ICH E8 Landscape Assessment

Results and Analysis from the TransCelerate ICH E8 Member Company Benchmarking Survey

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BACKGROUND ON THE SURVEY

TransCelerate's current Interpretation of Guidance and Regulations team is exploring implementation of ICH E8 (R1).

An external party has collected, blinded, and compilated the responses.

Sixteen member companies each submitted one response to the survey questions.

The information shared helped the TransCelerate's team in understanding the clinical study sponsors' needs and knowledge gaps in implementing ICH E8 (R1) when creating initiative deliverables.

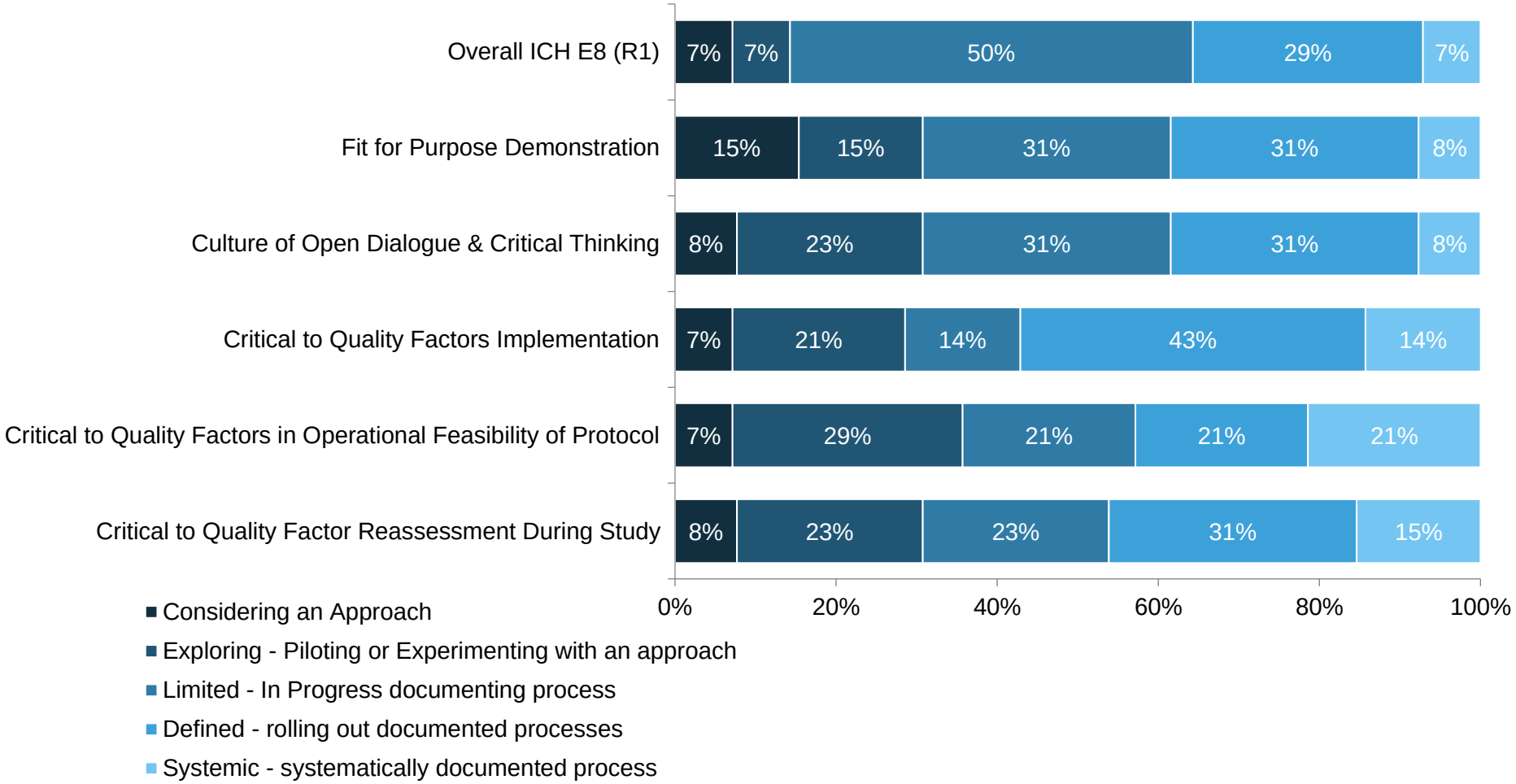
Key Concepts summarized within:

- Applying ICH E8 (R1)
- Key concepts
- Applying Critical to Quality Factors
- Understanding Open Dialogue and Critical Thinking
- Internal Stakeholder involvement
- External Stakeholder involvement
- Implementing ICH E8(R1)

Note: These responses reflect the current state at the responding companies at the time of the survey. These companies are at various points of implementation of ICH E8 (R1) and not all have fully implemented the concepts discussed.

Applying ICH E8 (R1)

At the time of the survey (Q2 2022), most companies were in progress of documenting or rolling out documented processes.



Key Concepts

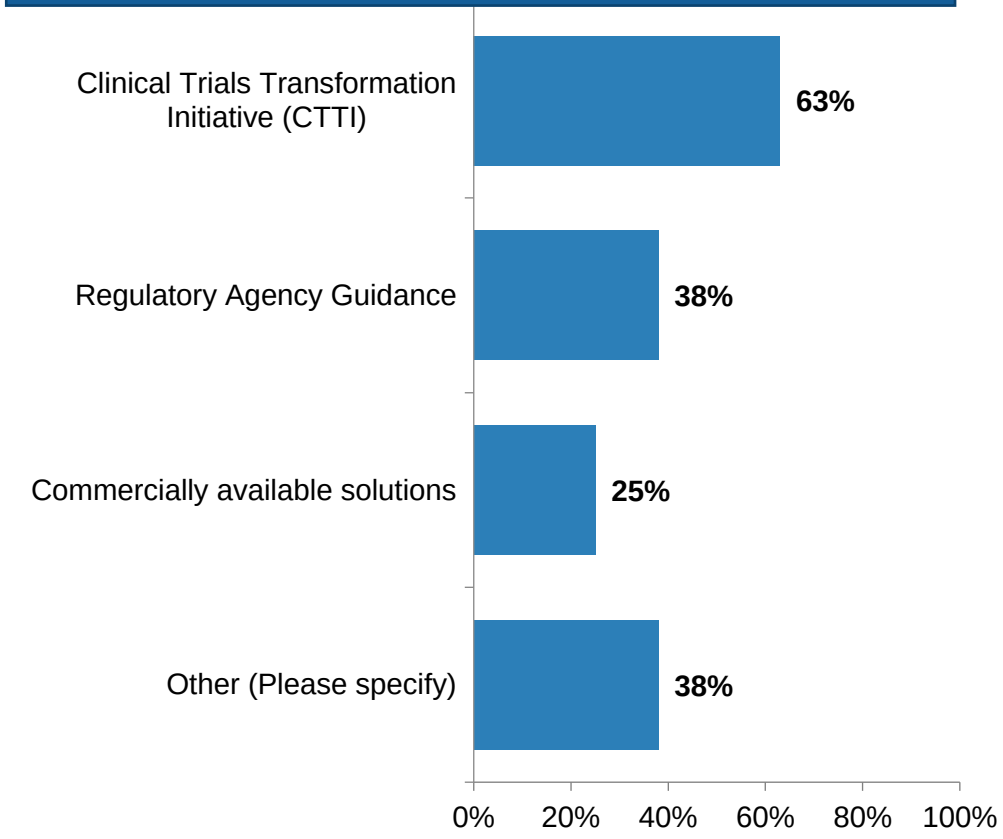
Are member companies defining key concepts from ICH E8 (R1)?

