

Ben Kaspar, Vice President, Regulatory Strategy

Ben Kaspar is Vice President, Regulatory Strategy at MMS, with over 16 years of experience in regulatory affairs, regulatory submissions, medical writing, and research.

He specializes in regulatory strategy, expedited approval pathways, and global submission planning, supporting sponsors across the full drug development lifecycle.

Ben has extensive experience with FDA and EU regulatory submissions, including INDs, NDAs, BLAs, and accelerated programs such as Fast Track, Breakthrough Therapy Designation, Priority Review, and Accelerated Approval. He holds a Master of Science in Biochemistry and a Bachelor of Science in Biology.



Stephine Keeton, Senior Director Biometrics

Stephine Keeton, Ph.D., is the Senior Director of Biometrics at MMS, where she leads strategic initiatives to advance the organization's biometric capabilities and deliver innovative solutions to meet the growing complexities of clinical data. With more than 19 years of leadership experience across regulatory agencies, contract research organizations, and the pharmaceutical industry, she brings deep expertise in statistical methodologies, data strategy, and cross-functional collaboration.

Dr. Keeton has held influential roles within several prominent professional societies, contributing to the advancement of industry standards and best practices. She earned her Ph.D. in Mathematics with a concentration in Statistics, providing a strong foundation for her work in driving scientific rigor and operational excellence in clinical development.





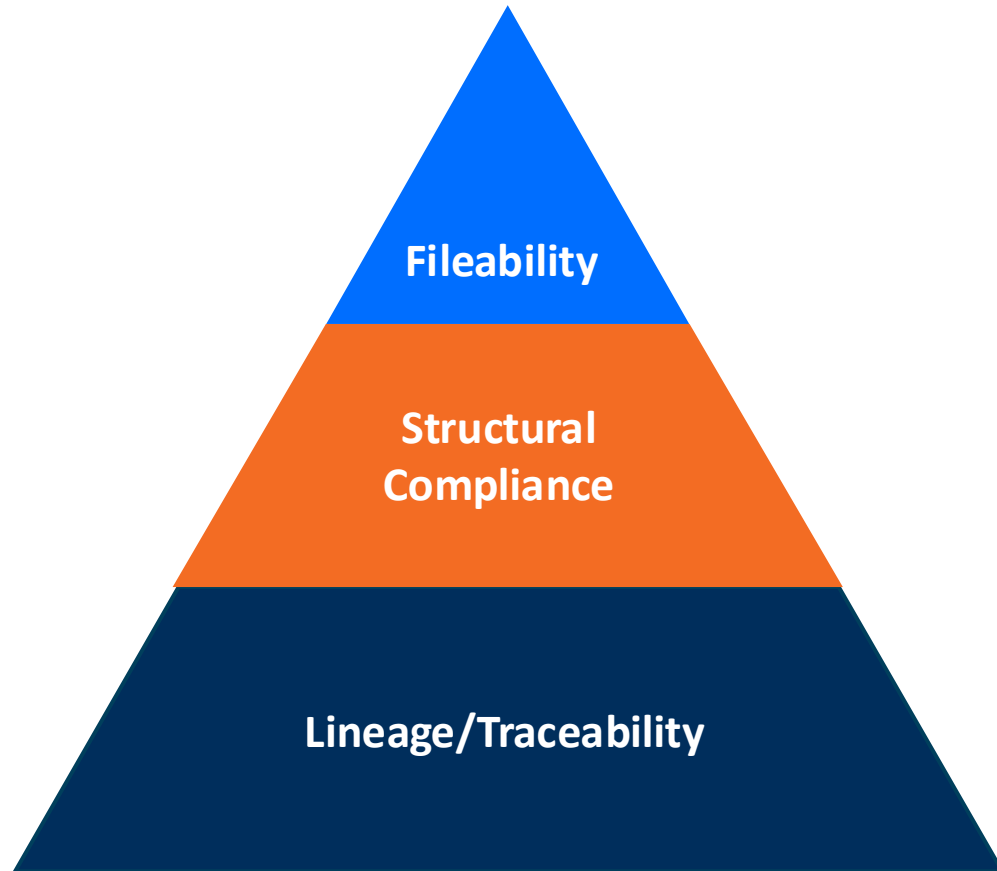
Building Cross Functional Regulatory and Programming Alignment for Successful Submissions

