Gerstner Sloan Kettering
Graduate School of Biomedical Sciences

Memorial Sloan Kettering
Cancer Center

Effective Documentation and Corrective and Preventive Plan (CAPA) Reviews

Ensuring Data Integrity, Compliance, and Continuous Improvement

Karima Yataghene, MD
Senior Director, Clinical Research Quality Assurance
Clinical Research Compliance

Effective Clinica Research Documentation

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Importance of Effective Documentation

Ensures **data integrity** and compliance with regulatory requirements (FDA, ICH-GCP, HIPAA).

Provides a **verifiable record** of all study activities and decisions.

Protects against audit findings and inspection observations.

Facilitates **continuity of care and research reproducibility**.

Key ICH E6(R3) Definitions

- **Data Integrity:**
  Data are **attributable, legible, contemporaneous, original, accurate, complete, secure, reliable, and fit for purpose**.

- **Essential Records:**
  Documents and data that enable **trial oversight, evaluation of conduct, and confirmation of compliance with GCP and regulations**.

- **Source Records:**
  Original documents or data, or **certified copies of the original**, irrespective of the media used. This may include:
  - Trial participants' medical/health records, notes, or charts
  - Data provided/entered by trial participants (e.g., electronic patient-reported outcomes, ePROs)
  - Healthcare professionals' records from pharmacies, laboratories, or other facilities involved in the trial
  - Data from automated instruments such as wearables and sensors

Core Principles of Good Documentation

Accuracy: Document facts, not assumptions or opinions.

Completeness: Include all relevant information (source data, protocol deviations, adverse events).

Timeliness: Record information **as close as possible to the time of observation**.

Legibility & clarity: Handwritten entries must be readable; electronic entries should follow formatting standards.

Traceability: Ensure all changes are tracked (audit trails for electronic records).

Attribution: Record who performed an action or made an entry.

ALCOA+: Ensure documentation is **Attributable, Legible, Contemporaneous, Original, Accurate, plus Complete, Consistent, Enduring, and Available**.

If it's not documented, it didn't happen: Reinforce that all actions, observations, and decisions must be recorded.

Document completed and omitted actions: Clearly indicate when a step was performed, skipped, or not applicable.

ALCOA+ Principles

- **Core ALCOA Principles**
  ALCOA stands for **Attributable, Legible, Contemporaneous, Original, and Accurate**, which are essential for **reliable clinical data**

- **Additional + Principles**
  The “+” ensures documentation is **comprehensive and durable** throughout the trial:
  - **Complete:** Include all necessary data, even if negative or zero results.
  - **Consistent:** Use uniform methods, formats, and terminology.
  - **Enduring:** Records are maintained in a durable format throughout the study.
  - **Available:** Documentation is accessible for review, audits, or inspections.

Principle	Description
Attributable	Entries are linked to the person performing the action or making the observation.
Legible	Records must be readable and understandable.
Contemporaneous	Document data as close as possible to the time of observation.
Original	Source records or certified copies are used.
Accurate	Information is correct, truthful, and reflects what actually occurred.

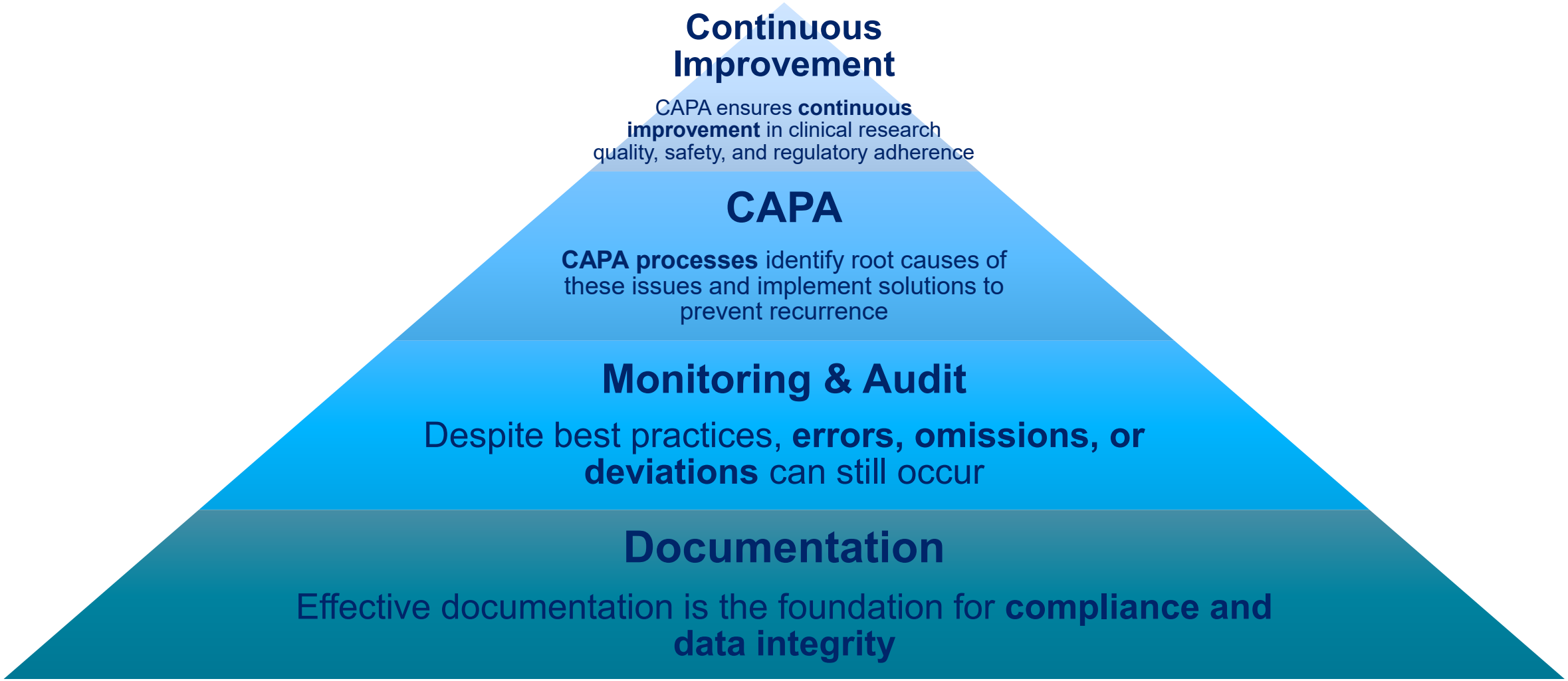
Most Common 483 Findings in Clinical Research

#	Observation / Issue	Why It Happens / What It Reflects
1	**Failure to comply with Form FDA 1572 requirements / failure to follow the investigational plan (protocol non-compliance / deviations)**	Inspectors often find that the site doesn't adhere strictly to the protocol or 1572 commitments: e.g., 1. Use of unapproved procedures, 2. Deviation without documentation or justification, 3. Enrolling ineligible subjects not meeting study entry criteria. 4. Missing study procedures indicated in the protocol, such as chest X-rays or electrocardiograms.
2	**Inadequate or inaccurate case history records / inadequate study records / source-data issues**	Common issues include: 1. Missing, incomplete, or inconsistent source data (e.g., medical records, CRFs, visit notes). 2. Failure to maintain adequate study records. 3. Dispensed drug amounts that do not match what the participant actually took. 4. Returned drug amounts that do not reconcile with what should have been returned.
3	**Informed consent / subject-protection deficiencies**	Problems include missing consent forms, use of outdated ICFs, failure to re-consent when needed (e.g., protocol amendments), or other lapses in subject rights protections.
4	**Poor accountability / control of investigational product (IP)**	Observations often involve missing or incomplete IP accountability records — e.g., no proper logs for receipt, dispensing, return or disposal; inadequate tracking of drug/device.
5	**Inadequate safety reporting / failure to report or record adverse events (AEs/SAEs)**	Issues: delayed or missing AE/SAE reporting, incomplete documentation of safety events, or failure to meet regulatory reporting timelines — compromising subject safety and data integrity.

Best Practices for Clinical Documentation

- **Informed Consent** – Document all consents (written or verbal) with signatures and dates; ongoing process.
- **Corrections/Addenda** – Use addenda for late entries or corrections; always signed and dated.
- **Case Report Forms (CRFs)** – Only use as source if specified in protocol.
- **External Medical Records** – Incorporate if relevant, with documented retrieval efforts.
- **Questionnaires** – Record who completed them and the method used.
- **Protocol Deviations** – Report timely; distinguish prospective, retrospective, and non-reportable.
- **Compliance Tools** – Use checklists, drug diaries, AE trackers, and follow-up logs.
- **Essential Records** – Maintain organized regulatory binders (electronic or paper), follow SOPs, and ensure quick retrieval.
- **Quality & Training** – Conduct internal audits, train staff, and implement electronic systems with audit trails.

From Documentation to CAPA: Ensuring Continuous Compliance



CAPA Overview

Purpose & Importance:

- Eliminates root causes of problems to **prevent recurrence**.
- Ensures **continuous improvement** in trial conduct, data integrity, and participant safety.

CAPA Process Steps:

1. **Identify deviations or issues** (from audits, monitoring, inspections, or documentation gaps).
2. **Perform root cause analysis** to understand why the issue occurred.
3. **Plan corrective and preventive actions**.
4. **Implement actions** and document steps taken.
5. **Verify effectiveness** to ensure the issue does not recur.

Regulatory Compliance:

- CAPA is **mandated by regulatory bodies** (FDA, ICH-GCP).
- Essential for maintaining **trial quality, safety, and compliance**.

CAPA Lifecycle Stages

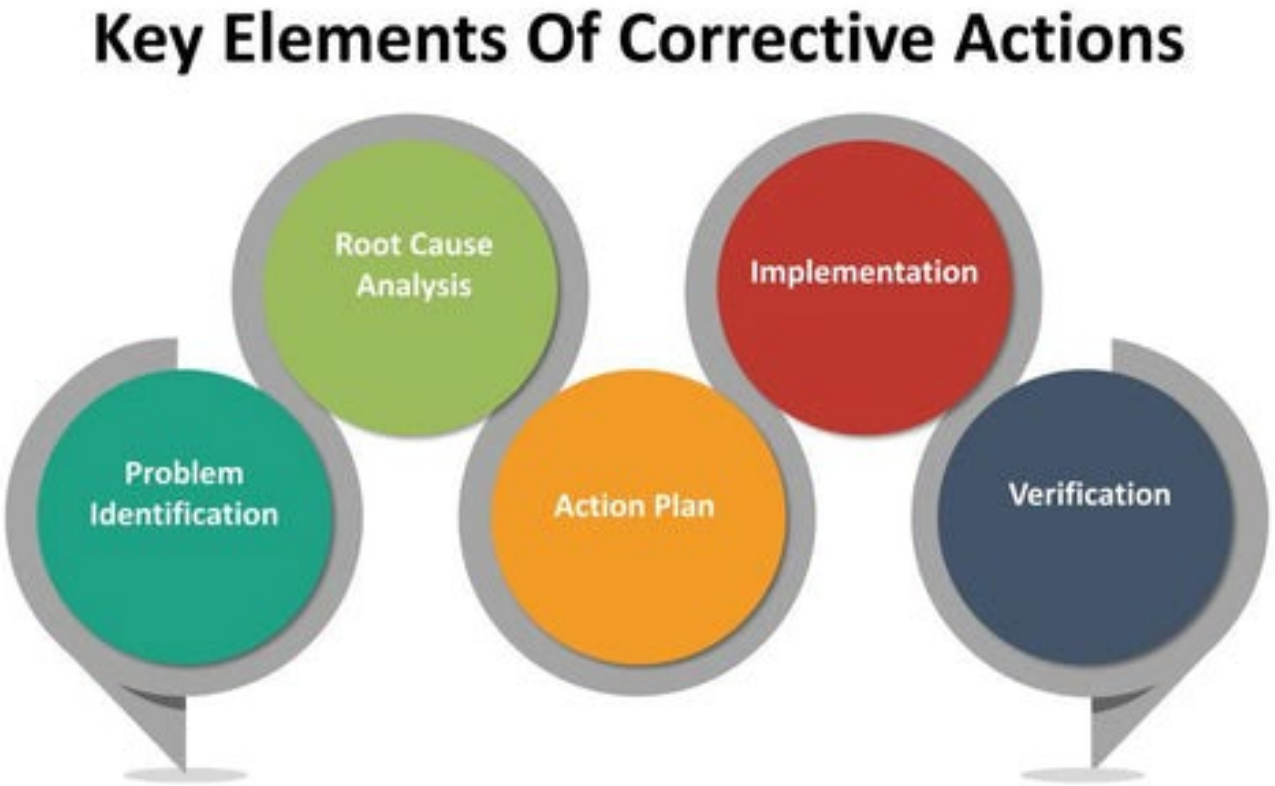
1. **Issue Identification**
Detect deviations or non-compliance to identify issues that require corrective action.

2. **Root Cause Analysis**
Determine underlying causes using tools like '5 Whys' and Fishbone diagrams.

3. **Action Plan Development**
Develop corrective and preventive measures with responsibilities and timelines assigned.

4. **Plan Implementation**
Execute the planned actions effectively to address the identified issues.

5. **Effectiveness Check**
Verify that actions resolved the issue and prevented recurrence through thorough review



CAPA in Action: Improving Clinical Research Quality

- **Prevents Recurrence** – Fixes gaps in documentation, protocol deviations, data handling
- **Enhances Data Integrity** – Corrective actions ensure complete and reliable data
- **Supports Regulatory Compliance** – Demonstrates proactive quality management
- **Drives Continuous Improvement** – Lessons feed back into SOPs, training, and systems

Key Takeaways

Document everything accurately and completely – your records should tell the participant's and study's story.

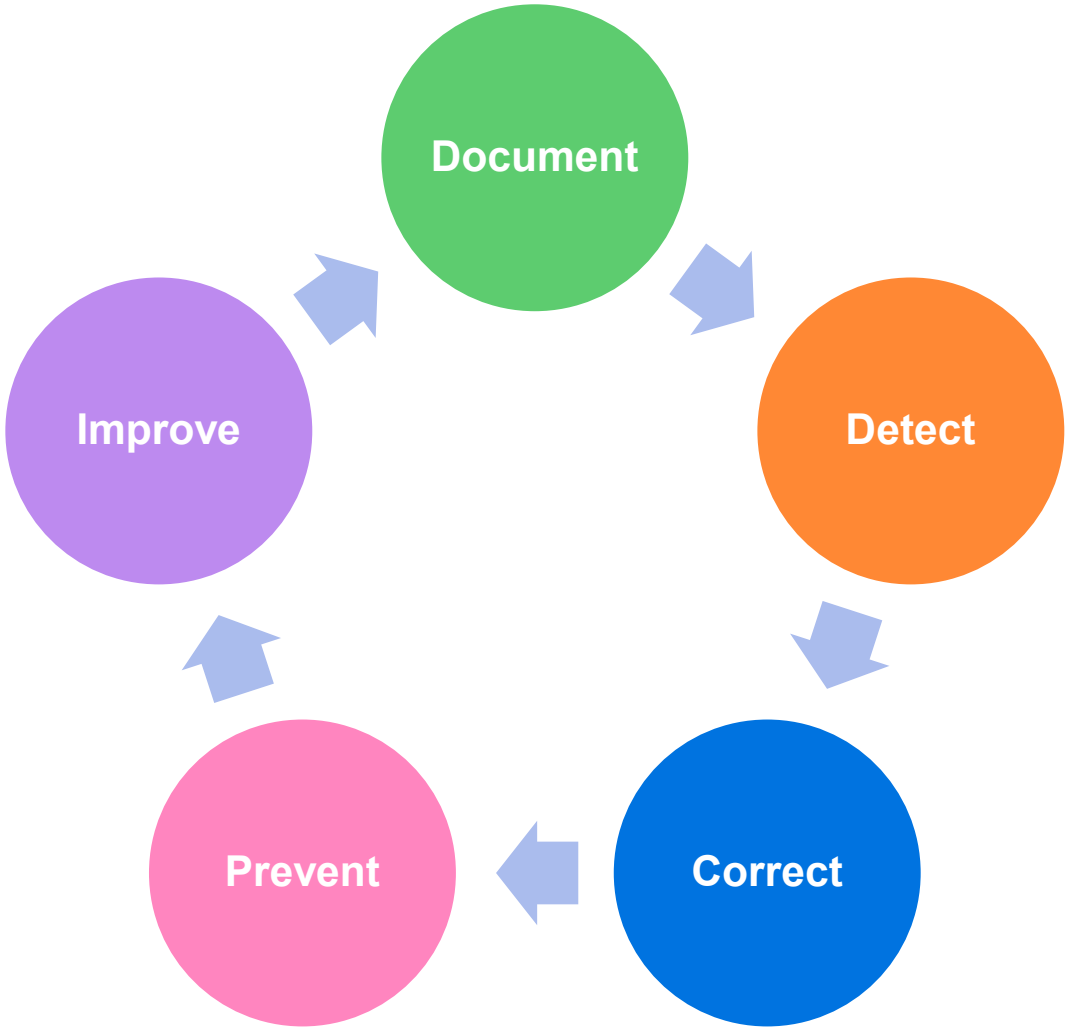
Follow ALCOA+ and SOPs to ensure quality, integrity, and compliance.

CAPA drives continuous improvement – identify gaps, correct issues, and prevent recurrence.

PI supervision is essential – active oversight ensures ethical, compliant, and high-quality conduct.

Handle errors and late entries properly – document, communicate, and implement preventive measures.

Continuous Improvement Loop



QUESTIONS

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Test Your Knowledge

Test your Knowledge

