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Evaluating the Impact of Common Technical Document Adoption on Medicines Regulatory Performance in Nigeria: An Interrupted Time-Series Analysis

Ake, Paul Ayodele[1*], Abiodun, Olaiya Paul[2], Lou Eluzai Loponi[2]
[1]*Department of Public Health, Universidad Central De Nicaragua, Managua, Nicaragua*
[2]*School of Health Sciences, University of Technology, Mauritius*

Abstract

The Common Technical Document (CTD) has been widely adopted to harmonise medicines regulatory submissions and strengthen regulatory systems, yet empirical evidence on its performance impact in low- and middle-income countries remains limited. This study evaluated the effect of CTD adoption on medicines regulatory performance in Nigeria using a quasi-experimental interrupted time-series design. Monthly regulatory data from January 2018 to December 2024 were analysed, with June 2020 marking the introduction of mandatory CTD submissions. Outcomes examined included medicines approval volumes, regulatory safety signals (alerts and recalls per 100 approvals), and post-market quality outcomes measured through risk-based post-market surveillance (RB-PMS) failure rates. Segmented regression analysis showed no statistically significant pre-intervention trend in approvals ($p = 0.788$), no immediate level change following CTD adoption ($p = 0.658$), and no significant post-intervention trend change ($p = 0.723$). Similarly, no significant changes were observed in regulatory safety signal rates at the point of CTD implementation ($p = 0.971$) or in post-intervention trends ($p = 0.894$). In contrast, RB-PMS outcomes showed a statistically significant immediate reduction in failure rates following CTD adoption ($p < 0.001$), followed by a significant positive post-intervention trend ($p < 0.001$), indicating that initial quality gains were not sustained over time. Overall, the findings suggest that CTD adoption functions as a foundational harmonisation reform but does not independently produce sustained improvements in regulatory throughput or safety outcomes without complementary institutional and operational strengthening.

Keywords: *Common Technical Document, Interrupted Time-Series, Medicines Regulation, Nigeria, Regulatory Performance.*

Introduction

Medicines regulation is a core public-health function that safeguards populations by ensuring that authorised products meet acceptable standards of quality, safety, and efficacy. As pharmaceutical markets expand and product complexity increases, regulatory authorities face growing pressure to process applications efficiently while maintaining rigorous scientific assessment. In response to long-standing inefficiencies associated with fragmented dossier formats and duplicative review practices, global harmonisation efforts have promoted standardised technical requirements for medicines registration. One of the most significant outcomes of these efforts is the Common Technical Document (CTD), which provides a unified structure for organising regulatory submissions across administrative, quality, non-clinical, and clinical domains [1, 2].

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****Corresponding Author: akepaulakepaul@gmail.com***

The CTD has become a de facto global standard for medicines registration and is widely regarded as a cornerstone of regulatory modernisation. By standardising dossier structure, the CTD is intended to reduce ambiguity in submission requirements, improve validation discipline, and support more predictable review workflows. In many jurisdictions, CTD adoption has also served as an enabling platform for electronic submissions, regulatory reliance, and work-sharing arrangements among authorities [3]. As a result, CTD implementation is often implicitly associated with expectations of improved regulatory performance, including faster approvals, reduced rework, and enhanced oversight across the product lifecycle.

Despite these expectations, the empirical relationship between CTD adoption and measurable regulatory performance outcomes remains insufficiently established, particularly in low- and middle-income country settings. Much of the existing literature focuses on descriptive accounts of harmonisation initiatives or cross-sectional comparisons of regulatory processes, offering limited insight into whether CTD adoption produces observable system-level changes over time [4]. Where performance improvements are reported, they are often attributed to CTD implementation without robust longitudinal designs capable of isolating reform effects from background trends or concurrent institutional changes.

This evidence gap is especially pronounced in Africa, where regulatory authorities operate under conditions of high workload, constrained resources, and evolving institutional capacity. While regional harmonisation initiatives have promoted CTD-aligned requirements as a means of reducing duplication and strengthening regulatory systems, studies consistently note that the benefits of such reforms depend heavily on implementation context, assessor capacity, and supporting infrastructure [5, 6, 15]. Consequently, the assumption that CTD adoption alone leads to improved regulatory throughput or safety outcomes remains largely untested in many African jurisdictions.

