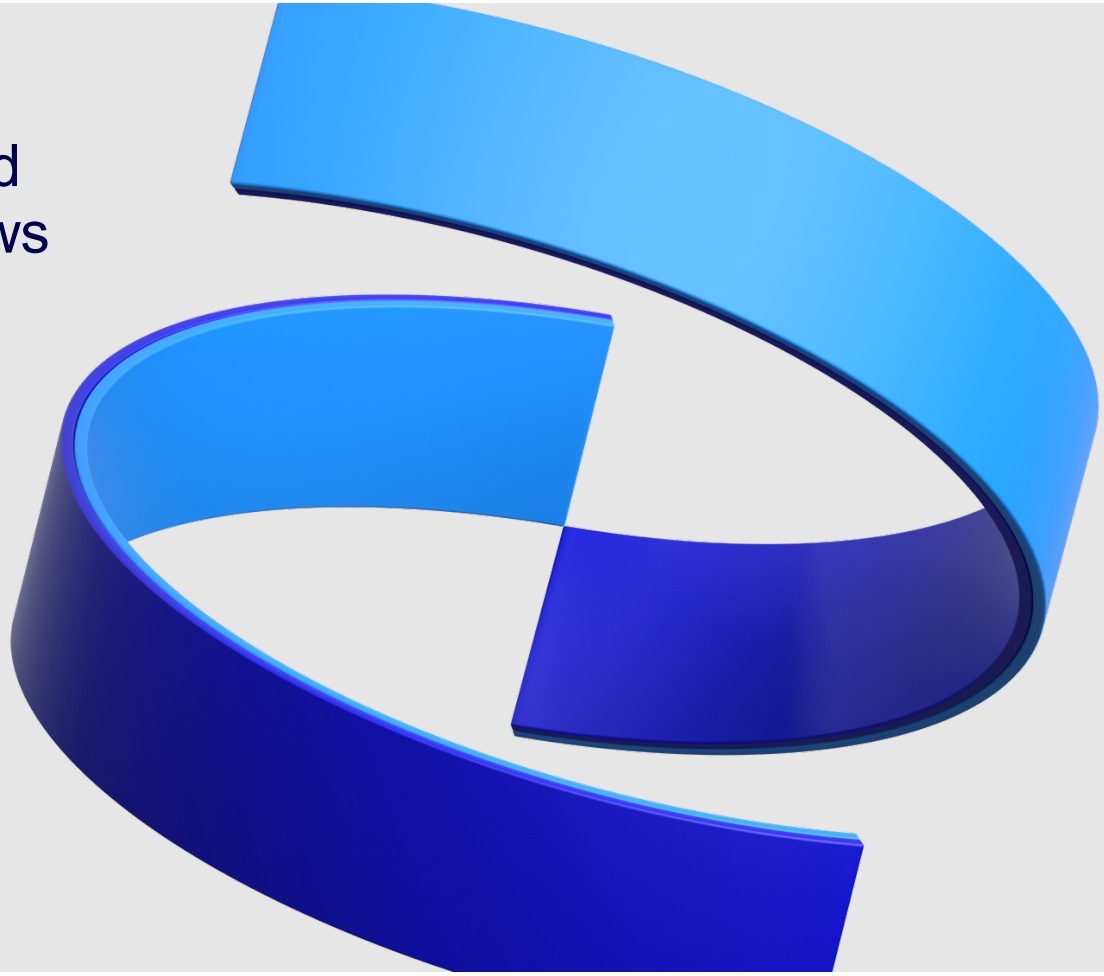
# Evolving the TMF Plan and Automating Quality Reviews

A Review of the Pfizer approach to streamline the quality and content review process through both process improvements and technology advancements



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# Agenda

eTMF Strategy
TMF Study Owner (SO) Transformation
Automation of Quality Review
Q&A

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# Pfizer eTMF Strategy

With the next generation of clinical trials and higher expectations from regulators, we need to be aggressive in adopting automation for TMF document management so that we can improve our **quality**, efficiency and inspection readiness while improving the user experience.

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# How Do We Measure TMF Quality?

