Audit/Inspection Readiness

A Presentation by Pharmaceutical Product Development (PPD)

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HELPING DELIVER LIFE-CHANGING THERAPIES

PPD

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Objectives

- Describe the difference between an Audit versus (vs.) Inspection
- Understand the Role of Quality Control (QC) and Quality Assurance (QA) in proper Quality Management (QM)
- Recognize the Role of QM in Site preparation for a Regulatory Inspection
- Gain insight into Preparation for a Regulatory Inspection utilizing practical tips for preparation

Audit versus Inspection

Audit versus Inspection

Audit

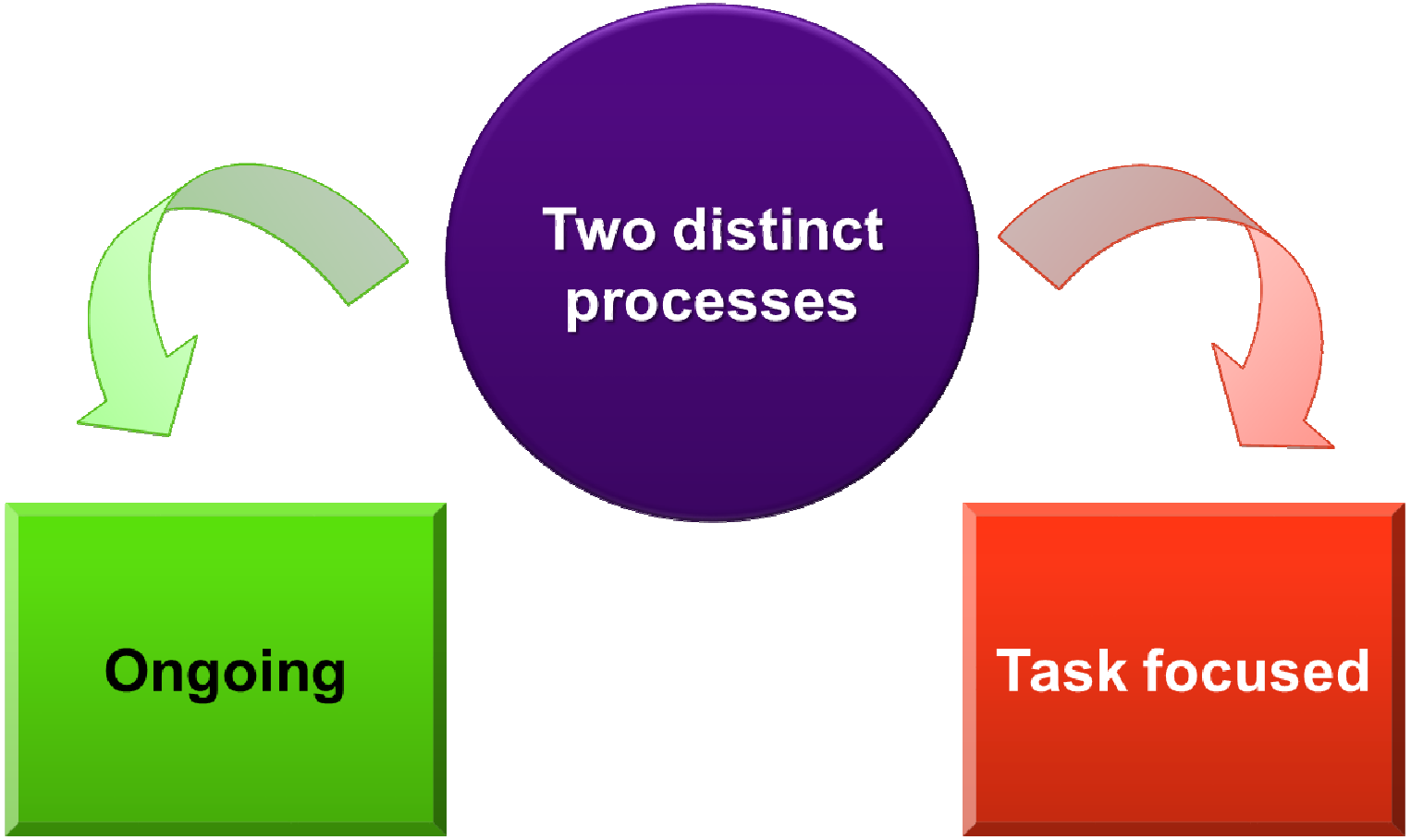
A systematic independent examination of trial related activities and documents, to determine whether the evaluated trial related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement

International Council for Harmonisation (ICH)-GCP 1.6

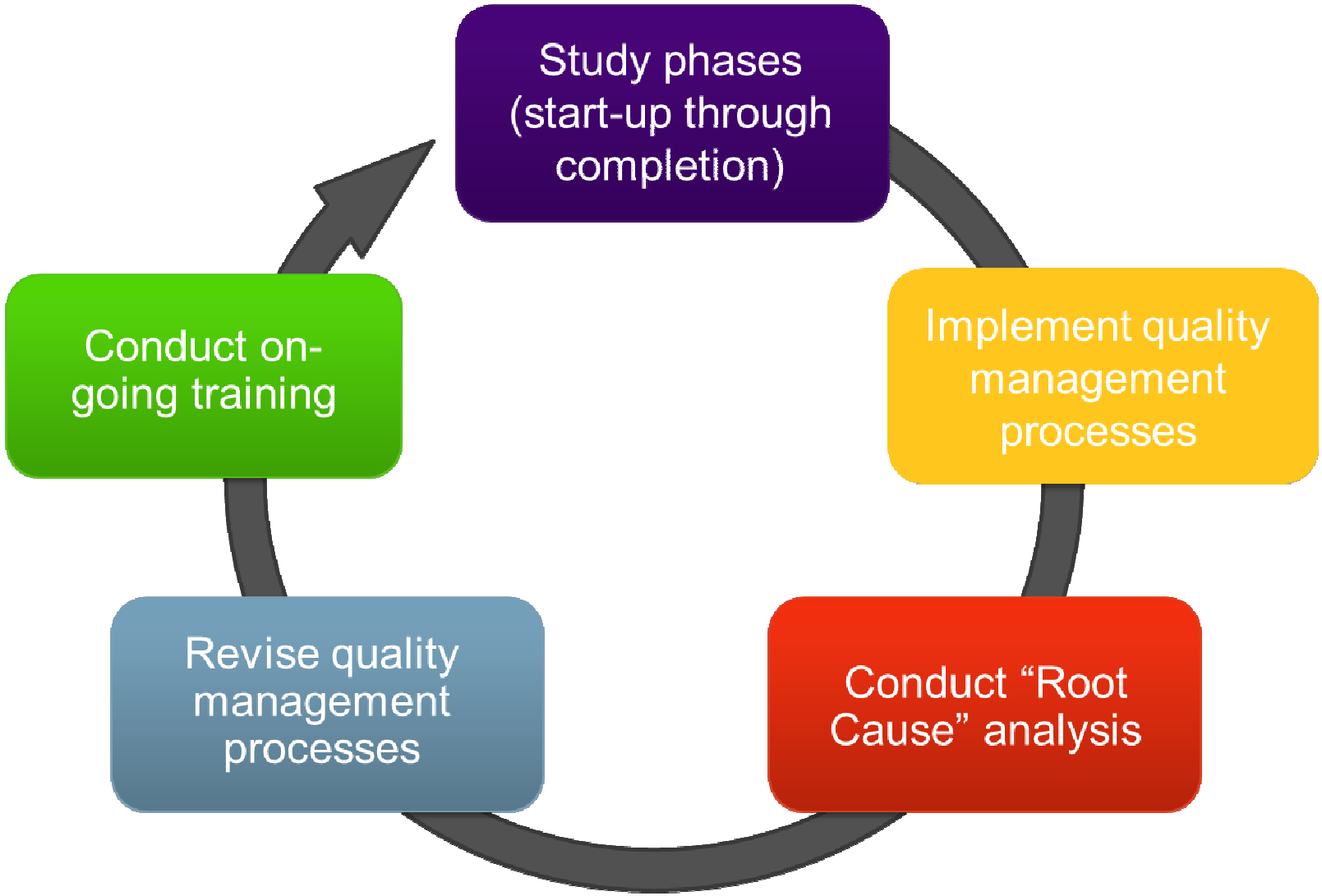
Inspection

The act by a regulatory authority of conducting an official review of documents, facilities, records, and any other resources that are deemed by the authority to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or Contract Research Organization (CRO) facilities, or at other establishments deemed appropriate by the regulatory authority

ICH-GCP 1.29


Two distinct processes
Ongoing
Task focused

Audit Readiness Life-Cycle



Quality Management and Audit Readiness

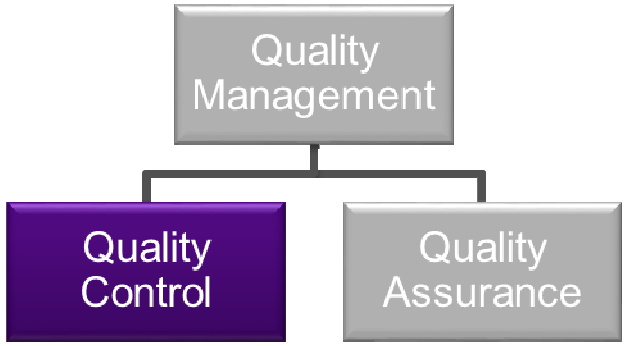
Quality Management

Quality Management is a term used to describe all the activities for ensuring consistent quality of a study or within an organization. The overall quality management function includes the objectives, responsibilities, processes and procedures needed to continually evaluate and improve the quality of the clinical research.

- Participant safety and data accuracy
- Effective protocol implementation
- Sponsor and regulatory compliance
- Audit readiness

Quality Control

Real-time, ongoing (day-to-day) observation and documentation of a site's work processes to ensure applicable procedures are being followed.



- Verify accurate completion of the Informed Consent process and documentation
- Review of eligibility criteria prior to enrollment
- Verification of study product management responsibilities
- Review of case report forms for accuracy prior to data entry or faxing
- Tracking and review of incoming and outgoing Institutional Review Board (IRB)/Ethics Committee (EC) communication (regulatory documents)

Quality Control (continued)

Example: Informed Consent Form (ICF) Review

- Participant provided ample time.
- Signed/dated properly.
- The participant has dated their own signature.
- A copy was provided.
- The person obtaining consent has been delegated to do so.
- Ensure that any local requirements are observed.
  - Example: 2017 Pennsylvania State Supreme Court ruling.

Quality Control (continued)

Example: Inclusion/Exclusion Criteria

- Each Participant must be qualified for the study by meeting all inclusion criteria and not meet any of the exclusion criteria.
- Screening procedure must take place after the ICF is signed.
- Each Inclusion Criteria (IC)/Exclusion Criteria (EC) criteria must be addressed.
- A blanket statement is not appropriate.

Quality Control (continued)

Proper conduction of the ICF process/documentation and Enrollment Adherence are critical to verify!