Agenda

- Key Learning Goals
- Why Submissions Fail
- The Disconnet: How Teams Drift Apart
- Achieving Internal Alignment Initiative
- Phased Alignment Framework
- Case Studies
- Lessons Learned / Practical Takeaways
- Summary



Key Learning Goals



- Design submissions that are fileable on their face, avoiding RTF actions
- Ensure data and eCTD structure meet section 745A(a) electronic format requirements
- Build traceability from CSR → SDTM/ADaM/SEND → tables and figures that supports efficient FDA review

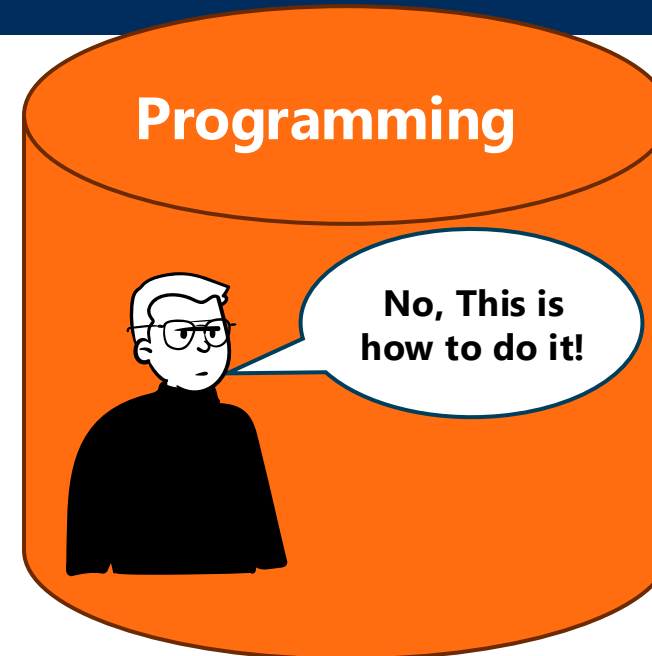
Why Submissions Fail

- **Common misconception:** submissions succeed or fail at the time of dossier assembly
- **Reality:** most failures occur due to decisions made months (or years) earlier
 - Siloed parallel workflows for Regulatory and programming working
 - Late surprises around pooling, standards, or analysis conventions
 - Rework during submission crunch and tight IR timelines