## TMF Completeness

- Measures the number of fulfilled placeholders vs. the total number of placeholders expected to be fulfilled at a point in time; document due dates are calculated using milestones or other dates

## TMF Timeliness

- Measures the number of documents that were activated within 35 calendar days of receipt or finalization; timeliness ensures that a study's TMF is contemporaneous

## TMF Document Quality

- Measures the number of documents that pass-through QC on the first submission

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# The Challenge of Completeness

I think my TMF is complete but how do I know?

I don't understand why the TMF completeness score is "green" for my study, but I've been told there are missing documents in the TMF.

I have a strong TMF process, defined requirements and a top-notch system. Why is my TMF not complete and inspection ready? What am I missing?

How is it the inspector found discrepancies and gaps in the TMF for my study when I don't see issues?

TMF Completeness is only an ***indicator*** of whether the TMF contains all expected documents. It will *not account for missing placeholders for new document versions, event driven documents or ad hoc documents*.

We rely on Quality Reviews to help us identify missing and excess placeholders

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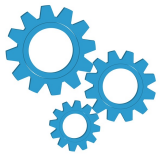
# TMF Quality Foundations



## Optimized Processes

Central Filing

Wizard-based study TMF creation

Event Management

**TMF SO Transformation**

## System Integrations

Auto-filing from source systems

Data feeds for milestones, sites, investigators

## Automation

Study Specific Document List

Relationships and Version

Quality Review

Placeholder creation

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# TMF Study Owner (SO) Transformation

- Adjust TMF Study Owner role
- Simplification of Quality Review
- Collaboration with Study Team Clinical Study Team Assistant (CSTA)

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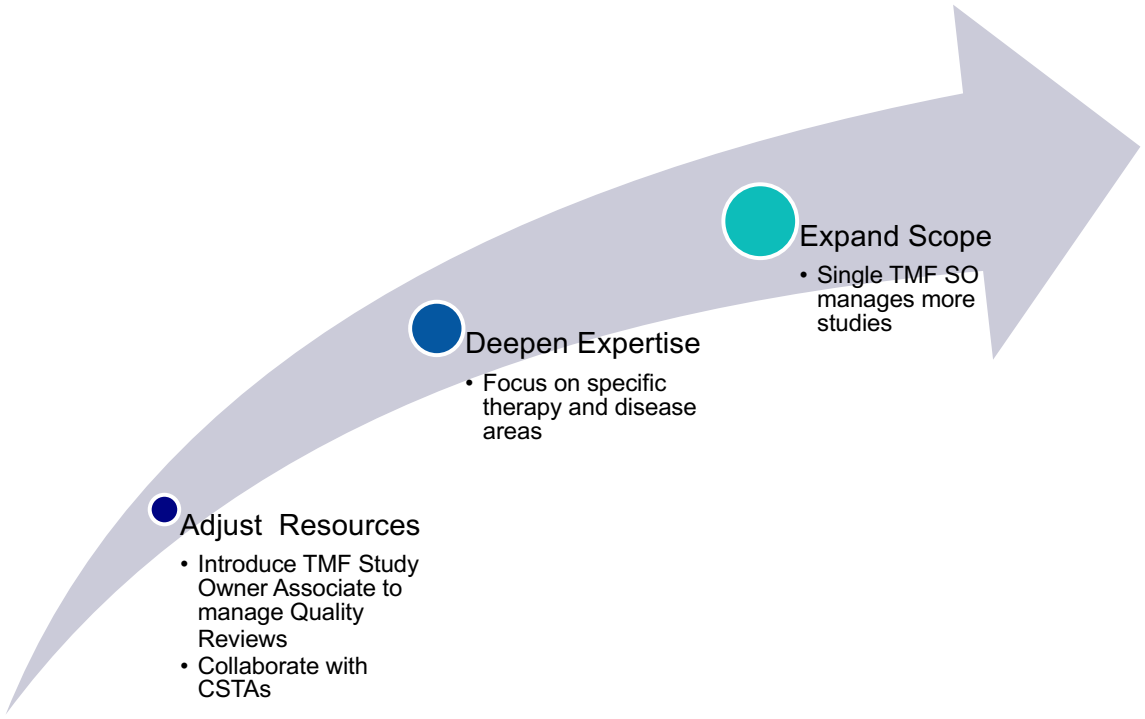
# Adjusting the TMF Study Owner Model