- Across all networks/countries (2017):
  - ICF Violations: 136
  - Enrollment Violations: 100

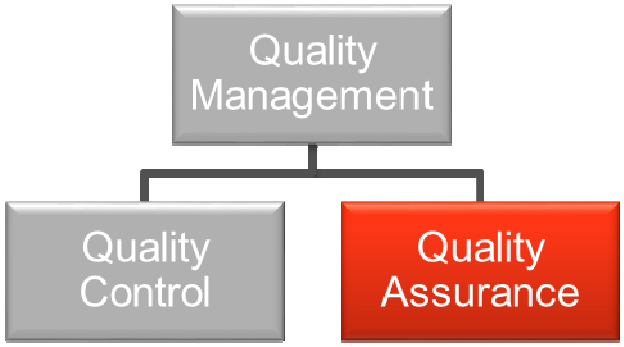
- Across only IMPAACT (2017):
  - ICF Violations: 10
  - Enrollment Violations: 2

Quality Control (continued)

- Regulatory Documents
  - Protocol and Informed Consent Form(s) approval present from all required regulatory bodies
  - Study-specific aides submitted to the IRB/EC and applicable regulatory authorities as required
  - Current Delegation of Responsibilities (DoR) Log
  - Training Documentation
  - Current Licensures and Curriculum Vitae (CVs)

Quality Assurance

Defined as a periodic, systematic, objective, and comprehensive examination of the total work effort to determine the level of compliance with all applicable laws and regulations governing clinical research.