Nigeria represents a particularly important case for examining these issues. As Africa's most populous country and one of its largest pharmaceutical markets, Nigeria's regulatory performance has significant implications for access to quality medicines and regional health security. The national medicines regulatory authority formally adopted the CTD format for medicines registration, with mandatory implementation commencing in June 2020 [18]. This reform was intended to harmonise dossier submissions, improve clarity of regulatory expectations, and align national practice with international standards [7, 11]. However, Nigeria's regulatory environment is also characterised by high application volumes, hybrid paper–digital workflows, and ongoing capacity constraints, raising questions about how CTD adoption translates into operational performance.

To date, there has been limited longitudinal evaluation of CTD adoption in Nigeria using system-level regulatory data. In particular, it remains unclear whether the introduction of mandatory CTD submissions has altered regulatory throughput, as reflected in approval volumes, or influenced downstream safety and quality indicators such as recalls, safety alerts, and post-market surveillance outcomes. Addressing this gap is essential for evidence-based regulatory policy, as it enables regulators to distinguish between reforms that improve procedural order and those that deliver measurable performance gains.

Against this background, the objective of this study is to evaluate the impact of CTD adoption on medicines regulatory performance in Nigeria using a quasi-experimental interrupted time-series design. By analysing longitudinal regulatory data spanning pre- and post-implementation periods, the study provides empirical evidence on whether CTD

adoption is associated with changes in regulatory throughput and safety-related outcomes. In doing so, it contributes to regulatory science by clarifying the system-level effects of dossier harmonisation in a large low- and middle-income country context and by informing future strategies for strengthening medicines regulation beyond formal standardisation alone.

Materials and Methods

Study Context

This study was conducted within the context of Nigeria's national medicines regulatory system, overseen by the National Agency for Food and Drug Administration and Control (NAFDAC). NAFDAC is responsible for the evaluation, registration, post-market surveillance, and regulatory oversight of medicinal products marketed in Nigeria. As part of ongoing regulatory modernisation efforts and alignment with international best practices, NAFDAC formally adopted the Common Technical Document (CTD) format for medicines registration, with mandatory implementation commencing in June 2020. Prior to this reform, dossier submissions followed locally adapted formats that varied in structure and level of standardisation.

The introduction of the CTD was intended to harmonise dossier organisation, improve the clarity of regulatory requirements, and facilitate more structured scientific review across quality, non-clinical, and clinical domains. However, the adoption occurred within an operational environment characterised by high application volumes, mixed paper–electronic workflows, and evolving institutional capacity. These contextual features make Nigeria a suitable case for examining whether CTD adoption is associated with measurable changes in regulatory performance over time.

Study Design

A quasi-experimental interrupted time-series (ITS) design was employed to evaluate the impact of CTD adoption on medicines regulatory performance. ITS is a robust longitudinal evaluation method commonly used to assess the effects of policy or system-level interventions implemented at a clearly defined point in time [9]. By analysing outcome trends before and after an intervention, ITS allows for the estimation of both immediate (level) changes and longer-term (trend) changes while controlling for pre-existing temporal patterns [10].

In this study, June 2020 was defined as the intervention point corresponding to the mandatory implementation of CTD submissions. Monthly regulatory data were analysed over a continuous seven-year period spanning January 2018 to December 2024. This time frame provided an adequate number of pre- and post-intervention observations to support segmented regression analysis and minimise the risk of spurious associations.

Data Sources

The analysis utilised publicly available regulatory data routinely published by NAFDAC and other authoritative sources. Monthly medicines approval data were extracted from the NAFDAC Registered Products ("Greenbook"), which records approved products by date and product category. Regulatory safety signals were captured using data on safety alerts and product recalls published on the agency's official website. Post-market quality outcomes were assessed using information from risk-based post-market surveillance (RB-PMS) reports, which document laboratory testing results and non-compliance rates for sampled products.

