RESEARCH PAPER

Comparative Regulatory Requirements And Strategic Decisions For Gcc, Mena & Africa Markets For Topical And Nasal Route Dosage Forms

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KEYWORDS

topical dosage forms; nasal formulations; regulatory convergence; eCTD/CTD; GCC; MENA; Africa; ZAZIBONA; EAC-MRH; African Medicines Agency; stability Zone IVb; reliance pathways

ABSTRACT:

Background:

Topical and nasal dosage forms constitute an important segment of pharmaceutical therapeutics due to their ability to deliver active ingredients directly to the site of action, provide a rapid onset of effect, and reduce systemic exposure relative to oral or parenteral routes. These advantages create unique regulatory expectations, especially with respect to excipient qualification, drug–device integration, in-use stability, and performance testing aligned with region-specific climatic and environmental conditions. The regulatory systems governing these dosage forms differ substantially among global regions. Markets within the Gulf Cooperation Council (GCC) have achieved partial harmonization through the GCC-Drug Registration framework, resulting in relatively predictable submission procedures. Conversely, the Middle East and North Africa (MENA) region remains characterized by fragmented regulatory processes with limited inter-agency alignment. Meanwhile, African regulatory systems are experiencing rapid modernization, accelerated digitization, and expanding reliance-based models; however, significant variability persists across national authorities.

Despite this progress, Africa remains highly diverse, with country-specific Module 1 requirements, varying dossier expectations, and different timelines for topical and nasal dosage forms[1-5]

Objectives The objective of this study is to perform a detailed comparative evaluation of regulatory requirements for topical and nasal dosage forms across GCC, MENA, and African regions. The analysis aims to identify divergences in dossier architecture, stability expectations, device-related requirements, GMP and quality standards, and administrative procedures. A further objective is to highlight how emerging harmonization initiatives influence approval pathways, reliance mechanisms, lifecycle management, and market-entry strategies.

Methods: A structured comparative review approach was adopted. Regulatory guidelines, Module 1 specifications, submission templates, and publicly available policies were collected from major authorities, including GCC-DR, the Saudi Food and Drug Authority (SFDA), the UAE Ministry of Health and Prevention (MOHAP), the Egyptian Drug Authority (EDA), and the Jordan Food and Drug Administration (JFDA). For African markets, documentation from

the South African Health Products Regulatory Authority (SAHPRA), the National Agency for Food and Drug Administration and Control (NAFDAC), and additional National Medicines Regulatory Authorities (NMRAs) was reviewed. Harmonization frameworks from ZAZIBONA, the East African Community Medicines Regulatory Harmonization initiative (EAC-MRH), and the African Medicines Agency (AMA) were assessed. Comparative extraction focused on submission format (eCTD/CTD), stability zone classification, device functionality testing, labelling and artwork requirements, GMP and quality expectations, and pathways utilizing reliance or work-sharing.

Results: The GCC region demonstrates moderate regulatory harmonization driven by GCC-DR, resulting in common requirements for eCTD format, Zone IVb stability studies, and standardized quality documentation. Nonetheless, national procedures—such as country-specific Module 1 requirements, fee structures, and administrative timelines—continue to influence approval predictability. The MENA region exhibits substantial heterogeneity, including varying CTD interpretations, divergent labelling rules, differing expectations for in vitro release testing for topical formulations, and inconsistent device-related testing requirements for nasal products. African markets reflect the highest degree of regulatory diversity; however, significant progress is underway. SAHPRA's full implementation of eCTD and stringent validation criteria has raised technical expectations. NAFDAC continues to refine CTD submission processes and strengthen GMP oversight. Regional platforms such as ZAZIBONA and EAC-MRH have reduced assessment duplication through joint dossier reviews and reliance models, supporting faster but technically rigorous approvals. The operational establishment of AMA represents a major step toward continental regulatory convergence with potential long-term implications for unified assessments.

Conclusion: GCC markets offer relatively predictable regulatory pathways due to partial harmonization, although national differences still necessitate localized planning. MENA markets require tailored, country-specific regulatory strategies owing to their fragmented and heterogeneous requirements. African markets, while currently the most diverse, demonstrate strong momentum toward modernization through digitization, reliance models, and regional coordination. Enhanced regulatory convergence across these regions has the potential to reduce technical review duplication, improve dossier assessment efficiency, and accelerate patient access to safe, high-quality topical and nasal pharmaceutical products. This comparative analysis provides a practical basis for optimizing submission strategies and anticipating regulatory challenges in these dynamic markets.

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1. Introduction

Topical and nasal dosage forms constitute a critical category within modern pharmaceutical therapeutics owing to their ability to provide localized delivery, rapid onset of action, and reduced systemic exposure compared with conventional oral or parenteral routes. Owing to these unique therapeutic and pharmacokinetic advantages, regulatory evaluation of such products requires comprehensive scrutiny of formulation attributes, excipient safety profiles, preservative systems, microbiological control strategies, device functionality, and manufacturing robustness. Additionally, their evaluation must consider stringent stability requirements under diverse climatic conditions—particularly in regions categorized under Climatic Zone IVb—along with adherence to WHO, ICH, and region-specific technical standards.

Over the past decade, the Gulf Cooperation Council (GCC) and the broader Middle East–North Africa (MENA) region have emerged as strategically significant pharmaceutical markets. This expansion has been driven by rapid population growth, rising chronic disease incidence, increasing healthcare expenditures, and substantial governmental investment in regulatory and healthcare infrastructure. Consequently, the demand for high-quality, internationally benchmarked medicines—

including complex formulations such as topical semisolids and nasal sprays—has grown steadily across these markets.

