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REGULATORY ADOPTION OF ECTD VERSION 4.0 IN THE ASIA-PACIFIC REGION: DOCUMENTATION REQUIREMENTS, SUBMISSION WORKFLOW, AND IMPLEMENTATION CHALLENGES

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ABSTRACT

The electronic Common Technical Document (eCTD) has become the global standard for electronic regulatory submissions in the pharmaceutical industry. The introduction of eCTD Version 4.0 under the International Council for Harmonization (ICH) M8 guideline represents a significant transformation, marking a regulatory shift from traditional document-based submissions toward a structured, data-driven framework. While early adoption activities were initiated in the United States and Europe, regulatory authorities in the Asia-Pacific region are increasingly aligning with eCTD v4.0 through pilot programs, phased implementation strategies, and region-specific guidance documents. This review provides a comprehensive analysis of the regulatory adoption of eCTD v4.0 in the Asia-Pacific region, with emphasis on documentation requirements, submission workflows, authority-driven implementation approaches, and practical challenges faced by industry stakeholders. Regulatory case studies from Japan, Singapore, and Australia are discussed to illustrate real-world application. The review further highlights the future regulatory implications of eCTD v4.0, positioning it as a foundational framework for next-generation digital regulatory submissions.

KEYWORDS: eCTD v4.0, Asia-Pacific, Regulatory submissions, ICH M8, Documentation, Lifecycle management.

1. INTRODUCTION

The globalization of pharmaceutical development has increased the demand for harmonized regulatory submission standards that enable efficient communication between sponsors and regulatory authorities [1]. Historically, regulatory dossiers were submitted in paper-based

formats, leading to duplication of effort, logistical inefficiencies, and prolonged review timelines [2]. To address these challenges, the International Council for Harmonization (ICH) introduced the Common Technical Document (CTD), followed by its electronic counterpart, the electronic Common Technical Document (eCTD) [1].

The eCTD format enables electronic regulatory submissions through a standardized structure supported by an XML-based framework., enabling lifecycle management across the product's regulatory history [3]. Over time, limitations associated with earlier eCTD versions, particularly version 3.2.2, became evident [2]. These limitations included fragmented XML structures, limited metadata utilization, and restricted support for structured data exchange [4]. In response, ICH developed eCTD Version 4.0, formalized through the ICH M8 guideline [5].

The Asia-Pacific region, characterized by diverse regulatory frameworks and varying levels of digital maturity, represents a critical area for eCTD v4.0 adoption. This review explores how regulatory authorities across Asia-Pacific are transitioning toward eCTD v4.0 and evaluates the regulatory, technical, and operational implications of this transition

Country / Region	**Regulatory Authority**	**Current eCTD Status**	**eCTD v4.0 Readiness / Status**
Japan	PMDA	Mandatory eCTD (v3.2.2)	Pilot implementation; early adoption aligned with ICH M8
Australia	TGA	Mandatory eCTD (v3.2.2)	Draft guidance issued; phased transition planned
Singapore	HAS	Mandatory eCTD	Test submission portals; gradual v4.0 preparedness
South Korea	MFDS	Mandatory eCTD	Exploratory stage; monitoring ICH M8 developments
China	NMPA	eCTD implemented for selected submissions	Transition phase; structured data initiatives ongoing
India	CDSCO	eCTD optional / hybrid submissions	Early digitalization stage; v4.0 under future consideration
Taiwan	TFDA	Mandatory eCTD	Early evaluation of next-generation eCTD
Hong Kong	Department of Health	eCTD accepted	No formal v4.0 implementation announced
Malaysia	NPRA	eCTD mandatory	v4.0 adoption under regulatory review
Thailand	Thai FDA	eCTD implemented	Future alignment expected with ICH M8

Source: Compiled by the authors based on ICH M8 guidance and official regulatory publications from PMDA, TGA, HSA, and other Asia-Pacific authorities.

As summarized in Table 1, regulatory readiness for eCTD Version 4.0 varies considerably across the Asia-Pacific region, with Japan, Australia, and Singapore demonstrating the most advanced adoption initiatives [6,7,8].

2. Evolution of eCTD and Regulatory Rationale for Version 4.0

The initial implementation of eCTD focused on replicating the paper CTD structure in an electronic environment, enabling sponsors to submit dossiers electronically while maintaining familiar document-based workflows [2]. eCTD v3.2.2 became the globally accepted standard, supporting lifecycle operations such as replace, append, and delete [9]. However, as regulatory submissions increased in complexity, the need for enhanced data integration and automation became apparent [2].