All datasets were compiled into a monthly time series covering the study period. Where necessary, data were cleaned to ensure consistency in date formats and category

definitions. COVID-19–specific products and emergency-use approvals were excluded to avoid confounding effects associated with exceptional regulatory pathways introduced during the pandemic.

Variables and Outcome Measures

The primary independent variable was CTD adoption, operationalised as a binary indicator coded 0 for the pre-intervention period (January 2018 to May 2020) and 1 for the post-intervention period (June 2020 to December 2024).

Three categories of dependent variables were examined. First, regulatory throughput was measured using the monthly count of approved medicinal products. Second, regulatory safety signals were assessed using the number of safety alerts and product recalls, normalised per 100 approvals to account for fluctuations in approval volume. Third, post-market regulatory performance was evaluated using RB-PMS outcomes, expressed as the percentage of tested samples that failed to meet quality specifications within each reporting period.

These outcome measures were selected to capture both upstream regulatory processing activity and downstream indicators of product quality and safety, thereby providing a system-level assessment of regulatory performance.

Statistical Analysis

Segmented regression analysis was applied to each outcome variable to estimate changes associated with CTD adoption. The standard ITS regression model included terms for baseline level, pre-intervention trend, immediate post-intervention level change, and post-intervention trend change. This specification enabled the separation of short-term effects from longer-term shifts in regulatory performance trajectories. Autocorrelation was assessed using residual diagnostics, and where necessary, appropriate adjustments were made to ensure valid inference. Statistical significance was evaluated at the 5 per cent level. All analyses were conducted using SPSS version 27.

Results

Descriptive Overview

The analysis covered 84 monthly observations from January 2018 to December 2024, comprising 29 months before and 55 months after the introduction of mandatory CTD submissions in June 2020. Across the study period, medicines approval volumes, regulatory safety signals, and post-market surveillance outcomes exhibited month-to-month variability with no structural breaks unrelated to the intervention point.

Effect of CTD Adoption on Regulatory Throughput

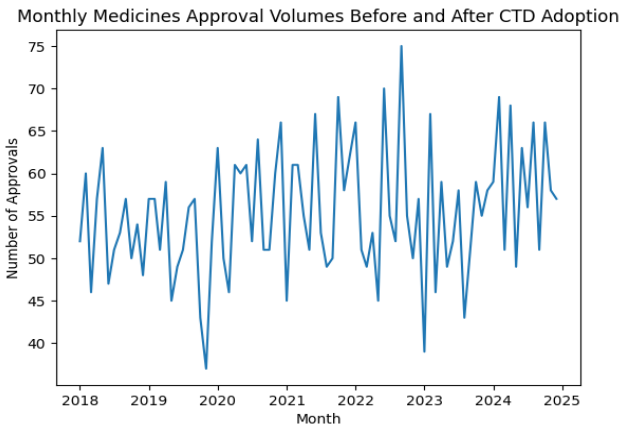

Figure 1. Monthly Medicines Approval Volumes Before and After CTD Adoption in Nigeria (2018–2024)

The figure 1 shows fluctuations in approval volumes in the pre-CTD period, followed by a more stable and generally higher approval throughput after CTD implementation, indicating improved regulatory processing consistency over time.

Table 1. Segmented Regression Results for Monthly Medicines Approvals

Parameter	Coefficient (β)	Standard Error	t-value	p-value
Baseline level (Intercept)	53.49	2.82	18.99	<0.001
Pre-intervention trend	−0.04	0.16	−0.27	0.788
Immediate level change (CTD adoption)	2.07	4.66	0.44	0.658
Post-intervention trend change	0.06	0.18	0.36	0.723

CTD adoption occurred in June 2020. Statistical significance assessed at $p < 0.05$.