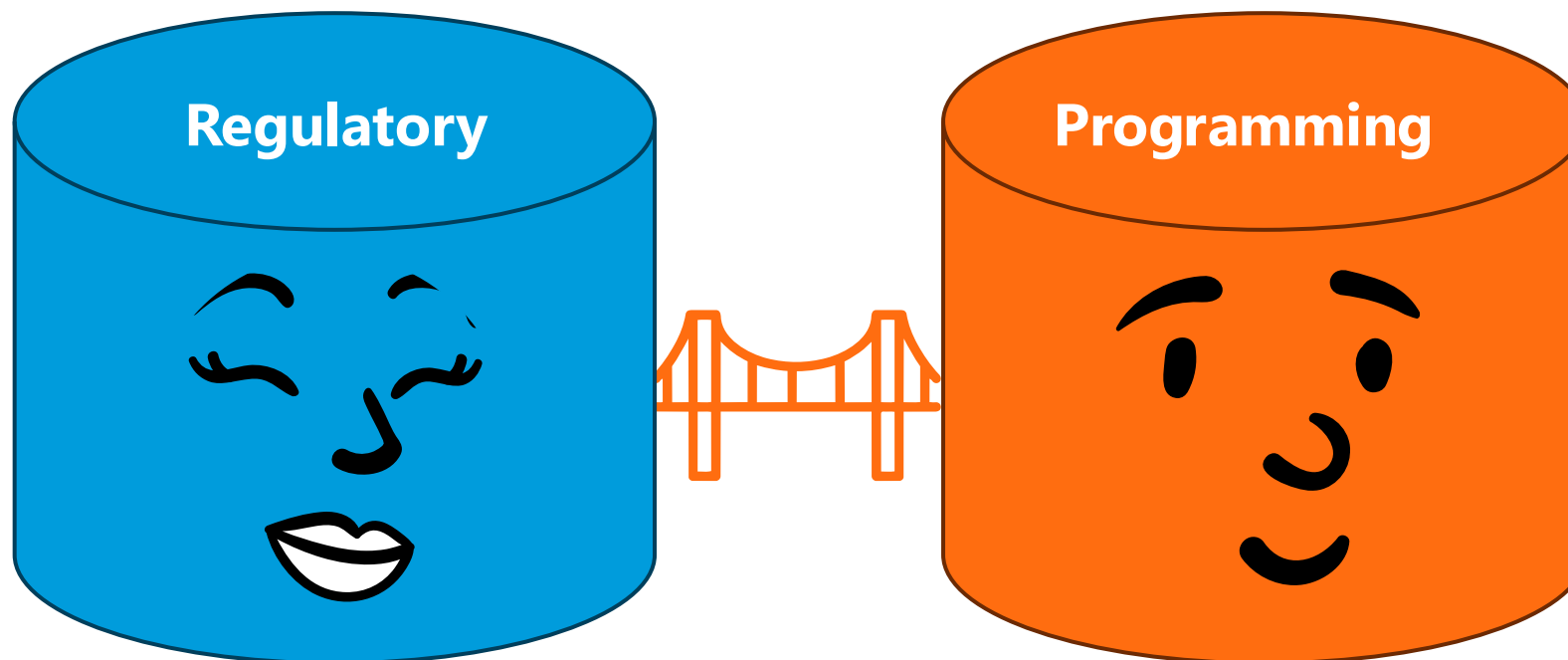
The Disconnect: How Teams Drift Apart

- How regulatory and programming teams are traditionally organized
- Different incentives, timelines, and definitions of 'done'
- Analysis datasets not optimized for submission narratives
- Pooling decisions deferred until late in the application process
- Traceability gaps between CSR, datasets, and Module 5
- Handoffs are often the root cause rather than capability gaps



Achieving Internal Alignment Initiative

- Embed RTF and standards thinking upstream in development
- Pair a Regulatory Strategist + Statistical Programming Lead as joint “submission owners”
 - Shared ownership of submission-critical decisions



The Phased Alignment Framework (High-Level Overview)

Phase 1

Early Planning — Design for fileability and data standards

Phase 2

Study Execution — Program with TRC and reviewer traceability in mind

Phase 3

Pre-Submission Integration — Stress-test completeness and conformance

Phase 4

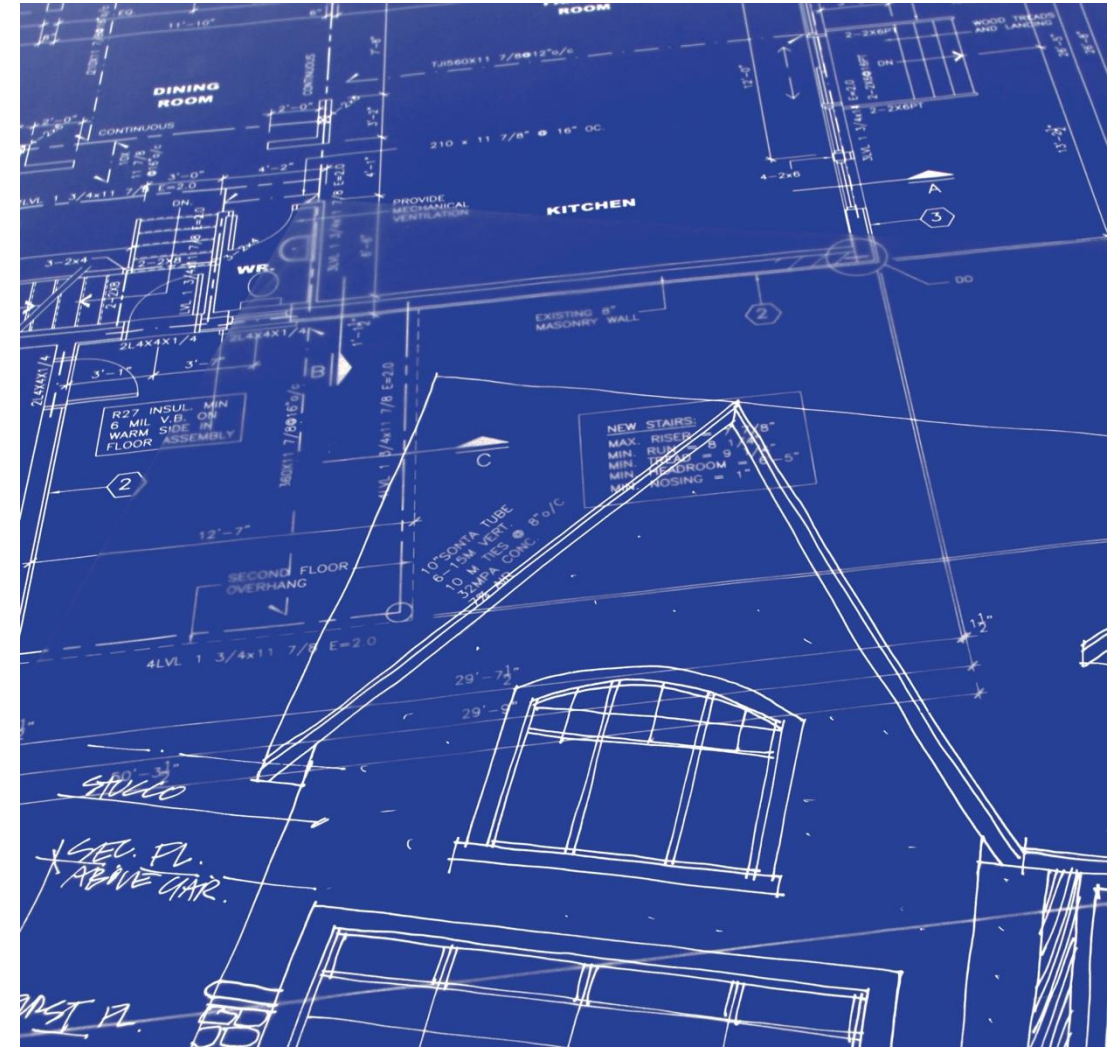
Submission & HA Interaction — Execute eCTD and manage IRs efficiently

