical	Nasal
In vitro permeation/absorption test	✓	✓
Microbial limit testing	✓	✓
Stability under actuation	✗	✓
Particle size distribution	✗	✓
Container closure integrity	✓	✓
Specific labeling	✓	✓

Table 3: Dosage Form-Specific Regulatory Expectations in ASEAN<sup>1,6</sup>

#### Timeline Analysis:

Country	Pre-Approval	Post-Approval Query
Singapore	30 calendar days	30 working days
Malaysia	30 working days	30 working days
Indonesia	30 calendar days	20–30 calendar days
Thailand	45 calendar days	30 calendar days
Vietnam	30–45 calendar days	20–30 calendar days
Philippines	60 calendar days	30 calendar days
Brunei	30 calendar days	30 calendar days
Laos	30 calendar days	30 calendar days

Table 4: Indicative Pre- and Post-Approval Query Response Timelines in ASEAN

Effective regulatory strategies should account for the discrepancies in safety and efficacy requirements, as well as the complex approval processes in each market. Strategies need to align the product's development with both regional and national regulatory frameworks to ensure timely approval and market access.

Approval Timelines	Topical	Nasal
Singapore	6–9 months	6–9 months
Malaysia	9–12 months	9–12 months
Indonesia	12–18 months	12–18 months
Thailand	9–12 months	12–15 months
Vietnam	12–18 months	12–18 months
Philippines	12–24 months	12–24 months
Brunei	9–12 months	9–12 months
Laos	9–12 months	9–12 months

Table 5: Approximate Regulatory Approval Timelines in ASEAN Countries

#### Discussion

The diverse regulatory requirements across ASEAN countries necessitate a flexible and strategic approach to market entry. Companies must adapt to the different regulatory landscapes, but at the same time, align with regional harmonization efforts. A thorough understanding of these regulatory frameworks allows companies to develop strategies that optimize the regulatory approval process.

By examining the regulatory standards across ASEAN member states, pharmaceutical companies can build a robust knowledge base, allowing them to respond more



effectively to the regions diverse market needs. This adaptability not only ensures compliance but can also enhance market access, leading to long-term profitability.

The regulatory environment across ASEAN member countries is characterized by a significant degree of diversity in requirements, processes, and expectations—especially for specialized dosage forms like topical and nasal formulations. This heterogeneity requires pharmaceutical companies to adopt a dynamic and tailored regulatory strategy to achieve efficient market entry and sustainable compliance across the region.

For instance, Thailand mandates the use of a locally marketed Thai Reference Product (PE) for bioequivalence (BE) studies, unlike countries such as Vietnam, Cambodia, and Myanmar, where reference product requirements are not mandatory. Similarly, while Thailand insists on product image submissions and detailed bioequivalence data including temperature loggers and PMATs, these are not compulsory in many other ASEAN countries. This directly influences dossier planning, clinical study design, and product comparability assessments.

Another area of regulatory divergence is the requirement for solvent use declarations, particularly for solvents such as IPA, methanol, and dichloromethane. These are discouraged across the region, and applicants must confirm acceptability with local agents—an important factor for formulation development and justifications. Furthermore, Thailand enforces extensive documentation such as Risk Management Plans (RMP), Post-Marketing Surveillance (PMS) plans, and detailed modules (Part III & IV) for new chemical entities (NCEs) and modified-release (MR) products in ASEAN CTD format, which are not mandatory in other member states.

Additionally, stringent requirements around COAs (Certificates of Analysis) and analytical raw data, including chromatograms and batch-specific documentation, are prevalent in Thailand, whereas countries like the Philippines or those in the Indochina region demonstrate more flexibility. Site-specific API/DMF (Drug Master File) data submission is another key regulatory expectation in Thailand, which may not be required in other ASEAN nations.

Finally, procedural formalities such as the need for wet ink-signed and stamped documents—mandatory in Vietnam, Cambodia, and Myanmar, but not required in Thailand or other markets—further exemplify the variability that must be managed.

This complex regulatory mosaic presents both challenges and strategic opportunities. Companies must remain flexible in their approach, customizing regulatory submissions based on each country's expectations, while simultaneously seeking opportunities for regional alignment through harmonized frameworks like the ASEAN Common Technical Dossier (ACTD) and Mutual Recognition Arrangements (MRAs).

A region-specific regulatory intelligence system—backed by cross-functional collaboration between regulatory, clinical, and quality teams—can significantly streamline development timelines. Engaging local agents and leveraging in-country expertise early in the development phase enables proactive risk identification and mitigation.

Ultimately, building regulatory agility through such tailored strategies not only reduces time to approval but also contributes to long-term commercial viability and enhanced patient access across ASEAN markets. In an environment marked by both convergence and divergence, regulatory adaptability becomes a critical success factor in unlocking the full potential of the ASEAN pharmaceutical sector.

Although the ACTD serves as a common format, ASEAN regulatory frameworks remain non-uniform in implementation, especially for complex dosage forms like topical creams/ointments and nasal sprays. Variability in reference product expectations, BE data, labeling norms and analytical documentation necessitates bespoke strategies per country. Thailand, Singapore, Philippines, Malaysia for example, has the most stringent dossier expectations, whereas Myanmar, Brunei, Cambodia or Laos offer more flexibility<sup>2,5</sup>.

Strategically, companies must:

- Plan dossier modules based on dosage complexity
- Engage local agents for updated regulatory intelligence
- Use regional reliance routes or harmonization mechanisms



- Maintain proactive query response protocols to reduce timeline variability

These actions can significantly minimize regulatory lag and ensure consistent commercial rollout across ASEAN.

## 5. Conclusion

Navigating the ASEAN regulatory environment demands a combination of technical expertise and regulatory agility. Topical and nasal formulations pose additional challenges due to in vitro testing, container specifications, and product-specific regulatory scrutiny.

A comprehensive strategy incorporating local expertise, harmonization tools, and proactive dossier planning is essential to succeed in this region.

Harmonization efforts at the regional level (e.g., ACTD and MRAs) are key to streamlining approval processes, thus ensuring that safe and effective medicines reach patients in a timely manner. By aligning regulatory timelines with local expectations, pharmaceutical companies can gain a competitive advantage while contributing to a more efficient healthcare infrastructure in ASEAN.

Achieving regulatory success in ASEAN markets requires a hybrid approach—one that respects both national nuances and regional harmonization frameworks. The use of harmonization tools such as the ASEAN Common Technical Dossier (ACTD) and Mutual Recognition Arrangements (MRAs) is instrumental in streamlining the registration process. MRAs in the ASEAN context serve as mechanisms to foster regulatory convergence, reduce duplicative assessments, and expedite product approvals across participating nations. A strategic, country-tailored regulatory roadmap—complemented by proactive engagement with local agencies—can significantly enhance the efficiency of product approvals for topical and nasal dosage forms in the ASEAN region.

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