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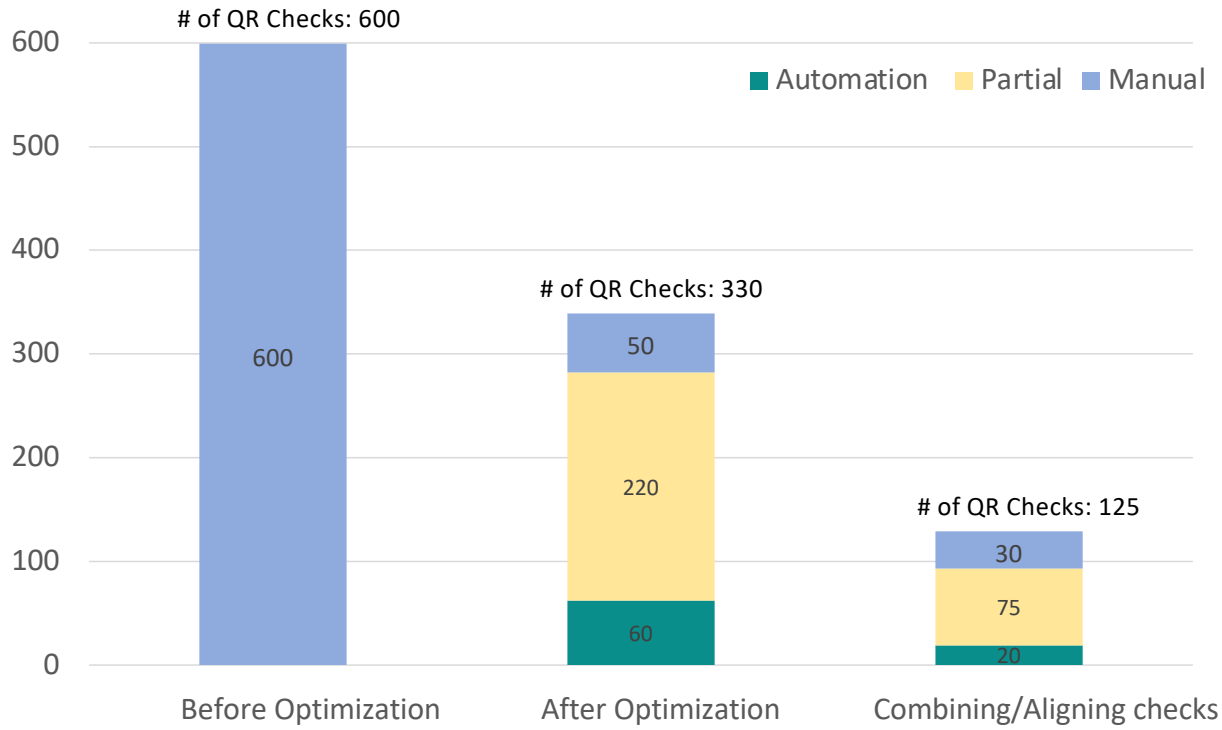
# Quality Review Checks Simplification

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# TMF Study Owner (SO) and CSTA Role Alignment

**Situation**

- Both TMF Operations and CD&O provide operational support for study TMFs

**Problem**

- Overlap in TMF SO and CSTA activities

**Action**

- Convene LDT to align the CSTA and TMF SO roles and responsibilities

**Result**

- New Model with updated RACI and Quick Reference Guide with performance metrics

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# TMF RACI and Quick Reference Guide

**PTMF Management Activities Matrix**

| RACI Legend |
|---|
| A: Accountable for activity completion; provides leadership |
| R: Responsible for completing activity or plays major role |
| A/R: Accountable and Responsible |
| C: Contributes significant support or input; not optional |
| I: Informed |

| Abbreviations | Term |
|---|---|
| TMF SO | TMF Study Owner |
| CSTA | Clinical Study Team Assistant |
| CSTL | Clinical Study Team Lead |
| SM | Study Manager |
| FLDO | Functional Line Document Owner |
| CRO | Contract Research Organization |