Principle

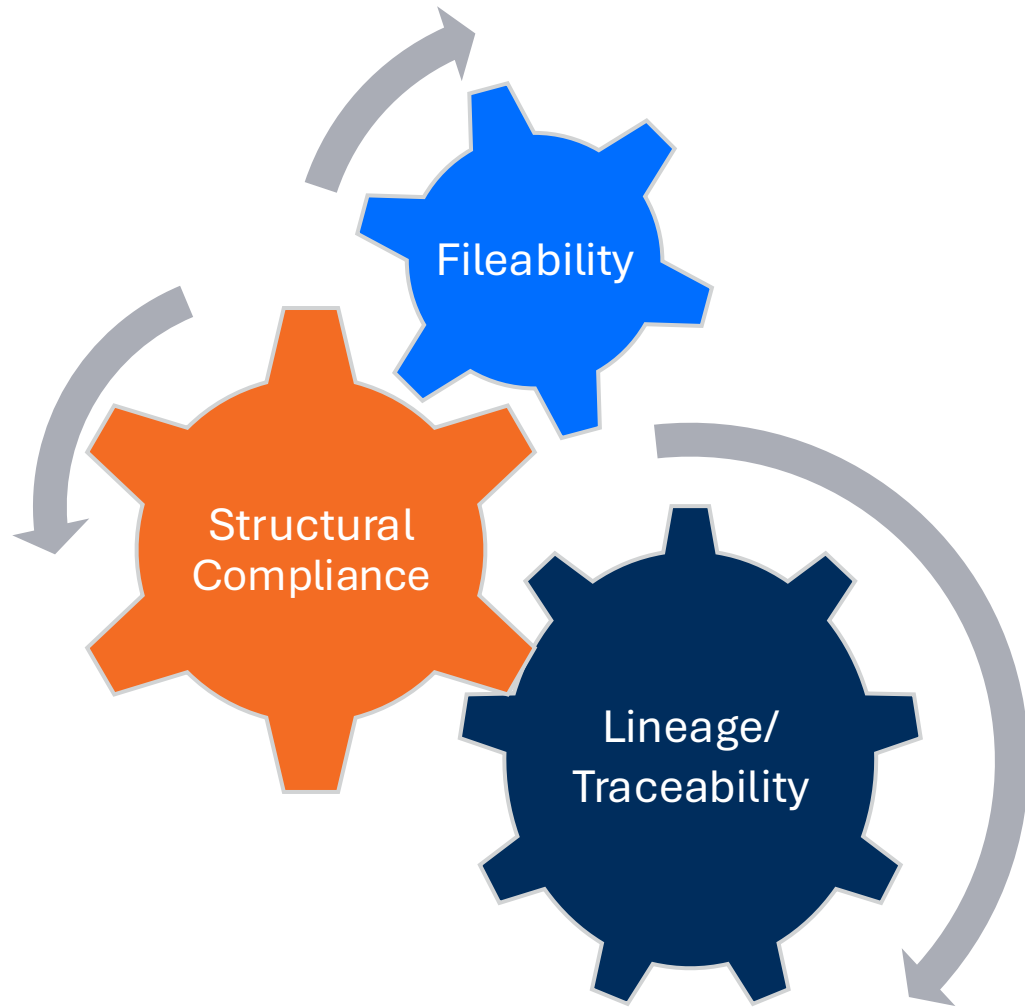
Every decision either reduces or increases RTF / TRC risk—there are no neutral choices