To overcome these limitations, eCTD v4.0 introduced a single, integrated XML message architecture [3]. This evolution reflects a broader regulatory shift toward data-driven review processes, improved interoperability, and long-term digital transformation [4]. The ICH M8 guideline provides the technical and regulatory foundation for this transition, emphasizing consistency, scalability, and future readiness [3,4].

3. Regulatory Architecture and Key Features of eCTD Version 4.0

From a regulatory perspective, eCTD v4.0 introduces several structural and functional enhancements that distinguish it from earlier versions [3]. One of the most significant changes is the adoption of a single XML message to describe the entire submission content, including all CTD modules [4]. This approach reduces redundancy and improves consistency across submissions [9].

Additional regulatory-relevant features include structured metadata that enables precise identification of document context, purpose, and relationships, as well as controlled vocabularies that standardize terminology across regions [3]. These features enhance regulatory review efficiency, facilitate lifecycle tracking, and support future integration with regulatory information management systems [10]. Collectively, these enhancements position eCTD v4.0 as a more robust and flexible regulatory submission framework [4].

4. Documentation Requirements under eCTD Version 4.0

Despite significant technical enhancements, the fundamental CTD structure remains unchanged under eCTD v4.0 [9]. Submissions continue to be organized into five modules:

Module 1 (administrative and prescribing information), Module 2 (summaries and overviews), Module 3 (quality), Module 4 (non-clinical), and Module 5 (clinical study reports) [9,10].

However, eCTD v4.0 introduces enriched documentation requirements through metadata and controlled vocabularies [3]. Each document is associated with structured attributes that describe its role within the dossier, enabling regulators to navigate submissions more efficiently [10]. This data-centric approach supports improved traceability and consistency throughout the product lifecycle [4].

5. Submission Workflow in the Asia-Pacific Regulatory Context

5.1 Japan – Pharmaceuticals and Medical Devices Agency (PMDA)

Japan has emerged as a **regional leader in the adoption of eCTD v4.0**, supported by strong alignment with ICH initiatives and advanced regulatory digitalization [6]. The Pharmaceuticals and Medical Devices Agency (PMDA) initiated structured **pilot testing programs** to evaluate both the technical feasibility and regulatory readiness of eCTD v4.0 submissions within the Japanese regulatory framework [6].

Under this workflow, sponsors participating in the pilot were required to prepare **test dossiers using eCTD v4.0 specifications**, including a unified XML backbone, structured metadata, and controlled vocabularies [6]. These submissions were not intended for regulatory approval but served as technical validation exercises [11]. PMDA assessed critical elements such as XML accuracy, lifecycle management operations, validation rule compliance, and system interoperability [6].

A key component of the PMDA workflow was the **feedback mechanism**. Sponsors received detailed feedback on deficiencies related to XML structure, metadata assignment, and lifecycle operations, enabling iterative improvement [11]. This interactive review process helped both regulators and industry stakeholders develop a shared understanding of submission expectations [6]. The PMDA workflow thus emphasizes early engagement, technical validation, and continuous refinement prior to full-scale implementation [11].

5.2 Singapore – Health Sciences Authority (HSA)

The Health Sciences Authority (HSA) of Singapore has adopted a **phased implementation approach** to eCTD v4.0, recognizing the need to balance regulatory innovation with operational readiness [7]. Central to this approach is the introduction of **eCTD test**

submission portals, which allow sponsors to familiarize themselves with electronic submission requirements in a controlled, non-evaluative environment [7].

Through these test portals, industry stakeholders can upload sample eCTD dossiers, conduct technical validation, and assess system compatibility without impacting active regulatory applications [7]. This workflow enables HSA to evaluate the robustness of validation rules, identify common submission errors, and refine internal review processes [12]. At the same time, sponsors gain hands-on experience with submission preparation, publishing tools, and lifecycle management [7].

The HSA workflow reflects a collaborative regulatory model, where iterative testing and stakeholder feedback play a central role in shaping future mandatory submission requirements [12]. Such phased adoption reduces transition risks and enhances overall regulatory efficiency [12].

5.3 Australia – Therapeutic Goods Administration (TGA)

Australia's Therapeutic Goods Administration (TGA) aligns its regulatory submission framework closely with **ICH guidelines**, including the ICH M8 specification for eCTD v4.0 [8]. Rather than immediate mandatory implementation, the TGA has adopted a **guidance-driven transition strategy** that supports gradual industry adoption [8].

The TGA has published regulatory guidance documents outlining expectations for eCTD v4.0 submissions and has developed **draft regional Module 1 specifications** tailored to Australian regulatory requirements. These documents provide clarity on administrative content, metadata usage, and submission structure [13], assisting sponsors in preparing compliant dossiers [13].