Term	Definition or Key Concepts Applied
Quality	• *Several companies surveyed had no definition of quality (cited by 25% of companies).*
Fit for Purpose	• *86% of companies surveyed did not have a definition.*
Quality by Design	• *67% of companies surveyed did not have a definition.*
Critical to Quality	• *53% of companies surveyed did not have a definition.*

Understanding and Applying Critical to Quality (CtQ) Factors

Over half of the responding companies surveyed use other sources beyond ICH to help with CtQ identifying and understanding.

References/tools to guide of CtQ understanding



Other included industry forums, professional meetings, TransCelerate Integrated Quality Risk Management Plan Framework

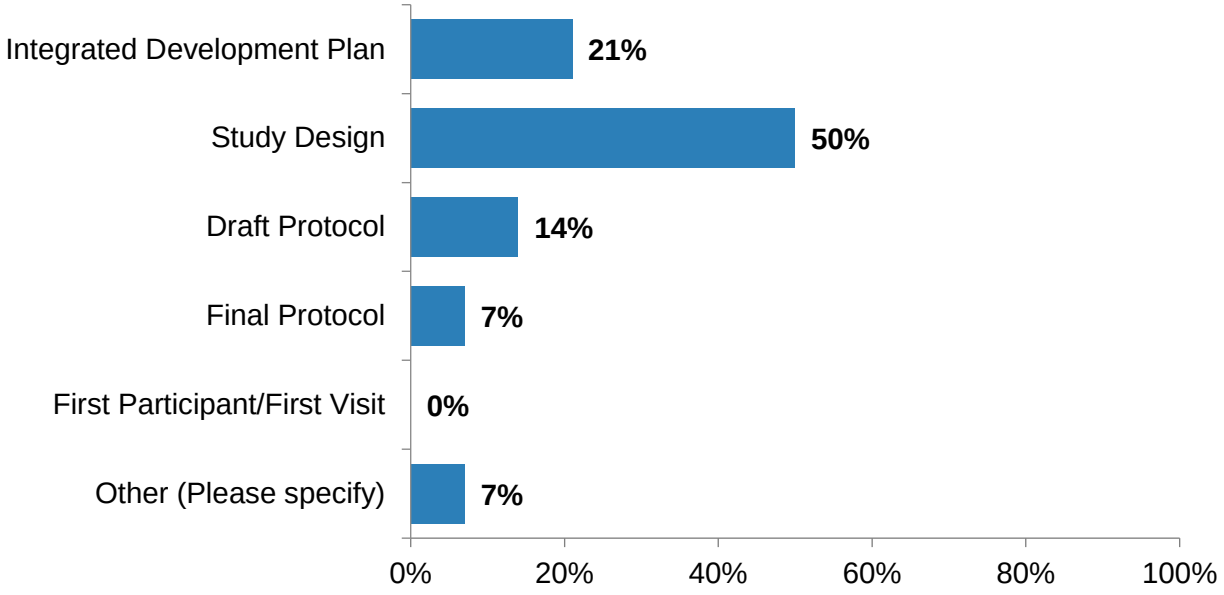
Top CtQ factors of focus

- Patient Safety data; adverse event collection, complete, consistent, timely
- Eligibility criteria; correct population is randomized/enrolled; inclusion/exclusion criteria
- Patients receive study treatment per protocol; completeness of planned intervention; IMP management
- Patients do not discontinue pre-maturely; loss to follow-up
- Quality, completeness, methods for primary endpoint (and key secondary endpoints) collection and assessment; Primary objective alignment with study design; Submission data use
- Data integrity; Data flow integrity (e.g., source to CRO to sponsor to CSR); Integrity and reliability of study results
- Management of protocol deviations; Protocol adherence; Compliance with regulations; Patient privacy/confidentiality
- Collection/handling/shipping/storage of samples
- Protocol/study design elements – number of participants, trigger for analysis, comparator arm appropriateness, reliability of results, scientific quality, subject protection, blinding, diverse populations
- Site staff qualifications
- PK Data

Applying Critical to Quality (CtQ) Factors

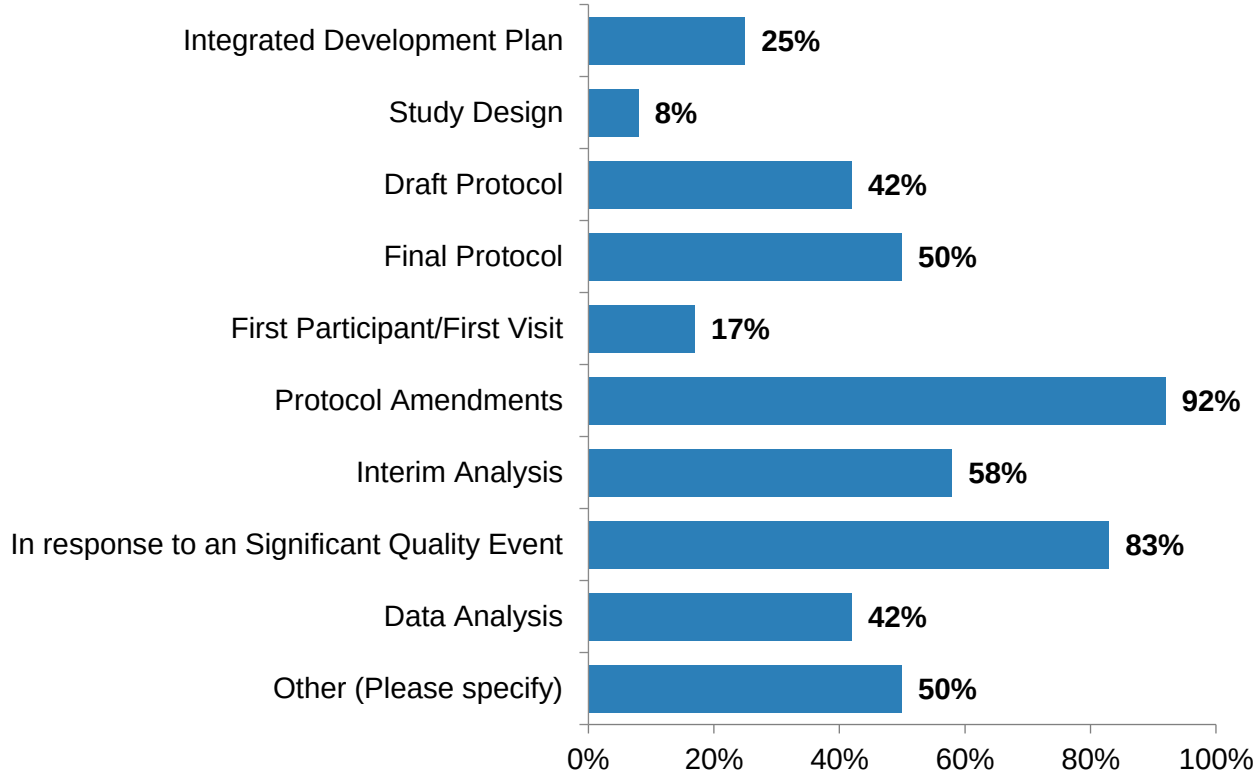
Half of responding companies first apply CtQs during study design.
87% of companies re-asses CtQ factors during the study.

Timepoint at which companies first determine CtQ factors in the life-cycle of a clinical study



Other included: Design concept sheet (similar to protocol synopsis)

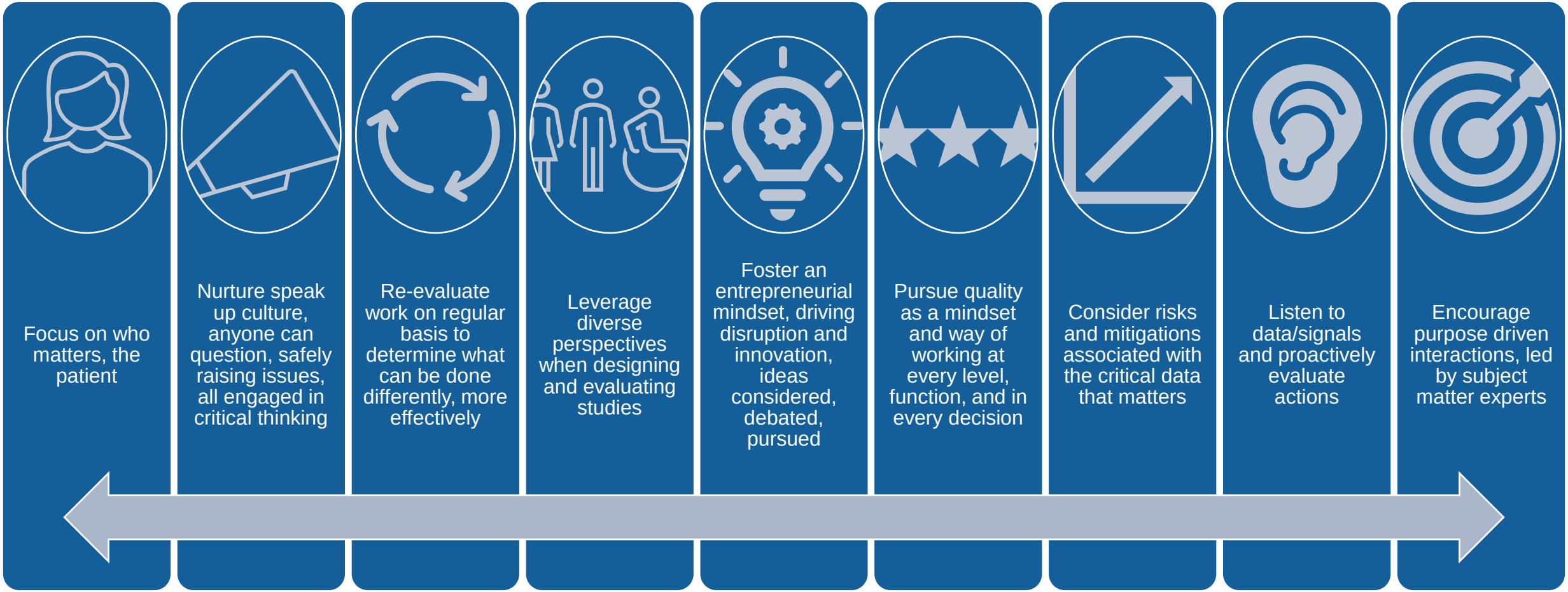
Timepoint at which companies reassess CtQ factors



Other included: Design concept sheet (similar to protocol synopsis), regular intervals, new external data, yearly, before critical database lock