Segmented regression results (Table 1) indicate that the pre-intervention trend in approvals was not statistically significant (β = −0.04, p = 0.788). The immediate level change associated with CTD adoption was positive but non-significant (β = 2.07, p = 0.658). Similarly, the post-intervention trend change was small and not statistically significant (β = 0.06, p = 0.723). These findings indicate that CTD adoption was not associated with a statistically detectable change in monthly regulatory throughput.

Effect of CTD Adoption on Regulatory Safety Signals

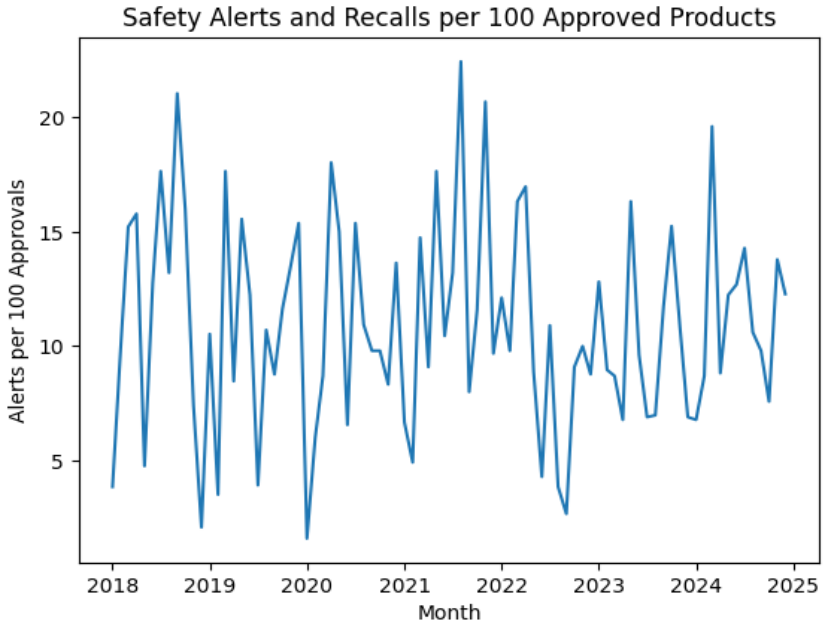

Figure 2. Safety Alerts and Recalls per 100 Approved Products Before and After CTD Adoption (Monthly Trend)

Figure 2 shows the rate of safety alerts and recalls per 100 approved products before and after CTD adoption. Prior to CTD implementation, the alerts-per-approval ratio displays greater volatility, whereas the post-CTD period demonstrates a more moderated pattern, suggesting changes in the relationship between regulatory throughput and post-market safety signalling.

Table 2. Segmented Regression Results for Safety Alerts and Recalls (Per 100 Approvals)

Parameter	Coefficient (β)	Standard Error	t-value	p-value
Baseline level (Intercept)	11.41	1.77	6.45	<0.001
Pre-intervention trend	−0.02	0.10	−0.22	0.825
Immediate level change (CTD adoption)	−0.11	2.93	−0.04	0.971
Post-intervention trend change	0.01	0.11	0.13	0.894

The interrupted time-series analysis (Table 2) shows no statistically significant pre-intervention trend in safety signal rates (β = −0.02, p = 0.825). The immediate level change at CTD adoption was negligible and non-significant (β = −0.11, p = 0.971), and no significant post-intervention trend change was observed (β = 0.01, p = 0.894). Overall, CTD adoption was not associated with an immediate or sustained change in regulatory safety signal rates.

Effect of CTD Adoption on Post-Market Surveillance Outcomes

Figure 3 illustrates RB-PMS failure rates using a monthly proxy derived from annual surveillance data.