In parallel, African pharmaceutical markets have undergone accelerated evolution, fueled by an increasing disease burden, expansion of local manufacturing capabilities, and noteworthy regulatory modernization. Several national regulatory authorities in Africa have introduced major structural reforms. For instance, the South African Health Products Regulatory Authority (SAHPRA) has implemented mandatory eCTD submissions, marking a transition toward digitized and globally aligned regulatory systems. Nigeria's National Agency for Food and Drug Administration and Control (NAFDAC) has similarly strengthened its CTD-based requirements and broadened its guideline portfolio to encompass drug registration, GMP compliance, storage and distribution practices, and bioequivalence assessment frameworks.

Beyond national-level reforms, Africa is experiencing significant regional regulatory transformation through harmonization and reliance initiatives. The ZAZIBONA Collaborative Procedure under the Southern African Development Community (SADC) has demonstrated measurable improvements in assessment timelines through joint reviews and work-sharing. Likewise, the East African Community's Medicines Regulatory Harmonization (EAC-MRH) initiative has established joint assessment and inspection platforms to reduce regulatory duplication. The most transformative development has been the operationalization of the African Medicines Agency (AMA), which commenced full activities in 2025 with the mandate to promote continental regulatory convergence, facilitate reliance pathways, and strengthen regulatory capacities across African Union member states.

Despite these advancements, the regulatory landscapes across the GCC, MENA, and African regions continue to differ significantly in terms of regulatory maturity, harmonization depth, dossier expectations, and procedural workflows. These variations pose practical challenges for manufacturers, especially for topical and nasal dosage forms that often require device-specific performance data, in vitro release and permeation testing, tight microbial control strategies, and stability studies tailored to high-temperature, high-humidity conditions typical of Climatic Zone IVb. Navigating these differences is essential for designing robust regulatory strategies, minimizing assessment delays, and ensuring timely market access.

Given this context, the present review provides a structured, comparative analysis of the regulatory frameworks governing topical and nasal dosage forms across the GCC, MENA, and key African markets. By synthesizing cross-regional requirements, harmonization efforts, and evolving regulatory practices, this review aims to support manufacturers and regulatory professionals in optimizing submission planning, enhancing predictability, and improving regulatory outcomes in diverse and rapidly evolving markets.

2. Scope and Review Methodology

2.1 Scope of the Review

This review examines the regulatory requirements that govern finished pharmaceutical products intended for topical and nasal administration across three major regions: the Gulf Cooperation Council (GCC), the Middle East and North Africa (MENA), and selected African markets. The primary emphasis is on understanding region-specific technical expectations, dossier structures, stability requirements, manufacturing controls, and administrative pathways that influence market authorization processes for these dosage forms.

The scope further incorporates the evolving regulatory landscape within Africa, where significant modernization efforts have reshaped national and regional approval mechanisms. Key African authorities—most notably the South African Health Products Regulatory Authority (SAHPRA) and Nigeria's National Agency for Food and Drug Administration and Control (NAFDAC)—have undertaken extensive regulatory reforms. These reforms include mandatory eCTD adoption, strengthened CTD-based frameworks, expanded GMP and quality-control guidance, and enhanced expectations for bioequivalence or in vitro performance demonstration for multisource products.

In addition to national changes, Africa is undergoing extensive structural transformation through regional harmonization programs such as the ZAZIBONA Collaborative Procedure under the Southern African Development Community, the East African Community Medicines Regulatory Harmonization (EAC-MRH) initiative, and the continent-wide African Medicines Agency (AMA). The AMA—fully operational since 2025—has laid the foundation for cross-border scientific reliance, joint reviews, and coordinated decision-making. Collectively, these developments have made African markets increasingly relevant for sponsors seeking predictable, streamlined pathways for topical and nasal products.

2.2 Data Sources

This review is grounded in a systematic analysis of primary and secondary regulatory sources.

Primary Data Sources

Primary documents were collected from official regulatory authorities, including:

- GCC-DR and individual GCC regulators
- Saudi Food and Drug Authority (SFDA)
- Egyptian Drug Authority (EDA)
- Jordan Food and Drug Administration (JFDA)
- South African Health Products Regulatory Authority (SAHPRA)
- National Agency for Food and Drug Administration and Control (NAFDAC), Nigeria
- Selected East, West, and Southern African National Medicines Regulatory Authorities participating in ZAZIBONA and EAC-MRH.

These sources provided the foundational regulatory requirements, procedural guidelines, and updated administrative rules governing dossier submission and product assessment.

Secondary Data Sources

Secondary materials included:

- WHO guidelines relevant to topical and nasal dosage forms
- ICH quality, stability, and CTD/eCTD guidance
- Regional harmonization documents published by ZAZIBONA, EAC-MRH, and AMA
- Peer-reviewed scientific literature related to comparative regulatory frameworks, generics evaluation, and drug-device combination products

These secondary sources supported contextual analysis and cross-regional comparison.