Phase 1: Early Planning — Designing for the Dossier

- Align on intended submission strategy and indication scope
- Define pooling strategy and key efficacy/safety narratives up front
- Data standards strategy
- Plan CSR, SDTM, ADaM, SEND, and define.xml traceability as a single package
- Practical tools: joint planning sessions & submission-focused analysis plans



Phase 2: Study Execution — Programming With the End in Mind



- Implement SDTM and ADaM during study conduct, not after CSR lock
- Maintain alignment through protocol amendments and interim analyses
- Build clean USUBJID / SUBJID and subject-level analysis datasets (ADSL) enabling pooling
- Ensure define.xml and reviewer guides evolve with the data
- Proactively check conformance with FDA business rules and validator rules

Phase 3: Pre-Submission Integration — Reducing Rework

- Run an internal filing review against FDA-like checklists
- Confirm presence and completeness of all required NDA/BLA sections
- Review cross-study pooling logic and consistency of SDTM / ADaM / SEND implementations
- Validate datasets against FDA Technical Rejection Criteria, business rules, and conformance guides
- Ensure CSR ↔ datasets ↔ tables figures are fully traceable and documented in reviewer guides



Phase 4: Submission & Health Authority Interaction

- Assemble the eCTD in line with current eCTD specs and validation criteria
- Transmit via the ESG and confirm technical acceptance
- Use traceable SDTM/ADaM/SEND to respond quickly to information requests
- Avoid additional review cycles driven by avoidable data issues
- Maintain a clean separation between filing issues and scientific review issues in HA dialogue



Case Example – Reactive Compliance and Organizational Learning After TRC Enforcement

Context

In the period immediately following FDA's enforcement of Technical Rejection Criteria (TRC) for study data, internal teams convened to address a rise in rejected submissions and near-miss validation failures. These discussions focused on understanding new rejection patterns and updating submission practices.

Failure Mode

Teams identified recurring issues related to **incorrect file tagging, missing required datasets, and inconsistent module placement** within eCTD submissions. These issues were unrelated to study outcomes or statistical validity but directly affected FDA's ability to process submissions electronically.

Case Example – Reactive Compliance and Organizational Learning After TRC Enforcement

Root Cause

The organization had historically treated eCTD publishing and study data standards as **downstream operational activities**, separate from clinical and programming ownership. As a result, compliance with TRC was addressed reactively—through training refreshers and submission-stage fixes—rather than through integrated planning at protocol development and analysis design stages.

Outcome and Lesson

This case highlights how **organizational structure and accountability models** influence filing success. The response to TRC enforcement required cultural change, emphasizing shared ownership between regulatory and programming teams. It reinforces the principle that filing risk is a structural risk, arising from how responsibilities are partitioned across the submission lifecycle.

Lessons Learned From 50+ NDA Submissions

- Robust early planning around RTF and standards consistently prevents fileability issues
- Applications still struggle when standards decisions and pooling logic are left too late
- Cultural shifts—shared accountability between regulatory and programming—matter more than tools
- Teams routinely underestimate the downstream impact of study start dates and Catalog updates



Practical Takeaways

- Add RTF and standards checkpoints at pre-IND, EOP2, and pre-NDA/BLA
- Map each key CSR conclusion to supporting SDTM/ADaM/SEND datasets and endpoints Adopt a shared, written definition of “submission-ready” that includes:
 - Required sections present and organized
 - eCTD and study data standards conformance checked
 - Traceability documented (CSRs, define.xml, reviewer guides)
 - Pilot this approach before scaling

Closing: From Parallel Tracks to Shared Ownership

- RTF and standards requirements are predictable, and we can design for them
- Submission-ready means complete, organized, standard-compliant, and traceable
- Regulatory and programming must co-own fileability and data conformance
- Submission success is designed, not assembled

Any questions?





Thank you

Get in touch:

 bkaspar@mms Holdings.com

Learn more on our website:

