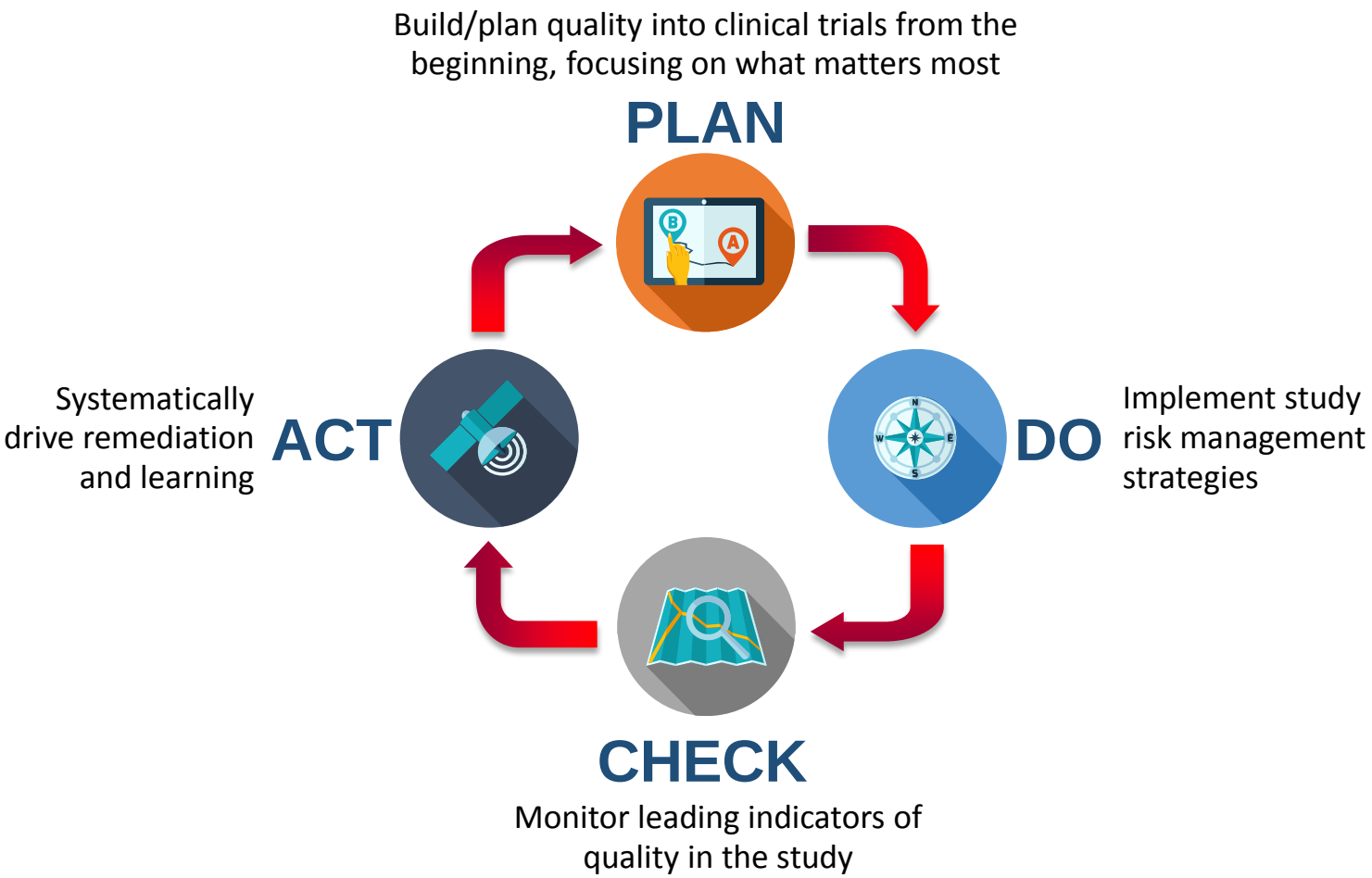
QUALITY BY DESIGN

CTTI recommends that quality be built into the scientific and operational design and conduct of clinical trials as follows:

1. **Create a culture that values and rewards critical thinking and open dialogue about quality**, and that goes beyond sole reliance on tools and checklists. Encourage proactive dialogue about what is critical to quality.
2. **Focus effort on activities that are essential to the credibility of the study outcomes**. Streamline study design wherever feasible. Consider whether nonessential activities may be eliminated from the study to simplify conduct.
3. **Involve the broad range of stakeholders** in protocol development and discussions around study quality, including staff and patients. Early engagement with regulators should be considered when a study has novel features.
4. **Prospectively identify and periodically review the critical to quality factors**. Use the Principles Document (summarized below) to identify those aspects in each study that are critical to generating reliable data and providing appropriate protections for research participants, and to develop strategies and actions to effectively and efficiently support quality in these critical areas.

QbD Implementation: Plan, Do, Check, Act



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CLINICAL TRIALS TRANSFORMATION INITIATIVE

QUALITY BY DESIGN

Critical to Quality Factors	Examples of Issues to Consider
Protocol Design • Eligibility Criteria • Randomization • Masking • Types of Controls • Data Quantity • Endpoints • Procedures Supporting Study Endpoints and Data Integrity • Investigational Product Handling and Administration	*Are all **criteria relevant** to ensuring the specific trial participant **population needed**?* *Is there **potential** for **bias**?* *What **actions** are to be taken if **unmasking** is discovered?* *Are there explicit **plans** for **minimizing risk** to the **study population** on the control arm?* *What is the **tolerance** for **error** in collection of **data points**?* *Does the primary **endpoint address** the study **aims**?* *How will device **malfunctions** be **recorded** and **reported**?* *Are there specific **storage considerations** for the product?*
Feasibility • Study and Site Feasibility • Accrual	*Do any of the sites pose concerns related to **data privacy laws**?* *Are there **external factors** (e.g., competing trials or seasonal variations) that might **affect accrual rates**?*
Patient Safety • Informed Consent • Withdrawal Criteria and Trial Participant Retention • Signal Detection and Safety Reporting • Data Monitoring Committee/Stopping Rules	*Will participants **understand** the **risk**?* *Are the **withdrawal criteria** described consistently throughout the protocol?* *How will **adverse event** information be elicited?* *Is the study governance structure clear—i.e., who is **ultimately accountable** for the decision to stop the study?*
Study Conduct • Training • Data Recording and Reporting • Data Monitoring and Management • Statistical Analysis	***Who** will be trained and **how** will **training** be **provided** and **documented**?* *Will self-evident **corrections** be **permitted**?* *Are there clearly defined **plans** for handling **missing data** in the study **protocol**?*
Study Reporting • Dissemination of Study Results	*Are there **specific** report content/format **requirements** that should be considered when **designing** data collection **tools**?*
Third-Party Engagement • Delegation of Sponsor Responsibilities • Collaborations	*Is **performance** by one third party **dependent** upon **inputs** from another?* *Who will have **responsibility** for **safety reporting**?*

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