| Study Stage | Bucket | Activity | Role | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | TMF SO | CSTA | CSTL | SM | Other FLDO | CRO | Notes |
| Start up | Study TMF Setup | SSDLs setup and activation | A/R | | A | C | C | | |
| | | TMF Management Plan finalization | A/R | | A | C | C | | FLDOs contribute to the confirmation of TMF Content Review details |
| Conduct | Document Management | File Pfizer owned TMF documents (e.g., study level documents) | | R | A/R | R | R | | Each functional line responsible for their own documents. |
| | | File CRO generated TMF documents (e.g., country & site level documents) | | I | | A/R | | R | CSTA helps SM to file docs for urgent case |
| | Study TMF Management | Process Request List Changes (RLCs); Manage Events (Assess/Run); Maintain Templates; Associate enterprise/program level documents; Process Deactivation Requests, etc. | A/R | | C | | | | |
| | | TMF Quality Review (PTMF 5.0 goes live) | A/R | C | A/R | | | | |
| | TMF Performance | Provide TMF metric reports to support oversight of study TMF metrics compliance | I | A/R | | | | | |
| | | Monitor study level past due placeholders | C | R | A/R | | | | |
| | | Monitor country and site level past due placeholders | C | R | C | A | | | |
| Close out | PTMF Lock | Ensure final TMF SSDL Quality Review conducted, and all issues resolved | A/R | C | A/R | | | | |
| | | Ensure PTMF lock timely | A/R | | R | | | | |

QUICK REFERENCE GUIDE

## TMF SO and CSTA TMF Management Collaboration

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4. Monitoring TMF Past Due Placeholders Process ..... 3
5. Communication Best Practices ..... 4


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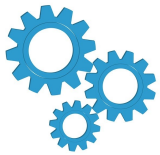
# TMF Quality Foundations



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# TMF Quality Review Principles

Quality reviews are conducted in the eTMF

Every study has a study specific quality review plan that outlines the checks to be performed

Quality check tasks are assigned to designated check performers at specified milestones

Checks are automated where possible

Every quality check task records finding and resolutions

# Study Specific Quality Review Plan (SSQRP) Guidance

Throughout the duration of the study, TMF quality reviewers are responsible for ensuring all required TMF documents for the study are available in the eTMF system at the time they are expected. This includes ensuring all versions of each document that pertain to the study have been filed and the absence of having duplicate documents.

The purpose of the TMF quality review is to confirm that the documentation necessary to reconstruct the study has been filed in the eTMF system

# TMF Quality Reviews User Stories

TMF Director : As a TMF Director I want to be able to assess the reviews that have been conducted for a study

So that I can monitor completeness and overall TMF Health

TMF Operations Lead: As a TMF Ops Lead I want to be able to monitor content and quality review checks

So that I can flag issues for a study to escalate to TMF SO Leads

TMF SO Lead: As a TMF SO Lead I want to monitor content and quality reviews for my studies

So that I can monitor performance of my TMF SOs

TMF SO: As a TMF SO I want a single place to manage and track quality reviews

So that I know what tasks should be performed for my studies

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# Types of Quality Checks

## Automated

The check conditions are configured and the eTMF runs the check automatically at specified intervals. The check either passes or fails. Failed checks are issued as tasks.

Cross check if the document type and its corresponding approval are present.
11.03.11 Subject Evaluability Criteria and Subject Classification
11.03.11 Subject Evaluability Criteria and Subject Classification Approval

Placeholder is only needed if Section 9 of the protocol indicates only certain populations will be included in the analysis. These placeholders are not needed if the protocol indicates all subjects treated with at least one dose will be analyzed (i.e., Intent to Treat (ITT) population).

## Partially Automated

The check conditions are configured as a query that is run at specified intervals. The query results are presented with the task to aid in assessment.

Refer to the Protocol Amendments section of the Registry to determine the number of amendments, confirm the following placeholders present for each protocol and amendments.

02.01.02 Protocol
02.01.02 Protocol Review and Approval
02.01.02 Clinical Protocol Approval Notification
02.01.04 Protocol Amendment
02.01.04 Protocol Amendment Summary of Changes
02.01.04 Protocol Amendment Review and Approval

## Manual

The check conditions are outlined in notes to guide the check performer in the assessment.

If an IRB/IEC may oversee some or all sites within a country (e.g., central/national/regional), confirm the following two placeholders are present, refer to TMF Country Requirements and Country Clinical Trial Intelligence (CCTI) to understand the requirements for other IRB/ IEC related document types
04.01.03: IRB or IEC Composition
04.01.05: RB or IEC Compliance Documentation

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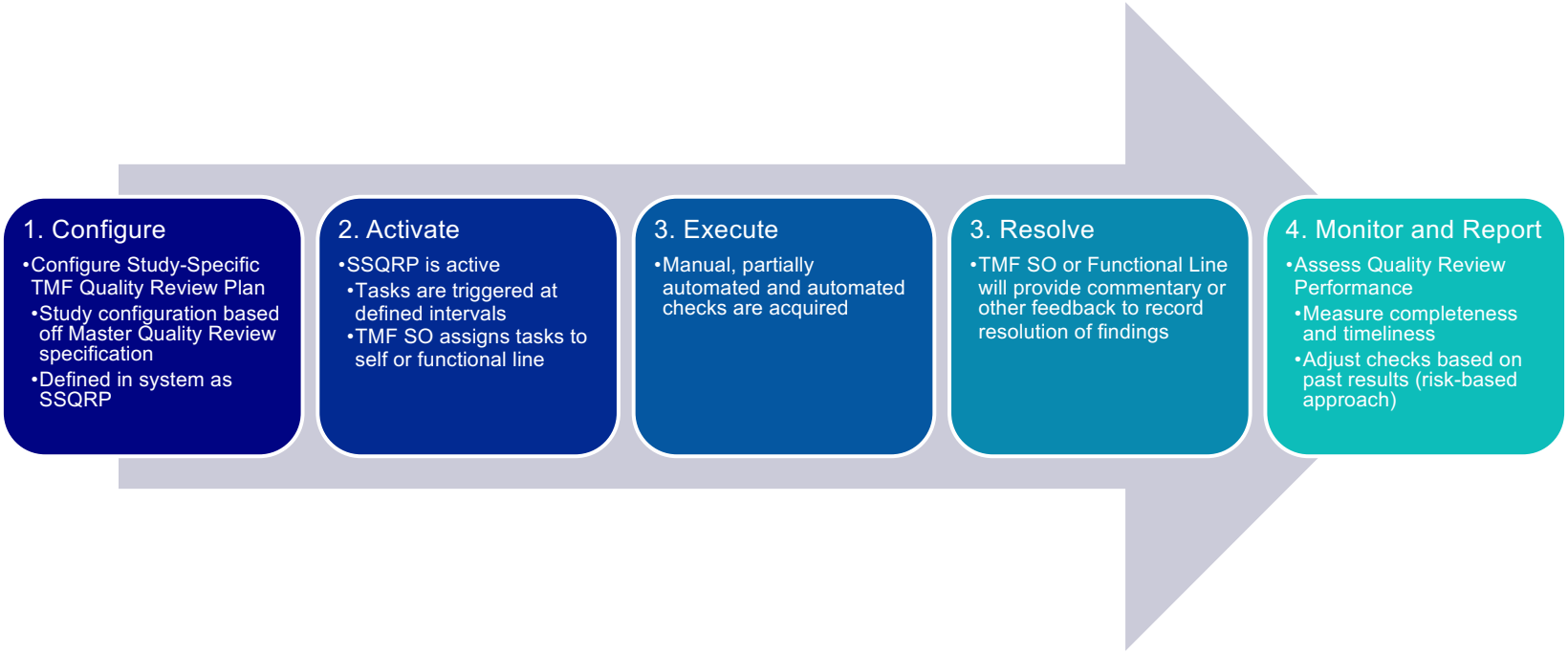
# Automation Patterns

| Pattern | Description | Options |
|---|---|---|
| Document Type(s) Check | This pattern will check for the existence of placeholders and documents for the configured document types (ID#s). | Scope can be set to Placeholder only or Placeholder and Document. |
| Cross Check | This pattern will check that the count of placeholders for a specific document type matches with the count of placeholders to the corresponding document type(s). | Scope can be set to Placeholder only or Placeholder and Document.<br><br>Ability to apply conditions on corresponding document types on Milestone\ SSDL Activation Date\Document Generation Date. |
| Relationship Check | This pattern will check for the presence of related placeholders and/or documents for the configured document types as per the document type definition. | Scope can be set to Placeholder only or Placeholder and Document.<br><br>Can be configured with specific document types (ID#s) or for all document types where "Relationship Expected = Yes".<br><br>Ability to define pass or fail criteria on the presence of “any”, “a specific” or “all” related documents. |
| Duplicate Document Check | The pattern shall allow to check for the potential duplicate documents for the configured document types (ID#s) by comparing the document attributes. | Scope can be set to Placeholder only or Placeholder and Document.<br><br>Ability to configure for all SSDL Documents or to a list of specific document types (ID#s) |
| Empty / Satisfied Ad-hoc Placeholder Check | This check shall allow to identify any empty or satisfied placeholders for configured ad-hoc document types. | Scope can be set to Placeholder only or Placeholder and Document.<br><br>Ability to configure for all ad-hoc document types or a list of specific ad-hoc document types (ID#s) |