2.3 Comparative Framework

To systematically assess regulatory differences, a qualitative comparative framework was developed focusing on key regulatory dimensions relevant to topical and nasal products. These included:

- Dossier format and submission systems: acceptance and implementation of CTD or eCTD structures and country-specific Module 1 adaptations
- Stability requirements: expectations for climatic Zones IVa and IVb, including long-term, accelerated, and in-use stability conditions
- Excipient acceptability: restrictions on preservatives, penetration enhancers, antioxidants, and region-specific allowable lists
- Labelling and serialization: language rules, artwork requirements, GS1 standards, and evolving e-labelling provisions
- Approval timelines and reliance pathways: standard vs. accelerated review processes and participation in reliance-based procedures

The Africa-specific component of the framework also integrated:

- Mandatory eCTD implementation (e.g., SAHPRA)
- CTD acceptance with NMRA-specific Module 1 variations (e.g., NAFDAC)
- Joint assessment and reliance mechanisms under ZAZIBONA and EAC-MRH
- Emerging AMA-coordinated scientific review models aimed at continental harmonization

This framework enabled consistent, comparative evaluation across regions.

2.4 Export Sales Trend Analysis (2019–2026):

In addition to regulatory comparison, a trend analysis was conducted to assess export performance for topical and nasal dosage forms across GCC, MENA, and African markets between 2019 and 2026.

Topical Dosage Forms

Export sales of topical formulations demonstrated a steady upward trajectory, increasing from USD 15,200 (2019) to USD 21,100 (2023), with projected growth reaching USD 24,900 by 2025. Their continued dominance is attributable to wide therapeutic applicability—particularly in dermatology—and well-established manufacturing capabilities across GCC, MENA, and African producers.

Nasal Dosage Forms

Nasal formulations exhibited a more accelerated growth pattern, rising from USD 4,570 (2019) to USD 5,850 (2023), with estimates of USD 6,720 by 2025. Although smaller in volume, this segment demonstrates a higher compound annual growth rate, reflecting increasing

adoption of non-invasive nasal drug delivery technologies for respiratory, systemic, and vaccine applications.

Market Distribution and Dynamics

By 2025, topical dosage forms are projected to represent approximately 61% of the total export value, with nasal products accounting for 39%. This shift indicates emerging competitiveness within nasal drug-delivery systems driven by:

- Increased demand for patient-centric delivery mechanisms
- Growth in respiratory and allergic disease prevalence
- Technological advancements enabling systemic delivery via nasal route

Influence of African Markets

African markets are expected to strengthen future export dynamics due to:

- Increasing regulatory predictability under SAHPRA, NAFDAC, and other NMRAs
- Rising import demand in Eastern and Western Africa
- Enhanced reliance pathways under EAC-MRH and ZAZIBONA
- Integration of AMA-led harmonization enabling streamlined cross-border marketing authorization

Year	Topical Dosage Forms (USD)	Nasal Dosage Forms (USD)
2019	15,200	4,570
2020	14,600	4,270
2021	17,800	5,120
2022	17,200	4,730
2023	21,100	5,850
2024	20,300	5,350
2025 (Projected)	24,900	6,720

Table 1: Export Sales Data: Topical vs Nasal Dosage Forms (2019–2025) for GCC,MENA and Africa Markets

These results underscore the importance for pharmaceutical manufacturers to prioritize both dosage forms in their regulatory and market strategies. While topical formulations remain the backbone of exports, the accelerating growth of nasal formulations presents an attractive opportunity for innovation and faster market entry in the GCC,MENA and Africa regions.

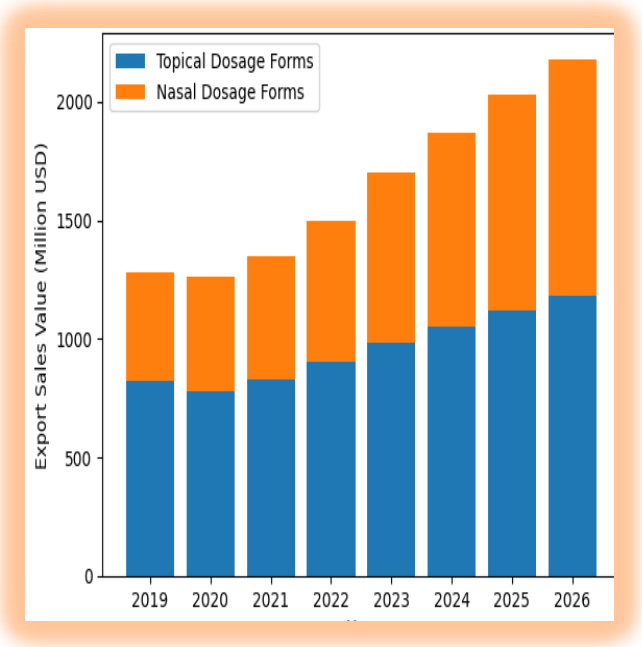

Figure 1. Export Sales Data for Topical vs Nasal Dosage Forms (2019–2026) for GCC,MENA and Africa Markets

Overall, the rising export volumes underscore the strategic importance for pharmaceutical manufacturers to prioritize both topical and nasal dosage forms within regulatory and commercial planning. While topical products remain foundational to regional export portfolios, the rapidly expanding nasal segment presents growing opportunities for innovation, differentiation, and faster market penetration across the GCC, MENA, and African regions.

3. Regulatory Frameworks in GCC, MENA, and Africa Regions

This section synthesizes information from publicly available regulatory documents, country-specific submission guidelines, and regional harmonization protocols (CTD/eCTD), covering GCC and MENA jurisdictions as well as key African markets. The comparative lens reflects the growing strategic relevance of these regions, driven by regulatory

reforms, digitalization of submissions, reliance mechanisms, and expanding pharmaceutical demand—factors that directly influence approval pathways for topical and nasal dosage forms.

For GCC and MENA, the analysis draws on guidance issued by the GCC Drug Registration (GCC-DR) system and leading national authorities, including SFDA (Saudi Arabia), MOHAP (United Arab Emirates), EDA (Egypt), and JFDA (Jordan). Practical insights are additionally informed by real-world submission experience and casework involving topical semisolids and device-dependent nasal products.

In Africa, the review evaluates authoritative publications and portals from national regulators and regional initiatives, reflecting rapid modernization:

- South Africa (SAHPRA) has instituted mandatory eCTD via its eCTD Portal with updated ZA-Module 1 specifications, representing one of the continent's most advanced digital regulatory ecosystems.
- Nigeria (NAFDAC) has reinforced CTD-based frameworks and maintains a comprehensive guidance set spanning registration, GMP, distribution practices, and bioequivalence expectations.
- ZAZIBONA (SADC) and EAC-MRH (East Africa) provide joint dossier assessment and coordinated GMP inspections, reducing duplication and supporting reliance.
- The African Medicines Agency (AMA)—now operational—aims to enable continent-wide regulatory convergence, reliance pathways, and coordinated scientific review.

Collectively, the inclusion of Africa broadens the comparative understanding: GCC exhibits partial harmonization with relatively predictable pathways; MENA remains diverse and nationally driven; Africa is heterogeneous yet rapidly modernizing through national reforms and regional reliance mechanisms that increasingly shape approval routes for topical and nasal products.

3.1 Regional Overview: Countries Covered

GCC Member Countries

Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and United Arab Emirates

Non-GCC MENA (selected Arab and adjacent markets)

Iraq, Egypt, Jordan, Lebanon, Palestine, Syria, Libya, Yemen, Iran (Persian)

Maghreb (French-administrative legacy)

Tunisia**,** Algeria**,** Morocco

Africa (illustrative set; ~46 markets referenced)

Angola, Benin, Botswana, Burkina Faso, Burundi, Cabo Verde, Cameroon, Central African Republic, Chad, Comoros, Congo, Democratic Republic of the Congo, Côte d'Ivoire, Equatorial Guinea, Eritrea, Eswatini, Ethiopia, Gabon, The Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Rwanda, São Tomé and Príncipe, Senegal, Sierra Leone, Somalia, South Africa, South Sudan, Tanzania, Togo, Uganda, Zambia, Zimbabwe.

French speaking ('Francophone') African countries (21)

Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Comoros, Congo, Côte d'Ivoire, Djibouti, DRC, Gabon, Guinea, Madagascar, Mali, Mauritania, Niger, Rwanda, Senegal, Togo, (plus Mauritius as bilingual in practice).

Note: Linguistic and administrative legacies affect labelling, language of submission, and serialization conventions.

3.2 Typical Steps in Marketing Authorization (MA)

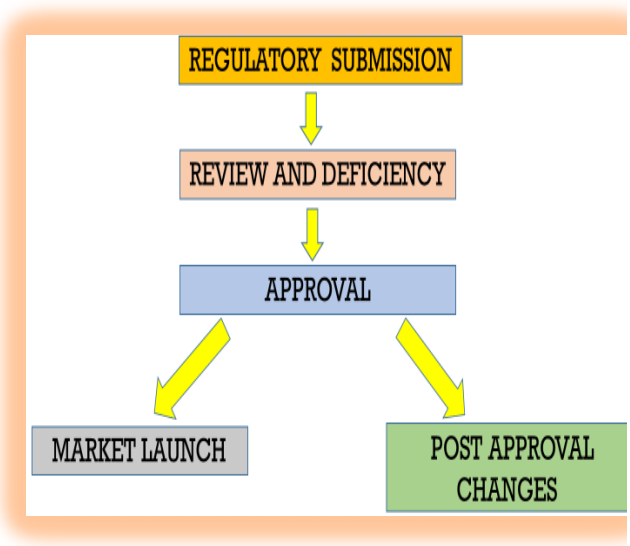

Figure 2. Indicative regulatory pathway for GCC, MENA, and Africa

1. Appointment of local trade partner or distributor through agreement or letter of authorization.
2. Submission of dossier according to country-specific MOH requirements.
3. Dossier review by regulatory committees covering quality, stability, pharmacology, bioequivalence, and analytical aspects.
4. Site inspection and bioequivalence accreditation where applicable.
5. Product analytical testing by regulatory laboratories.
6. Pricing approval.
7. Resolution of regulatory queries and deficiencies.
8. Grant of Marketing Authorization.

3.3 GCC-DR and Regional Harmonization

The GCC-Drug Registration (GCC-DR) pathway enables unified scientific assessment followed by national implementation in member states. Hallmarks include eCTD submissions, ICH-aligned technical guidelines, and harmonized expectations for Zone IVb stability, quality documentation, and, for device-dependent nasal products, performance verification. These elements improve predictability, reduce duplication, and can accelerate review cycles across the Gulf.

In parallel, Africa's reliance architecture is advancing:

- ZAZIBONA (SADC) supports joint assessments and coordinated GMP inspections, with ongoing moves toward portal-based submissions and more standardized procedures.
- EAC-MRH applies unified technical expectations and conducts shared assessments/inspections, while each member state retains MA issuance authority.
- AMA seeks to establish a continental scientific coordination mechanism, strengthening reliance and progressively harmonizing regulatory frameworks, analogous in intent to GCC-DR's role within the Gulf.

Implication: These mechanisms—GCC-DR in the Gulf and AMA/ZAZIBONA/EAC-MRH in Africa—exemplify a global trend toward collaborative assessment, technical convergence, and reliance-based pathways that directly affect topical and nasal approvals.