Which of the following is *not* a core principle of good clinical research documentation?
A. Accuracy
B. Timeliness
C. Legibility
D. Popularity of the researcher

Answer: D

True or False:
“If it’s not documented, it didn’t happen.”

Answer: True

What are source records?
A. Copies of documents used for convenience
B. Original documents or certified copies, including medical records, participant-reported data, and lab results
C. Only electronic records
D. Only signed consent forms

Answer: B

Test your Knowledge

What is the main purpose of CAPA in clinical research?
A. To replace documentation practices
B. To eliminate root causes of problems, prevent recurrence, and ensure continuous improvement
C. To provide optional training for staff
D. To delay audits

Answer: B

True or False:
CAPA is mandated by regulatory bodies such as the FDA and ICH-GCP.

Answer: True

How does CAPA support data integrity in clinical research?
A. By eliminating the need for source documents
B. By correcting inaccuracies and preventing future issues
C. By providing optional staff guidance
D. By automating all data entry

Answer: B

Test your Knowledge

Which of the following is NOT part of ALCOA principles?

A) Attributable
B) Logical
C) Original
D) Accurate

Answer: B

What is the primary purpose of a CAPA plan?

A) To document adverse events
B) To prevent recurrence of issues and improve processes
C) To train site staff on GCP
D) To archive trial documents

Answer: B

Which step comes first in the CAPA lifecycle?