# High-Level Quality Review Flow

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# Q & A

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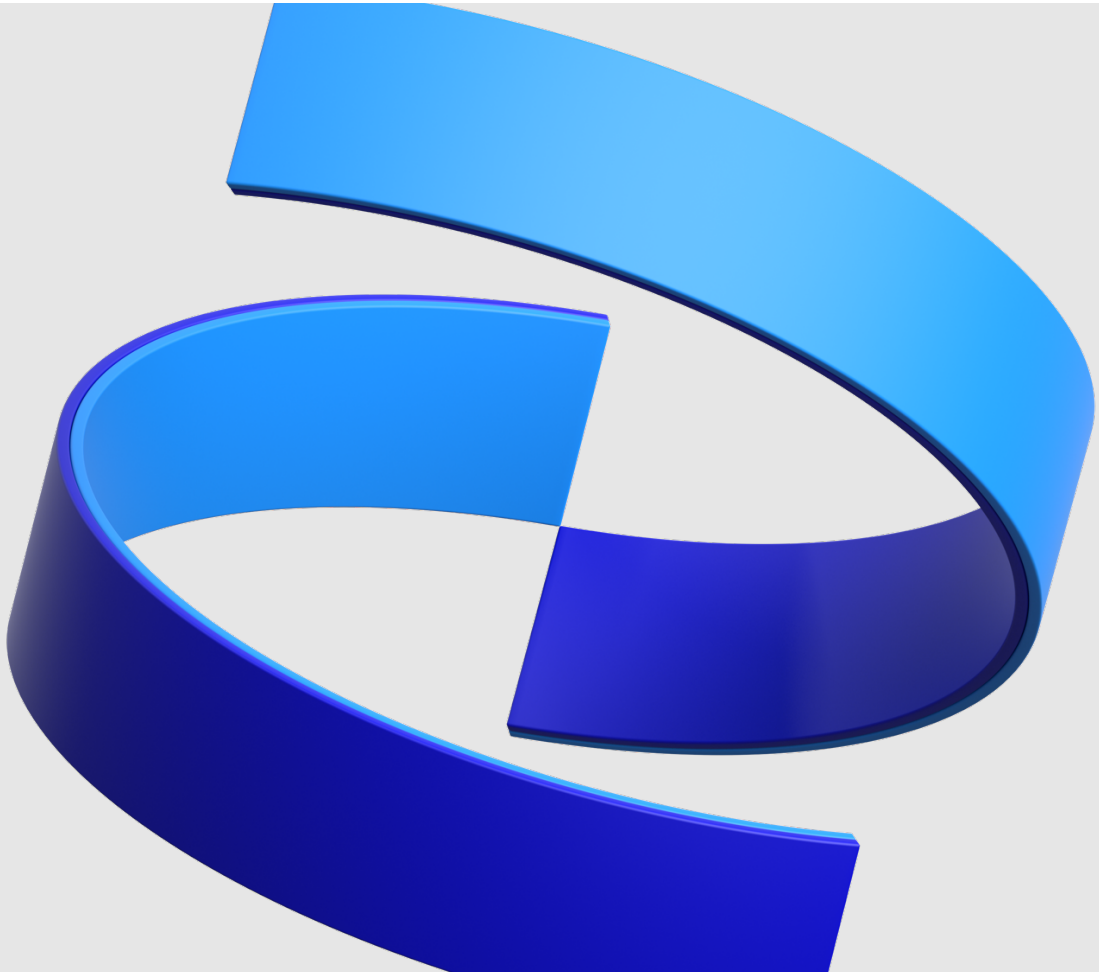
# Thank You!



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