3.4 Country-Specific Requirements

Despite harmonization efforts, national variations remain material to planning and timelines.

GCC examples

- SFDA and MOHAP maintain distinct Module 1 administrative lists, labelling standards (including Arabic language and serialization), pricing documentation, and Halal compliance (alcohol-free/porcine-free verification).
- Manufacturing sites must meet GCC expectations; audits may be performed prior to acceptance; local sample testing may apply.

Africa examples

- SAHPRA mandates eCTD for human medicines and ZA-specific Module 1; strict pre-submission validation and detailed labelling are enforced—critical for device performance data and Zone IVb stability in nasal products.
- NAFDAC accepts CTD with country-specific Module 1; may require import permits, GMP certificates, legalized CPP, specific labelling/quality documentation, and bioequivalence where applicable (e.g., certain nasal solutions/sprays).
- ZAZIBONA participants may request supplemental national elements post joint opinion (PIL localization, language adaptations, country fees).
- EAC-MRH retains national MA issuance; applicants file EAC-aligned dossiers alongside country-specific Module 1 components.

Submission evaluation nuances

- **Nasal** products: device performance (dose uniformity, plume/spray pattern, droplet/particle size), extractables/leachables (as applicable), in-use stability.
- **Topical** products: Q3 equivalence concepts (where recognized), IVRT/IVPT expectations (jurisdiction-dependent), microbial limits and preservative efficacy testing.

MENA	• Local OCQ testing variability; review timelines and certificate validity differ; language and serialization standards vary
Africa	Multiple online submission portals (e.g., Tanzania, Kenya, Uganda); variable timelines; multilingual requirements (e.g., French; Spanish in limited contexts); national supplements after reliance decisions

Table 3. Sources of diversification (submission and post-approval)

3.5 Pre-Approval: Common Elements vs. Points of Divergence

Region	Common Elements
GCC	• eCTD format; Arabic language requirements; Halal (alcohol/porcine-free) compliance; Zone IVb stability; frequent request for CEP (where applicable) and DMF (open/restricted) alignment
MENA	• Zone II or Zone IVb stability depending on country; tender-linked import permissions may precede full registration in some markets; stringent BE acceptance in select jurisdictions
Africa	• Reliance concepts increasing; Zone II/IVb stability based on climate; broad acceptance of French across Francophone markets; CEP/DMF alignment commonly requested

Table 2. Pre-approval common elements (illustrative)

Region	Diversification / Region-Specific Factors
GCC	• Review timelines vary; SFDA guidance and procedures often more prescriptive than peers; variability in site audit/registration steps; local sample testing differences

3.6 Lifecycle Management: Comparative Considerations

Region	Diversification / Region-Specific
GCC, MENA and Africa	**Administrative** • Cover letter requesting variation approval • MAH letter describing change, assumptions, API manufacturer details, implementation date **Declarations** • No change in API synthetic route/QC procedures/specifications • Cross-reference of current vs. proposed synthesis routes **API Change Assessment** • Comparative synthesis (old vs new) • Physicochemical properties (incl. polymorphs, solubility) • Comparative specifications and impurity profiles • COAs: API (new vendor) and finished product (old vs new API) • Scientific risk assessment (impact on finished product quality) • Stability data (e.g., Type 1) using API from new manufacturer **Certificates & Supporting**

	• Valid CEP (if applicable) or GMP certificate for API site **Batch & Analysis** • ≥2 comparative API lots; finished product COAs (old vs new) **Specifications & CTD Updates** • Updated API specs; change request per national categorization • Updated CTD sections and product information (if impacted) **DMF / S-Part** • S-part/DMF for new API manufacturer (as required)

Table 4. Documentation checklist (illustrative) for API manufacturer change (topical/nasal).

Region	Lifecycle Nuances
GCC & MENA	Timelines vary; SFDA vs. other GCC guidance differences; tabulated "current vs proposed" changes often requested; nitrosamine declarations frequently sought; Halal, TSE/BSE documentation; Arabic translation
Africa	Distinct national portals and templates; variable timelines; multilingual submissions (e.g., English/French); reliance outcomes may still require national supplements

Table 4. Documentation checklist (illustrative) for API manufacturer change (topical/nasal).

3.7 Case Studies (Lifecycle Management for Topical/Nasal)

Case A — Packaging Variation: *Acyclovir Ointment, USP 5%, 30-g tube*

Objective: Update tube dimensions (immediate packaging) without altering material of construction.

Rationale: Machine fit/line feasibility and improved presentation; no change in container composition.

Regulatory pathway: Minor variation (country classification-dependent) focusing on dimensional drawings, compatibility confirmation, label/artwork updates if impacted, and confirmation that CQAs remain unaffected.

Figure 3: Acyclovir Ointment, USP 5% 30 gm Tube

Case B — Packaging Variation: Azelastine Hydrochloride Nasal Spray 0.1% (HDPE/PET bottle + metered-dose actuator)
Objective: Update dimensional specifications of bottle and actuator (pump + nozzle) while retaining identical materials.
Rationale: Filling/capping-line feasibility, assembly accuracy, and aesthetic improvements.
Regulatory pathway: Minor variation with device performance verification (dose uniformity, spray pattern, plume geometry), unchanged E/L risk profile (if materials unchanged), in-use stability confirmation, artwork updates as needed.
Case C — Alternative Vendor Development (AVD): *Topical and Nasal Portfolio*
Scenario: Introduce alternate vendor (and in-house capability) for API/excipients to strengthen supply continuity and cost efficiency; execute pilot batches at reduced commercial lot size.
Topical focus: Physicochemical attributes, particle size distribution, purity/related substances, base compatibility; pilot manufacture executed.
Nasal focus: API solubility, pH compatibility, microbial quality, spray performance (pattern, plume, droplet size); no formulation/process changes proposed.