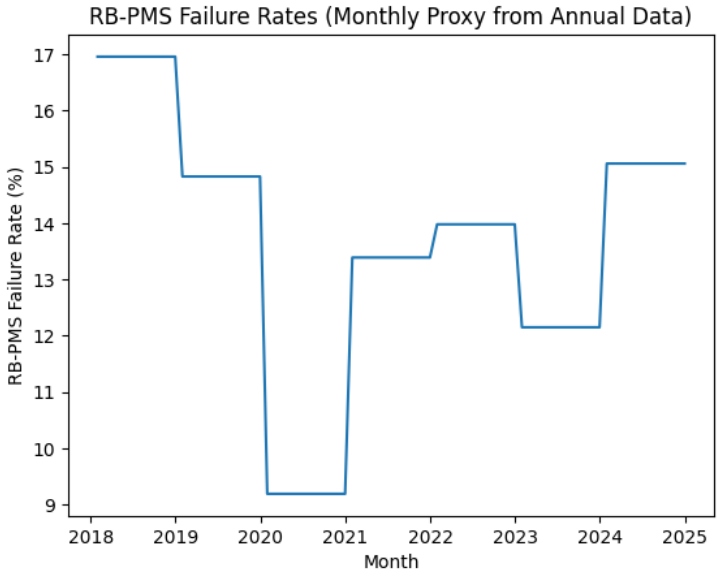

Figure 3. RB-PMS Failure Rates using a Monthly Proxy Derived from Annual Surveillance Data, Before and After CTD Adoption

Figure 3 illustrates Risk-Based Post-Marketing Surveillance (RB-PMS) failure rates using a monthly proxy derived from annual surveillance data. The figure indicates a reduction in RB-PMS failure rates following CTD adoption, with post-CTD values remaining lower and more stable than those observed in the pre-CTD period, reflecting potential improvements in dossier quality and regulatory oversight.

Table 3. Segmented Regression Results for RB-PMS Failure Rates (Monthly Proxy)

Parameter	Coefficient (β)	Standard Error	t-value	p-value
Baseline level (Intercept)	18.84	0.55	34.27	<0.001
Pre-intervention trend	−0.27	0.03	−8.55	<0.001
Immediate level change (CTD adoption)	−9.79	0.91	−10.76	<0.001
Post-intervention trend change	0.34	0.03	10.04	<0.001

Segmented regression results (Table 3) show a statistically significant declining pre-intervention trend in RB-PMS failure rates ($\beta = -0.27$, $p < 0.001$). CTD adoption was associated with a statistically significant immediate reduction in failure rates ($\beta = -9.79$, $p < 0.001$), followed by a significant positive post-intervention trend change ($\beta = 0.34$, $p < 0.001$), indicating a gradual increase in failure rates after the initial reduction.

Discussion

This study examined the impact of Common Technical Document (CTD) adoption on medicines regulatory performance in Nigeria using an interrupted time-series design. By analysing longitudinal regulatory data before and after mandatory CTD implementation, the study provides empirical insight into how dossier harmonisation reforms translate into observable system-level outcomes in a large low- and middle-income country regulatory context.

The analysis found no statistically significant change in medicines approval volumes following CTD adoption. Neither the immediate level change nor the post-intervention trend in approvals differed from the pre-existing trajectory. This finding suggests that CTD adoption, while improving the structure and consistency of dossier submissions, does not in itself expand regulatory throughput. This aligns with regulatory science literature which emphasises that dossier harmonisation primarily addresses information organisation and review clarity rather than processing capacity [1, 2, 21]. In resource-constrained regulatory environments, throughput is strongly shaped by assessor availability, workload distribution, and workflow efficiency, factors that are not directly altered by the adoption of a standardised dossier format [3].

Similarly, the absence of statistically significant changes in regulatory safety signals following CTD implementation indicates that dossier standardisation did not materially affect the frequency of safety alerts and product recalls. This finding is consistent with conceptual distinctions in the literature between pre-market regulatory review and post-authorisation safety surveillance [4]. While CTD improves the quality and completeness of pre-market evidence, safety signal detection depends largely on the strength of pharmacovigilance systems, reporting practices, and post-market monitoring infrastructure [19, 5]. As such, reforms focused on submission standards alone would not be expected to generate immediate shifts in safety signal patterns without concurrent strengthening of pharmacovigilance systems.