Understanding of Open Dialogue and Critical Thinking

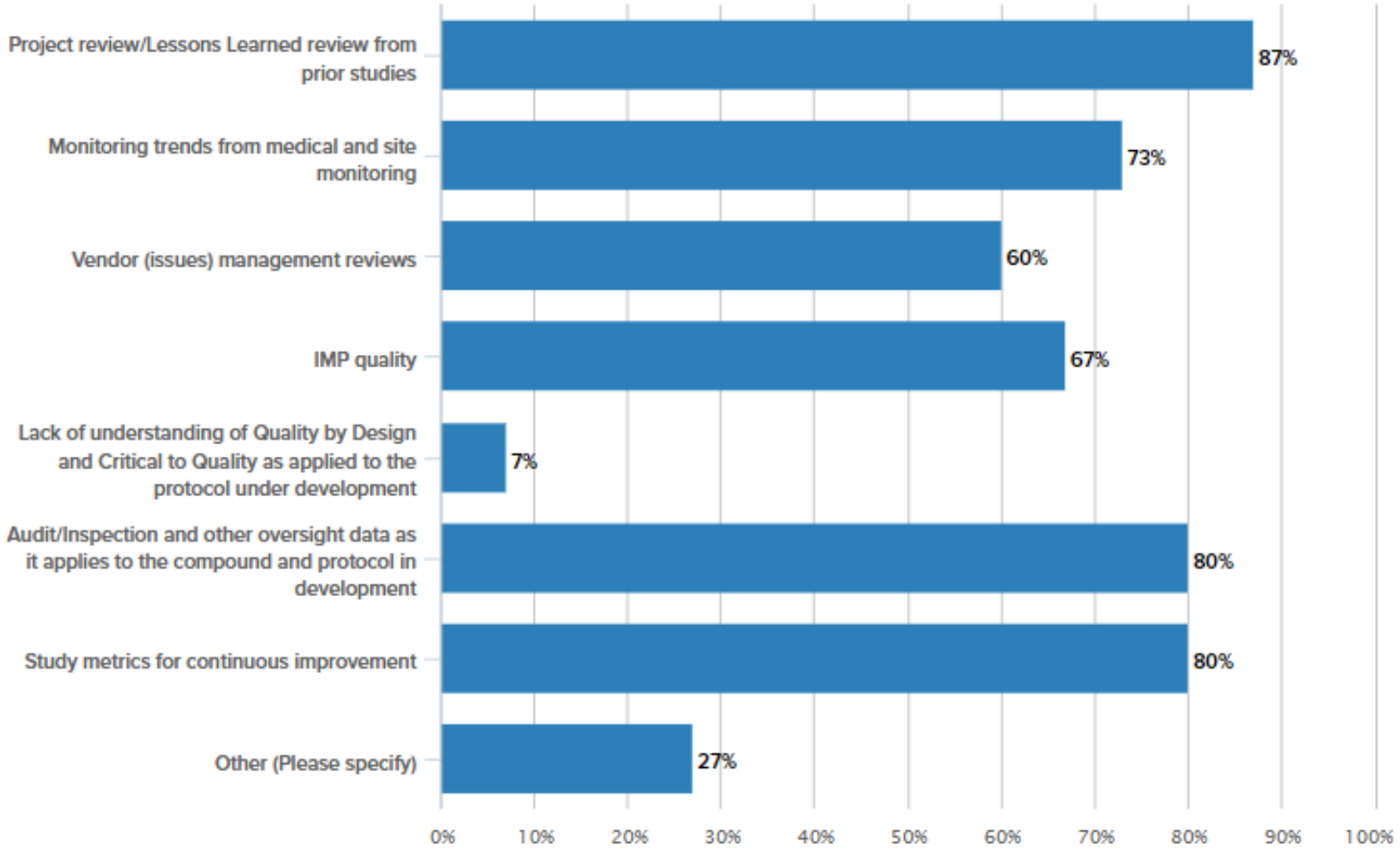
Survey responses had common threads when identifying principles for fostering open dialogue and critical thinking.



Applying Open Dialogue and Critical Thinking

Responding companies are learning from previous studies, identifying trends and issues.

How member companies are capturing issues when designing a new protocol for the same program



Other included: Risk tracking via risk register, risk assessment outcomes, risks observed within CtQ factors.

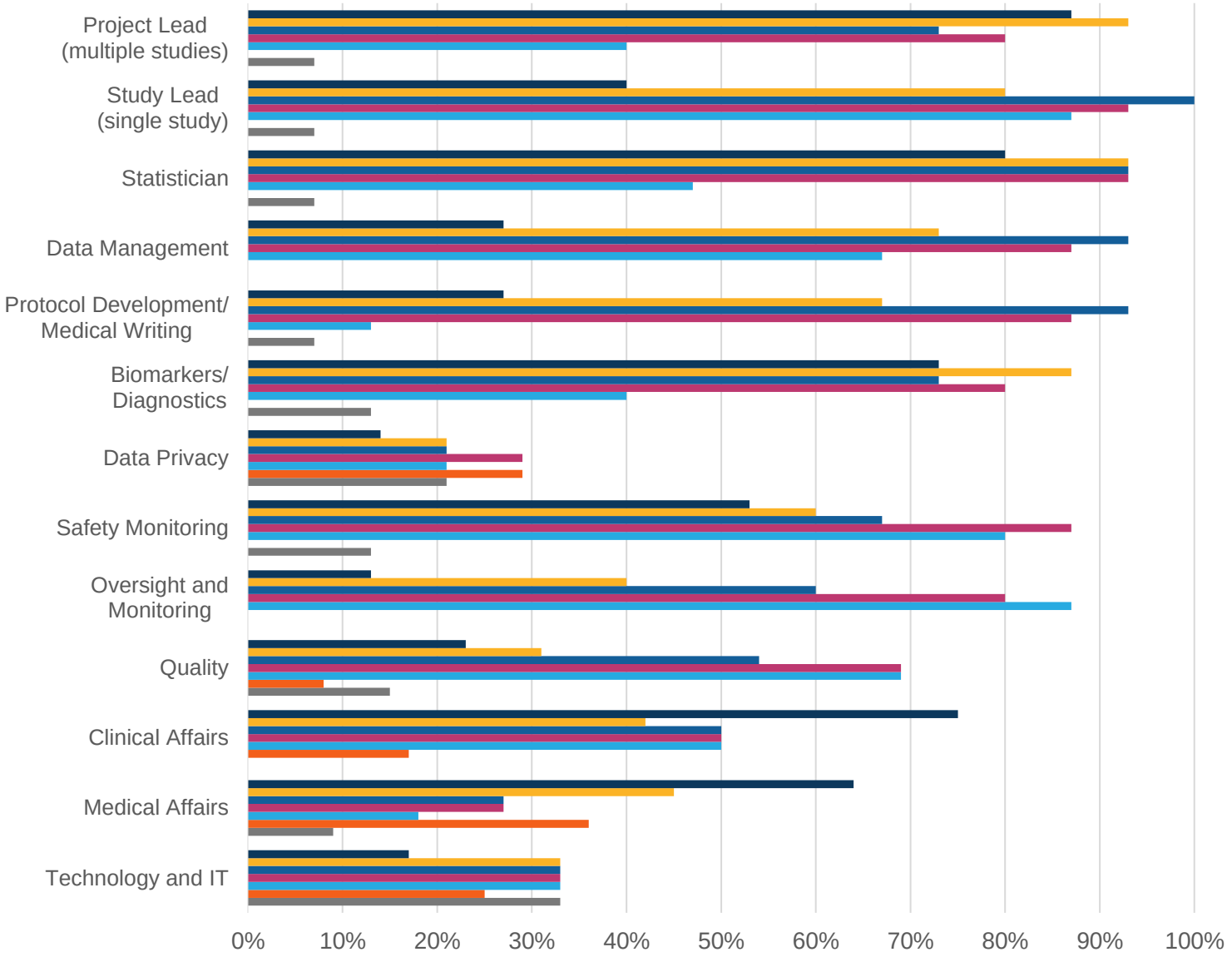
Internal Stakeholder Group Involvement in Clinical Development Process

During integrated development planning, most companies align on internal strategy with involvement from the project lead, statistician, biomarkers/diagnostics, clinical affairs and medical affairs.

Most internal stakeholders are involved in study design/draft protocol/final protocol stage.

Companies largely follow same approach that certain core roles are involved at first participant/first visit stage, inclusive of study lead, data management, safety monitoring, quality.