Figure 4: Azelastine Hydrochloride Nasal Spray, 0.1%

Impact Assessment:

- Comparative API characterization within specs; no change in product CQAs
- Stability profile comparable; no process parameter changes required
- Regulatory impact: Typically minor variation (where specs/materials and manufacturer status are equivalent)

Way Forward & Documentation:

- Vendor qualified (GMP/supply capability reviewed)
- Reduced pilot batch results appended; comparative COAs attached
- Stability summaries (Zone II/IVb; accelerated, 3 batches where applicable)
- Batch records, PV protocol/report, FMEA risk assessment
- Regulatory impact assessment and updated CTD modules

3.8 Practical Takeaways

- Plan nationally within regional systems: Even under GCC-DR, EAC-MRH, or ZAZIBONA, national Module 1 specifics and local supplements drive timelines.
- Device-related rigor for nasal: Anticipate comprehensive device performance and in-use stability packages.
- Topical equivalence strategies: Prepare for IVRT/IVPT or Q3 comparability where recognized.
- Lifecycle agility: Minor variations (packaging/vendor) are feasible with robust comparability dossiers; align early with Halal, labelling, and serialization rules to avoid delays.
- Leverage reliance: Where available, reliance and joint assessment can compress timelines, but country-level follow-through remains essential.

4. Review and Deficiency Identification

Upon submission, regulatory authorities undertake detailed administrative and scientific assessments to verify compliance with national and regional requirements. Review timelines vary substantially across the GCC, MENA, and African regions due to differences in regulatory maturity, dossier evaluation capacity, and reliance pathways. For nasal dosage forms, authorities commonly require extensive device-related performance data, including spray pattern, plume geometry, droplet and particle-size distribution, delivered-dose uniformity, and in-use stability. These data expectations are well established within GCC and MENA jurisdictions and are emphasized in African markets such as South Africa, where SAHPRA's quality and bioequivalence guidelines mandate rigorous performance documentation for products incorporating aerosolization mechanisms.

For topical semisolid formulations, regulators in all three regions may require in vitro performance data—particularly when formulation differences exist relative to a reference product. In line with CTD-based quality expectations, agencies such as NAFDAC require excipient justification, microbiological quality data, and comparative in vitro release or permeation testing where relevant to product equivalence or safety.

Regulatory authorities across GCC, MENA, and Africa may also request:

- Container–closure integrity testing (CCIT) for multidose nasal and topical packaging.
- In vitro permeation or release studies (IVPT/IVRT) for topical semisolids to support equivalence assessments.
- Device compatibility and material-interaction studies for nasal sprays and pump-actuated systems.
- Microbial-limits testing, antimicrobial preservative-effectiveness studies, and Zone IVb stability data, which are particularly important in hot, humid environments typical of these regions.

In the African context, regional joint-assessment mechanisms—notably ZAZIBONA and EAC-MRH—add a coordinated layer to the review process. Under these collaborative procedures, multiple national authorities conduct parallel evaluations of the same dossier and issue consolidated deficiency letters. While this enhances consistency and reduces assessment redundancy, it requires sponsors to prepare harmonized responses that satisfy several regulatory agencies simultaneously.

Across all regions, the efficiency of the review process is strongly influenced by the quality of responses to deficiency letters. Timely, structured, and scientifically substantiated replies—accompanied by updated CTD sections, justifications, and additional stability or performance data where required—are essential for preventing extended clock-stops and minimizing approval delays.

4.1 Regulatory Diversity

The **MENA region** does not operate under a single, unified medicines regulatory framework. Instead, **national authorities** apply their own processes and Module-1 administrative requirements, even as many adopt the **CTD/eCTD** technical backbone in practice. For example, **Egypt's EDA** publishes detailed CTD guidance and Module-1 checklists, while **Jordan's JFDA** accepts eCTD with a Jordan-specific Module-1 specification; the **UAE (MOHAP)** requires eCTD for product registration. Implementations, document formats, and labeling rules, however, remain country-specific.

Figure 5 Topical and Nasal Route Dosage form Portfolio

4.2 Stability and Labelling Requirements

Hot/humid conditions across the Gulf and much of North Africa/Levant drive frequent reliance on **Zone IVb** stability (e.g., **30 °C/75 % RH** long-term; **40 °C/75 % RH** accelerated), though **mixed climatic expectations** persist in some North African markets. **Arabic or bilingual** labeling is typically required in the Gulf (Arabic–English), with **country-specific** bilingual expectations across the wider MENA (e.g., MOHAP prescribes bilingual Arabic–English submission and labeling). [sfda.gov.sa], [istitlaa.ncc.gov.sa], [mohap.gov.ae]

Regulatory Requirement	GCC,MENA and Africa Markets
Stability Condition and Duration: 3 consecutive batches	Accelerated: 40 °C ± 2 °C / 75 % ± 5 % RH (6 months) & Long-term: 30 °C ± 2 °C / 75 % ± 5 % RH (minimum 12 months, Zone IVB)
Bioequivalence (BE) Study	Generally waived for topical products; nasal products require in-vitro/device performance data; comparative data may be requested by some authorities
Labelling	GCC: Arabic & English mandatory MENA: Arabic or bilingual Arabic/English Maghreb: Arabic and/or French (often bilingual Arabic/French) Africa: Regular English/Spanish in some countries Francophone: Regular English and Frech

Table 4-A. Common Regulatory Requirements Across GCC, MENA, and Africa (Topical/Nasal)

Regulatory Requirement	GCC	MENA	Africa
Site registration & audit	✓	*	*
Alcohol / pork content declaration	✓	✕	✕
Quality control (QC) testing	✓	*	✕
BE / clinical study accreditation	✓	✕	✕
Halal compliance	✓	✕	✕
Sample dispatch	✓	*	✓
Price certificate	✓	✕	✕
Patent declaration	✓	✕	✕
GMO / Non-GMO declaration	✓	✕	✕
Expert declaration	✓	✕	✓
COPP / GMP certification	✓	✓	✓

Table 4-B. Selected Administrative/Technical Requirements (Indicative)

Regulatory Requirement	Topical	Nasal
In-vitro permeation / absorption testing	✓	✓
Microbial limit testing	✓	✓
Stability under actuation	✕	✓
Particle size distribution	✕	✓
Container-closure integrity	✓	✓
Specific labelling requirements	✓	✓
Spray pattern analysis	✕	✓
Delivered dose uniformity	✕	✓

Table 4-C. Dosage-Form–Specific Technical Expectations (Topical vs. Nasal)

4.3 Timeline Analysis (Sponsor-Reported/Indicative)
The timeline values below reflect your internal experience and are presented as indicative planning ranges. Authorities' workloads, completeness of submissions, reliance pathways, and pricing/MAH steps can materially affect actual timelines.

Country	Pre-Approval	Post-Approval
Algeria	30 calendar days	30 working days
Egypt	30 working days	30 working days
Iraq	30 calendar days	20–30 calendar days
Jordan	45 calendar days	30 calendar days
Lebanon	30–45 calendar days	20–30 calendar days
Morocco	60 calendar days	30 calendar days
Palestine	30 calendar days	30 calendar days
Tunisia	30 calendar days	30 calendar days
GCC (centralized)	60 calendar days	30 calendar days
Africa (ZAZIBONA)	60 calendar days	30 calendar days

Table 4-D. Indicative Pre- and Post-Approval Query Response Windows

Approval Timelines*	**Topical**	**Nasal**
Algeria	6–9 months	6–9 months
Egypt	9–12 months	9–12 months
Iraq	12–18 months	12–18 months
Jordan	9–12 months	12–15 months
Lebanon	12–18 months	12–18 months
Morocco	12–24 months	12–24 months
Palestine	9–12 months	9–12 months
Tunisia	9–12 months	9–12 months

Table 4-E. Approximate Regulatory Approval Timelines — MENA

Approval Timelines*	**Topical**	**Nasal**
Bahrain	Generic : 18-24 Months Fast track: 6-8 Months Human New Drugs not registered in GCC: 24-36 M Mfg. Site and MAH Registration: 3-6 Months SRA approval can help shorten the regulatory timeline.	
Kuwait		
Oman		
Qatar		
Saudi Arabia		
UAE		

Table 4-F. Approximate Regulatory Approval Timelines — GCC

Approval Timelines*	**Topical**	**Nasal**
South Africa (SAHPRA)	12–24 months	12–26 months
Nigeria (NAFDAC)	12–18months	12–20 months
ZAZIBONA (SADC Collaborative Route)	Joint review+ National approval: 9–12 months	6–14 months
EAC-MRH (East Africa Joint Assessment)	Joint assessment: + sign-off : 8–14 months	8–14 months
Other African Markets	12–24 months	12–24 months

Table 4-G. Approximate Regulatory Approval Timelines — Africa

4.4 Unique Regulatory Requirements for Topical Route Dosage Forms—Regulatory Perspective

Key quality/performance attributes and CMC/development documentation expected for common topical/nasal categories.

Dosage Form	Critical Quality & Performance Attributes	CMC / Development Requirements
Topical Semisolids (Creams, Ointments, Gels)	• Rheology (viscosity, thixotropy) • pH, appearance, odour • Globule/particle size • Content uniformity • In-vitro release/permeation (IVRT/IVPT) • Spreadability/extrudability • Microbial limits & preservative efficacy	• QbD/PDR development report • Specs, STP, COA, AMV • Process validation • Impurity & elemental impurity analysis • Stability (accelerated + Zone IVB) • Extractables/Leachables (E&L) • Nitrosamine risk
Topical Solutions / Lotions	• pH, clarity, colour, odour • Content uniformity • Preservative levels & efficacy • Viscosity (if thickened) • Microbial quality	• Method validation (assay, preservative) • Transport & in-use stability • Impurity qualification • Microbiology & challenge studies
Nasal Sprays / Nasal Solutions	• Delivered-dose uniformity (DDU) • Spray pattern / plume geometry • Droplet/particle size distribution • Device performance & priming/re-priming • Microbial limits & preservative efficacy	• Device–formulation compatibility • E&L for pump/actuator • Delivered-dose testing across life-cycle • Particle size/spray pattern validation • In-use stability (multi-dose containers)
Transdermal Patches (TTS)	• Adhesion (peel, tack, shear) • Drug content per area • In-vitro flux/permeation • Residual drug	• Adhesion & wear studies • Flux studies (in-vitro permeation) • Residual drug stability

	content • Polymer/adhesive integrity • Backing/liner compatibility	• E&L (backing/liner/adhesive) • Irritation & sensitization studies • Cold-flow assessment
Medicated Shampoos / Washes	• pH, viscosity • Foaming properties • Drug content uniformity • Preservative level • Microbial quality	• Method validation • Preservative challenge • Transport/in-use stability • Microbiological quality

Table 4-F.Unique Regulatory Requirements for Topical Route Dosage Forms—Regulatory Perspective

5. Strategic Considerations for Regulatory Planning

5.1 Market Prioritization and Sequencing

Prioritize markets where dossier format (CTD/eCTD), stability zone, and labeling rules best match your baseline package; leverage **GCC-DR** or **reliance**-based routes where available (e.g., ZAZIBONA/EAC-MRH) to minimize duplication. [ghc.sa], [zazibona.com], [tmda.go.tz]

5.2 Formulation Adaptation

Design for **Zone IVb** robustness, in-use stability for multidose nasal systems, and microbiological control consistent with regional climates; ensure device–formulation compatibility and performance (DDU, spray metrics) are demonstrated up-front. [sfda.gov.sa], [sahpra.org.za]

5.3 Post-Approval Management

Build a variation playbook (site transfer, packaging/IFU updates, excipient source changes) aligned with national procedures (e.g., **SAHPRA eCTD** sequences; **NAFDAC** variation documentation; **SFDA** verification/abridged pathways). [sahpra.org.za], [nafdac.gov.ng], [istitlaa.ncc.gov.sa]

6. Opportunities for Regulatory Convergence and Reliance

Broader adoption of reliance and convergence mechanisms—**GCC-DR**, **ZAZIBONA**, **EAC-MRH**, and the operational **AMA**—can reduce duplication, shorten approval timelines, and harmonize expectations for stability (Zone IVb), device performance (nasal), and microbiological quality (topical). While **CTD/eCTD** usage is expanding, Module-1 and procedural implementations remain nationally defined, particularly in MENA and several African NMRAs. [ghc.sa], [zazibona.com], [tmda.go.tz], [gna.org.gh], [ich.org]

Strategic actions:

- Align dossier architecture with **product complexity** and **target-region** requirements.
- Utilize **local agents/MAHs** to maintain current regulatory intelligence.
- Select **reliance routes** proactively (GCC-DR, ZAZIBONA, EAC-MRH; national reliance options).
- Implement strong **query-management SOPs** to minimize clock-stops.

7. Discussion

This comparative analysis underscores the need for **differentiated regulatory strategies**:

- **GCC:** Partial harmonization via **GCC-DR** improves predictability, although national Module-1/pricing/labeling differences remain. [ghc.sa]
- **MENA:** Significant **national diversity** in dossier, labeling, and procedural expectations necessitates **localized expertise** (e.g., MOHAP/EDA/JFDA specifics). [mohap.gov.ae], [edaegypt.gov.eg], [ectdtool.com]

- **Africa:** Rapid **modernization** (e.g., **SAHPRA** eCTD mandate; **NAFDAC** CTD with national Module-1) coexists with **regional work-sharing** (**ZAZIBONA**, **EAC-MRH**) and emerging **AMA** coordination. [sahpra.org.za], [nafdac.gov.ng], [zazibona.com], [tmda.go.tz], [gna.org.gh]

Challenges & way forward (operational):

- Maintain a **global CTD baseline** and generate **country-specific Module-1** packages; use secure portals or authorized channels for document exchange as required by each NMRA.
- Prepare for **portal-based** submissions where mandated (e.g., SAHPRA eCTD Portal), and tailor dossier granularity accordingly. [sahpra.org.za]
- Seek **informal presubmission/scientific advice** where available; otherwise, build Q&A resolution into early sequences.
- Use **biowaiver/intake** discussions via local agents to confirm acceptability of IVRT/IVPT, BCS-based waivers, or literature-based justifications, consistent with national policies.

8. Conclusion

Regulatory success for **topical and nasal** products across **GCC, MENA, and Africa** hinges on **strategic sequencing**, robust **Zone IVb-fit** CMC packages, and early attention to **device performance** for nasal systems. Convergence mechanisms—**GCC-DR** in the Gulf, **ZAZIBONA/EAC-MRH** in Africa, and the operational **AMA**—provide realistic opportunities to **reduce duplication** and **accelerate approvals**, even as national Module-1 and labeling requirements remain diverse. Continued alignment on **CTD/eCTD**, stability design, and **topical/nasal performance standards** will further streamline multi-regional access.

9. Abbreviations:

BE — Bioequivalence
COPP — Certificate of Pharmaceutical Product
CTD — Common Technical Dossier
DMF — Drug Master File
eCTD — Electronic Common Technical Dossier
EDA — Egyptian Drug Authority
GCC — Gulf Cooperation Council
GCC-DR — Gulf Central Committee for Drug Registration (Centralized Procedure)
GMP — Good Manufacturing Practice
GMO — Genetically Modified Organism
JFDA — Jordan Food and Drug Administration
LOA — Letter of Authorization
MA — Marketing Authorization
MAH — Marketing Authorization Holder
MENA — Middle East and North Africa
MOH — Ministry of Health
MOHAP — Ministry of Health and Prevention (United Arab Emirates)
NCE — New Chemical Entity
PMS — Post-Marketing Surveillance
QC — Quality Control
RMP — Risk Management Plan
SFDA — Saudi Food and Drug Authority
SRA — Stringent Regulatory Authority

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