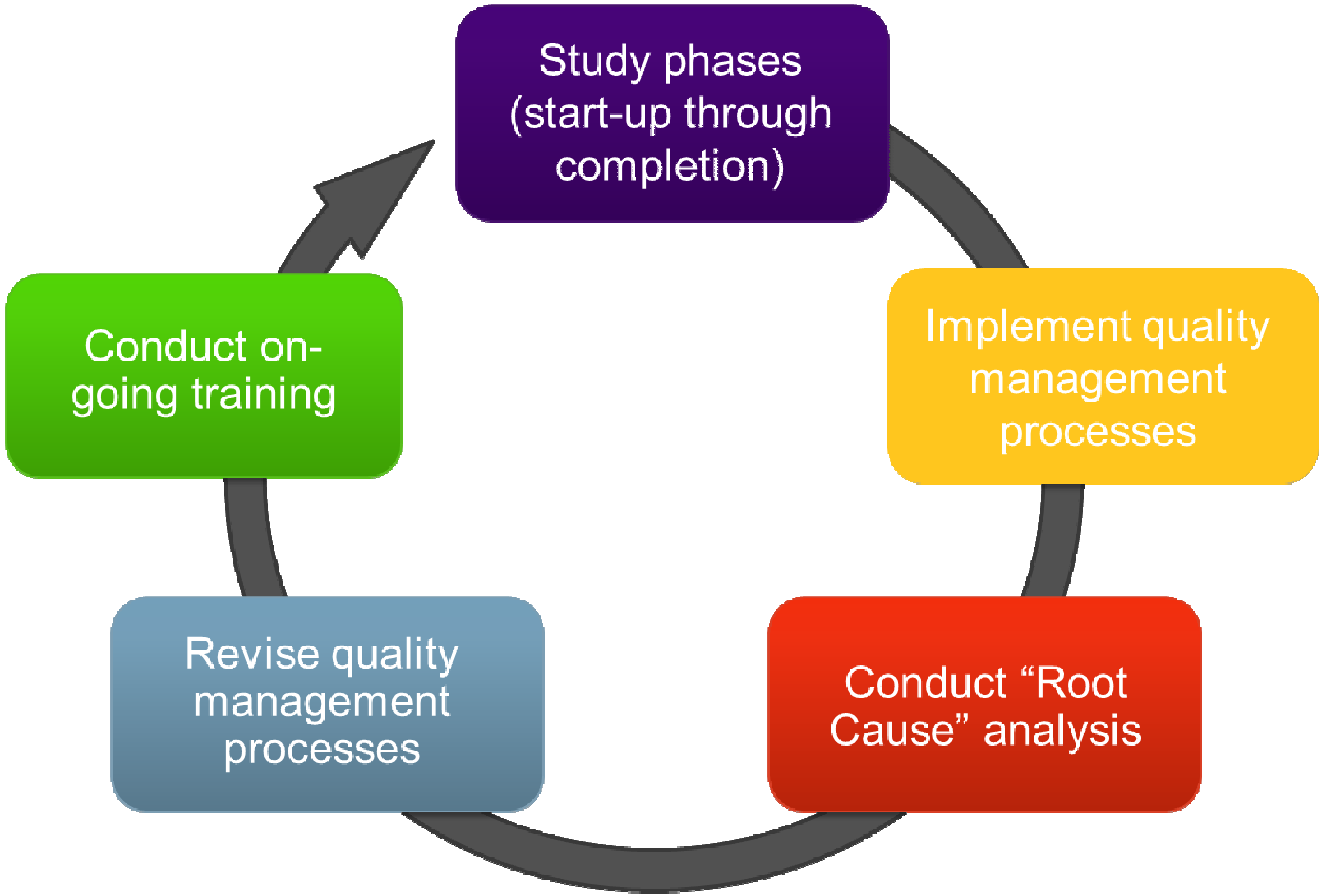


- A review of the research records for the first five (5) participants enrolled in the study comparing source documents to case report forms and the protocol for accuracy
- Quarterly verification of regulatory or essential documents
- Monthly review and comparison of study product accountability logs, shipping records, and inventory
- Quarterly verification of current policies, procedures, forms, etcetera (etc.)

Quality Management Tips

- Create tools before the trial that can be modified to become protocol-specific
  - For example, ICF process checklists, eligibility checklists, protocol-tracking tools, chart review tools, QC checklists
- Develop SOPs to facilitate the process
  - For example, Informed Consent process and tracking, training algorithms
- Maintain all study related documents in an organized and centralized location (where applicable)

Audit Readiness Life-Cycle



Regulatory Authority Inspections

Before the Inspection

Inspections can be Announced or Unannounced

When Notified of an Inspection (Announced):

- Notify the Sponsor (DAIDS)
- Plan for:
  - Responsibilities of team members
  - Availability of team members
  - Where the Inspectors will work

During the Inspection

Work with the Inspector to set expectations:

- How long does the Inspector plan to be at the site?
- Will the Inspector need access to any facilities?
- What is the scope of the inspection?
- What hours should the site staff plan to be available?
- What is the possibility of daily debriefing?

Tip: A daily debriefing can help you know the direction of the inspection.