A) Effectiveness check
B) Root cause analysis
C) Implementation
D) Identification of issue

Answer: D

Resources

Clinical Research: https://mskcc.sharepoint.com/sites/pub-ClinResearch

Clinical Research Quality Assurance Portal: https://mskcc.sharepoint.com/sites/pub-ClinResearch/SitePages/CRQA--Clinical-Research-Quality-Assurance.aspx

FDA Form 483 Frequently Asked Questions: https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/fda-form-483-frequently-asked-questions

Frequently Asked Questions – Statement of Investigator (Form FDA 1572): https://www.fda.gov/regulatory-information/search-fda-guidance-documents/frequently-asked-questions-statement-investigator-form-fda-1572

ICH Harmonized Guidelines E6(R3): https://database.ich.org/sites/default/files/ICH_E6%28R3%29_Step4_FinalGuideline_2025_0106.pdf

Thank you

Karima Yataghene, MD
Senior Director, Clinical Research Quality Assurance
Clinical Research Compliance
Clinical Research Administration
yataghek@mskcc.org

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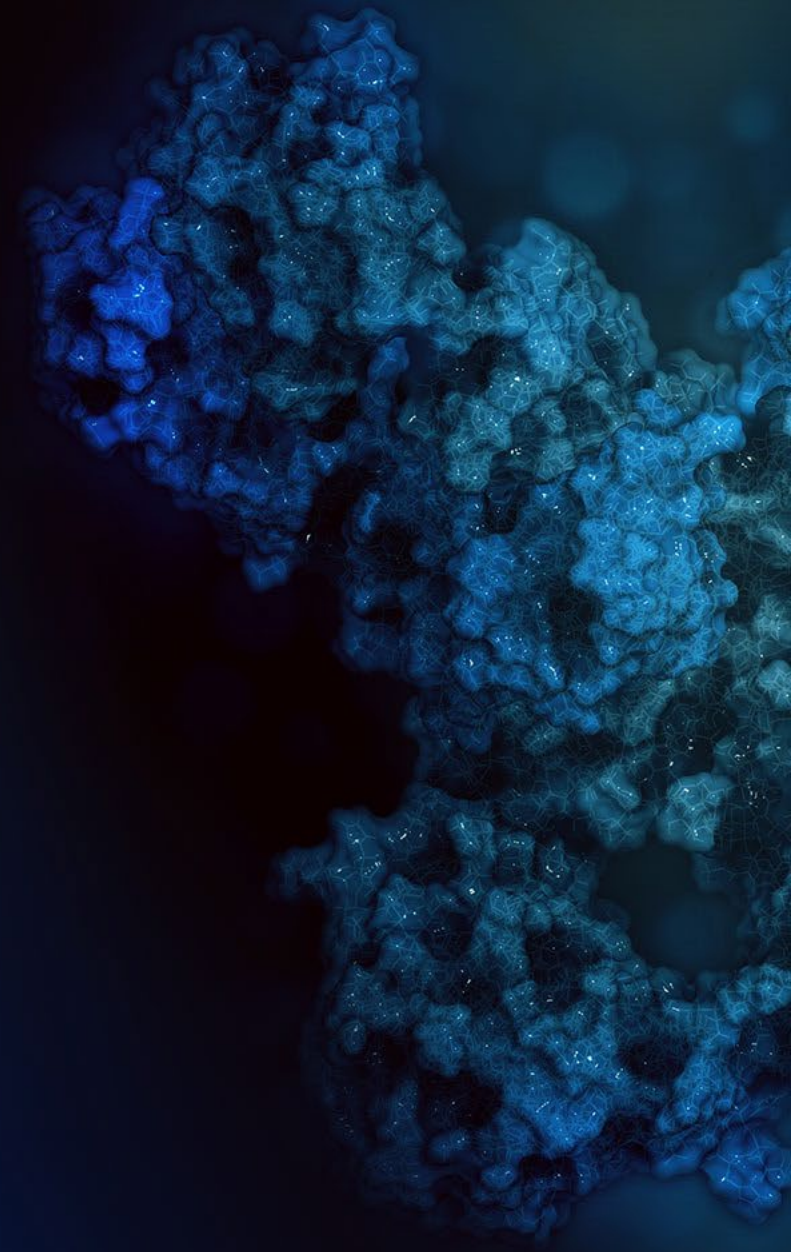

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