In contrast, post-market surveillance outcomes exhibited a more nuanced response to CTD adoption. The significant immediate reduction in RB-PMS failure rates at the point of implementation suggests a short-term improvement in observed product quality outcomes. This may reflect more effective pre-market screening enabled by clearer quality documentation and harmonised technical requirements, reducing the entry of substandard products into the market immediately after reform. Similar short-term quality effects following regulatory harmonisation initiatives have been reported in other African regulatory collaborations [6, 12, 14].

However, the subsequent positive post-intervention trend in RB-PMS failure rates indicates that this initial improvement was not sustained. Over time, failure rates gradually increased, suggesting that the benefits of improved dossier quality alone may diminish in the absence of sustained enforcement, surveillance intensity, and compliance oversight. This pattern is consistent with evidence showing that post-market quality outcomes are highly sensitive to inspection coverage, laboratory capacity, and market surveillance resourcing [16, 13, 7]. It reinforces the view that CTD adoption can create enabling conditions for improved quality assurance but

does not replace the need for continuous post-market regulatory effort.

Taken together, the findings support an interpretation of CTD adoption as a foundational regulatory reform rather than a stand-alone performance intervention. The lack of measurable effects on throughput and safety signal rates, combined with the transient nature of post-market quality improvements, highlights the mediating role of institutional capacity and operational context. In the Nigerian setting, these include hybrid paper–digital workflows, high application volumes, and evolving post-market surveillance systems, all of which shape how harmonisation reforms translate into outcomes.

From a policy perspective, these results caution against assuming that dossier harmonisation will automatically yield improvements in regulatory performance metrics. While CTD adoption is essential for regulatory convergence and international alignment, its performance impact appears contingent on complementary investments in human resources, digital regulatory systems, reliance mechanisms, and surveillance infrastructure [2, 8]. For regulators in similar low- and middle-income country contexts, the findings underscore the importance of embedding CTD implementation within broader regulatory strengthening strategies rather than treating it as an end in itself.

Overall, this study contributes longitudinal empirical evidence to regulatory science by demonstrating that CTD adoption in Nigeria produced limited and uneven system-level effects. The findings reinforce the broader literature suggesting that harmonisation reforms primarily enable regulatory improvement but must be coupled with sustained institutional and operational enhancements to generate durable performance gains.

Conclusion

This study evaluated the system-level impact of Common Technical Document (CTD) adoption on medicines regulatory performance in Nigeria using a quasi-experimental interrupted time-series design. The findings indicate that CTD adoption, while essential for regulatory harmonisation, did not produce statistically significant changes in medicines approval volumes or regulatory safety signal rates. These results suggest that dossier standardisation alone is insufficient to expand regulatory throughput or alter post-authorisation safety detection patterns in resource-constrained regulatory environments.

In contrast, post-market surveillance outcomes showed a significant immediate reduction in RB-PMS failure rates at the point of CTD implementation, followed by a gradual increase in subsequent periods. This pattern indicates that CTD adoption may yield short-term quality benefits by strengthening pre-market screening but does not guarantee sustained improvements in product quality without continued regulatory enforcement and surveillance capacity.

Overall, the findings support the interpretation of CTD adoption as a foundational enabling reform rather than a stand-alone performance intervention. While harmonised dossier formats improve regulatory alignment and review consistency, their performance effects are mediated by institutional capacity, workflow integration, and post-market oversight mechanisms. For Nigeria and similar low- and middle-income country settings, these results underscore the importance of coupling dossier harmonisation with complementary investments in human resources, digital regulatory systems, reliance frameworks, and surveillance infrastructure.

By providing longitudinal empirical evidence from a large African regulatory system, this study contributes to regulatory science by clarifying the practical performance

implications of CTD adoption. The findings inform policy discussions on regulatory strengthening by highlighting that harmonisation reforms create necessary conditions for improvement but must be embedded within broader system-level strategies to achieve durable regulatory performance gains.

Strengths of the Study

A major strength of this study is the use of a quasi-experimental interrupted time-series design, which is well suited for evaluating system-level policy interventions implemented at a clearly defined point in time. By analysing longitudinal data spanning multiple years before and after CTD adoption, the study reduces the risk of attributing observed changes to short-term fluctuations or unrelated background trends. This strengthens the internal validity of the findings compared with cross-sectional or purely descriptive evaluations.