Tip: Make every effort to mitigate an Inspector's finding during the inspection if possible.

During the Inspection

Inspectors may request additional documents or need help locating documents that have been provided.

Tip: Designate a team member to be the site contact

Role of site contact includes:

- Making sure Inspector has everything needed.
- Accompany Inspector around site if necessary.
- Take notes of discussions, questions, requests, etc.
- Makes copies for Inspector (make duplicates).

During the Inspection

Inspectors may also wish to speak to individual team members for clarification of events.

Tip: Listen to what is asked;
Answer only the question that is asked;
Do not answer for another team member;
Be confident, truthful, factual, and concise.

After the Inspection

Inspectors will request a time to debrief the site staff. At this time, the Inspector will notify the site of the next step [issue a Form Food and Drug Administration (FDA) 483, etc.].

Respond promptly to any findings.

References

- Code of Federal Regulations (CFR) Title 45, Part 46
- Division of Acquired Immunodeficiency Syndrome (DAIDS) Requirements for Clinical Quality Management Plans (DWD-POL-CL-009.04)
- DAIDS Source Documentation Requirements, Appendix 1 (DWD-POL-CL-04.00A1)
- DAIDS Essential Documents Recordingkeeping Requirements, Appendix 1 (DWD-POL-RA-03.00A1)
- DAIDS Protocol Registration Procedures Manual, Version 3.0 dated Apr/2015
- Food and Drug (FDA) Guidance for Industry Integrated Addendum to ICH Guidelines for Good Clinical Practice (E6) (R2)

QUESTIONS?