Within the Australian workflow, sponsors are encouraged to align internal publishing systems with eCTD v4.0 standards while maintaining compatibility with legacy formats during the transition period. This approach supports regulatory continuity and minimizes disruption to ongoing regulatory activities [8].

Collectively, the submission workflows adopted by PMDA, HSA, and TGA demonstrate a **progressive, risk-based regulatory transition** toward eCTD v4.0 in the Asia-Pacific region. Pilot testing, test submissions, and phased guidance-based implementation serve as key mechanisms for ensuring successful regulatory adoption [6,7,8].

6. Case Study: PMDA eCTD v4.0 Pilot Implementation

A significant and well-documented regulatory case study within the Asia-Pacific region is the **eCTD Version 4.0 pilot implementation conducted by Japan's Pharmaceuticals and Medical Devices Agency (PMDA)**. This pilot program represents one of the earliest structured attempts by a regional authority to operationalize the ICH M8 guideline in a real regulatory environment [6]. The primary objective of the PMDA pilot was to evaluate the practical feasibility of eCTD v4.0 submissions before broader regulatory adoption [6].

The pilot program was designed with multiple regulatory and technical goals. First, it aimed to **evaluate the technical feasibility** of eCTD v4.0 by assessing the functionality of the unified XML backbone, metadata implementation, controlled vocabularies, and lifecycle operations [6]. Sponsors participating in the pilot were required to generate sample submission dossiers using eCTD v4.0 specifications, enabling PMDA to verify system compatibility, XML accuracy, and validation performance [11].

Second, the pilot sought to **assess industry readiness** for transitioning from eCTD v3.2.2 to eCTD v4.0 [11]. This included evaluating the availability of compliant publishing tools, the level of sponsor expertise in structured data management, and the effectiveness of internal quality control processes [6]. Feedback from industry participants highlighted key training needs and resource gaps, which informed subsequent regulatory guidance [11].

Third, the PMDA pilot program focused on **refining regional implementation guidelines** aligned with Japan's regulatory framework [6]. Observations from pilot submissions were used to update validation rules, clarify metadata requirements, and improve technical checklists [11]. This iterative process ensured that both regulators and industry stakeholders shared a common understanding of submission expectations [6].

The outcomes of the PMDA pilot demonstrated the value of a collaborative regulatory approach [11]. Lessons learned from the pilot contributed to enhanced validation tools, clearer guidance documents, and improved readiness for full-scale implementation [6]. Importantly, the PMDA experience serves as a practical model for other Asia-Pacific regulatory authorities, illustrating how phased pilot testing and stakeholder engagement can facilitate the smooth adoption of eCTD v4.0 within diverse regulatory systems [11].

7. Implementation Challenges in eCTD v4.0 Adoption

Despite the strategic advantages of eCTD Version 4.0, its implementation across the Asia-Pacific region presents several regulatory, technical, and organizational challenges [14]. One of the primary challenges is **technological readiness**. Migration from eCTD v3.2.2 to v4.0

necessitates substantial modernization of regulatory information technology systems, including XML processing systems, validation engines, and document management platforms [3]. Regulatory authorities and industry sponsors must ensure system interoperability and data integrity, which can be resource-intensive [2].

Another major challenge is **industry preparedness and skill gaps**. eCTD v4.0 introduces a data-driven submission model that relies heavily on structured metadata and controlled vocabularies [4]. Many sponsors face difficulties in adapting existing publishing workflows and training regulatory personnel to manage complex XML-based submissions [2]. This learning curve may initially increase submission errors and validation failures [14].

Regulatory harmonization also remains a challenge within the Asia-Pacific region. While eCTD v4.0 is based on ICH standards, regional variations in Module 1 requirements necessitate customized implementation strategies [8]. Differences in timelines, validation criteria, and technical specifications across regulatory agencies can complicate global submission planning for multinational sponsors [14]. Similar variability in country-specific registration and documentation requirements has also been reported for generic drug submissions across Rest-of-World markets, underscoring the broader challenge of achieving harmonized global regulatory strategies [15].

Additionally, **change management and transition risks** pose practical concerns. During the coexistence period of eCTD v3.2.2 and v4.0, sponsors must maintain dual systems, increasing operational complexity and cost [11]. Regulatory authorities must carefully manage this transition to avoid disruption to ongoing submissions and reviews [6].

Finally, **data governance and lifecycle management complexities** emerge as new challenges. While eCTD v4.0 enhances lifecycle transparency, improper metadata management or incorrect lifecycle operations can have broader impacts on submission integrity [4]. Robust quality control processes and clear regulatory guidance are essential to mitigate these risks [3].