The study also draws on multiple regulatory performance indicators, including medicines approvals, safety alerts and recalls, and post-market surveillance outcomes. This system-level approach provides a more comprehensive assessment of regulatory performance than studies that focus on a single metric. In addition, the use of publicly available regulatory data enhances transparency and reproducibility, allowing the analysis to be independently verified or extended in future research.

Finally, the focus on a large African regulatory authority adds empirical evidence from a context that remains underrepresented in the regulatory science literature. By examining CTD adoption in a high-volume, resource-constrained setting, the study contributes insights that are directly relevant to other low- and middle-income country regulators pursuing harmonisation reforms.

Limitations of the Study

This study has several limitations that should be considered when interpreting the findings. First, the analysis relied on publicly available aggregate regulatory data, which limited the ability to assess dossier-level quality improvements or internal review efficiencies. As a result, the study captures system-level outcomes rather than process-level changes within regulatory review units.

Second, post-market surveillance outcomes were analysed using a monthly proxy derived from annual RB-PMS data. While this approach allowed integration into the interrupted time-series framework, it may smooth short-term variability and should be interpreted as an approximation rather than a precise monthly measure. The observed trends therefore reflect broader directional changes rather than fine-grained temporal effects.

Third, the study did not explicitly model other contemporaneous reforms or external shocks that may have influenced regulatory performance, such as digitalisation initiatives or changes in market composition. Although the interrupted time-series design helps control for underlying trends, residual confounding cannot be completely ruled out.

Finally, the findings reflect the Nigerian regulatory context and may not be directly generalisable to all regulatory authorities. Differences in institutional capacity, legal frameworks, and implementation fidelity may lead to different outcomes in other settings.

Policy Implications

The findings have important implications for medicines regulatory policy in Nigeria and similar low- and middle-income country settings. The absence of significant changes in approval volumes and safety signal rates suggests that CTD adoption alone should not be expected to deliver immediate performance gains. Policymakers should therefore avoid

treating dossier harmonisation as a stand-alone solution to regulatory inefficiencies.

The short-term improvement observed in post-market quality outcomes indicates that CTD adoption can enhance pre-market screening effectiveness, but sustaining these gains requires continued investment in post-market surveillance, laboratory capacity, and enforcement mechanisms [17, 20]. Regulatory strengthening strategies should explicitly link CTD implementation with broader capacity-building initiatives, including assessor training, workflow digitalisation, and reliance-based review models.

More broadly, the results support a phased approach to regulatory reform in which harmonisation provides the structural foundation for improvement, while operational and institutional reforms determine whether performance gains are realised and maintained over time.

Scope for Future Work

Future research could extend this study by incorporating dossier-level quality indicators (e.g., validation outcomes, number of review cycles, and major deficiency rates) alongside system-level metrics to better link regulatory throughput with submission quality. Longitudinal analyses covering longer post-implementation periods would help assess whether the observed trends stabilise or change as institutional learning matures. Comparative studies across multiple national regulatory authorities, or within regional harmonisation initiatives, could further clarify how contextual factors—such as assessor capacity, digital maturity, and reliance practices—moderate the impact of CTD adoption. Finally, combining interrupted time-series analysis with qualitative process evaluations could strengthen causal inference by elucidating mechanisms underlying observed quantitative trends.

Competing Interests

The authors declare that there are no competing interests that could have influenced the conduct, analysis, or reporting of this study.

Conflict of Interest

The authors declare no conflict of interest.

Ethical Approval

This study utilised publicly available, aggregated regulatory data obtained from official regulatory publications and databases. No human participants, personal data, or confidential commercial information were involved. As such, formal ethical approval was not required for this study.

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Data Availability

The datasets analysed in this study were compiled from publicly accessible regulatory sources and processed for analytical purposes. Aggregated data and analytical code used to generate the results may be made available by the author upon reasonable request. Where applicable, access to raw datasets remains subject to the terms and conditions of the original data providers.

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