8. Future Outcomes and Regulatory Impact

The widespread adoption of eCTD Version 4.0 across the Asia-Pacific region is expected to generate significant long-term regulatory and operational outcomes [14]. One of the most important future outcomes is the enhanced standardization of regulatory submissions [16]. The unified XML backbone and structured metadata model of eCTD v4.0 will enable regulators to process submissions more consistently, reducing variability in dossier structure and improving review predictability [14].

Another key outcome is the **improvement in regulatory efficiency and review quality**. With better lifecycle management and data traceability, regulators can more easily track changes across submission sequences, leading to faster identification of updates, reduced review redundancy, and improved decision-making [14]. Over time, this may contribute to shortened approval timelines and more efficient resource utilization within regulatory agencies [16].

Adoption of eCTD v4.0 establishes a foundation for future regulatory digitalization, including advanced analytics and automation-driven review processes [14]. Structured data elements can support future innovations such as automated validation, artificial intelligence–assisted dossier review, and cross-submission data reuse [16]. These capabilities align with broader regulatory modernization initiatives across the Asia-Pacific region [16].

From an industry perspective, long-term outcomes include **greater submission flexibility and global alignment**. Sponsors will benefit from a single, harmonized submission standard that supports multi-regional regulatory strategies [14]. Although initial implementation costs are high, long-term gains are expected through reduced rework, improved lifecycle control, and streamlined global submissions [16].

Finally, the successful implementation of eCTD v4.0 is expected to strengthen **regulatory convergence and collaboration** among Asia-Pacific authorities. Shared technical standards and aligned submission models will facilitate information exchange and reliance mechanisms, supporting regional regulatory cooperation [14].

9. CONCLUSION

eCTD Version 4.0 represents a transformative advancement in regulatory submission standards, marking a shift from document-centric to data-driven regulatory ecosystems. In the Asia-Pacific region, regulatory authorities such as PMDA, HSA, and TGA have demonstrated structured, phased adoption strategies through pilot programs, test submissions, and guidance-driven transitions.

This review highlights that while implementation challenges related to infrastructure, skills, and harmonization remain, the future outcomes of eCTD v4.0 adoption—including enhanced regulatory efficiency, improved data quality, and greater global alignment—offer substantial long-term benefits. Continued collaboration between regulators, industry stakeholders, and international organizations will be essential to fully realize the potential of eCTD v4.0 and to support the evolution of next-generation regulatory submission frameworks.

REFERENCES

1. Reddy P, Kumar S. Electronic common technical document: regulatory perspective and global adoption. J Regul Sci. 2022;10(2):45-52.
2. Patel D, Shah R, Mehta A. Evolution of eCTD submissions and regulatory challenges. Asian J Pharm Clin Res. 2021;14(6):120-126.
3. International Council for Harmonisation (ICH). eCTD specification and implementation guide. Geneva: ICH; 2024.
4. Sudesamithiran N. A review on next generation eCTD – eCTD v4.0. Int J Drug Regul Aff. 2023;11(4):1-7.
5. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). ICH harmonised guideline M8: electronic common technical document (eCTD). Geneva: ICH; 2023.
6. Pharmaceuticals and Medical Devices Agency. Pilot testing of eCTD version 4.0 based on ICH M8 guideline. Tokyo: PMDA; 2023.
7. Health Sciences Authority. eCTD submissions: regulatory updates. Singapore: HSA; 2024.
8. Therapeutic Goods Administration. Adoption of ICH eCTD version 4.0: regulatory guidance. Canberra: Australian Government Department of Health; 2024.
9. U.S. Food and Drug Administration. eCTD version 4.0 technical conformance guide. Silver Spring (MD): FDA; 2024.
10. U.S. Food and Drug Administration. Electronic regulatory submissions and review: eCTD v4.0 overview. Silver Spring (MD): FDA; 2023.
11. Pharmaceuticals and Medical Devices Agency. Guidance on electronic submissions based on ICH eCTD standards. Tokyo: PMDA; 2024.
12. Health Sciences Authority. Launch of eCTD portal for test submissions. Singapore: HSA; 2025.
13. Therapeutic Goods Administration. International scientific guidelines: eCTD version 4.0. Canberra: TGA; 2024.
14. Nagar K, Choudhary M, Sharma R. The future of regulatory submissions: transition to eCTD 4.0. Int J Drug Regul Aff. 2024;12(1):15-22.
15. Pashikanti S, Koribilli N. Generic drug registration requirements in ROW countries. J Pharm Sci Res. 2021;13(10).
16. Certara Inc. Embracing the future of regulatory submissions: eCTD 4.0. Princeton (NJ): Certara; 2023.