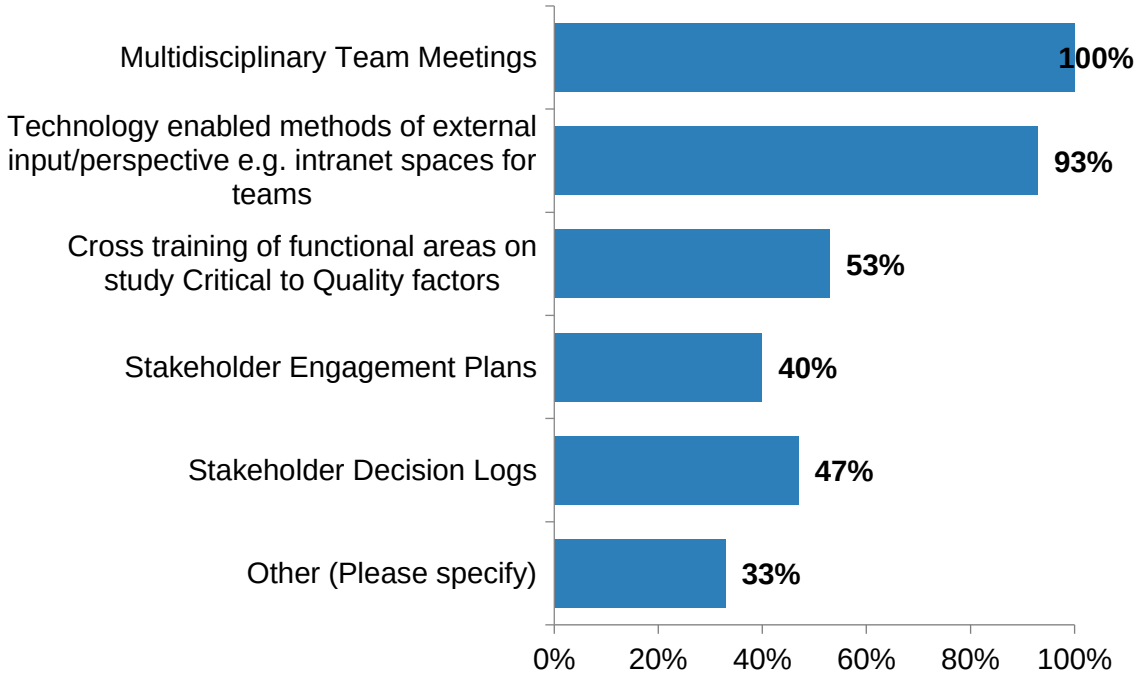
No clear trend was observed with use of Data privacy, and technology/IT.



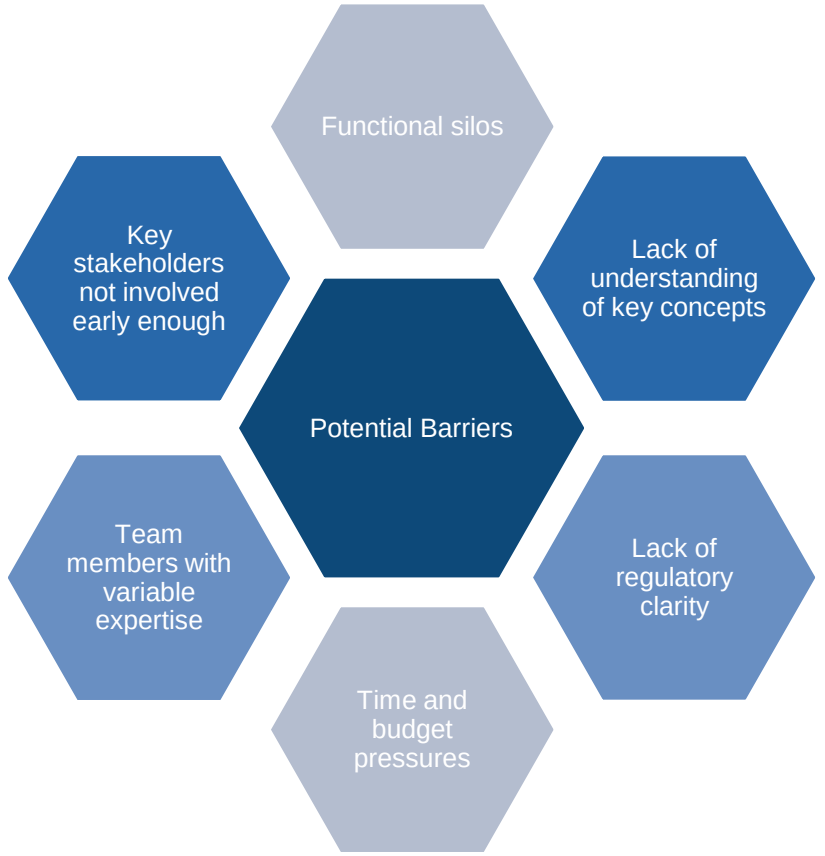
Internal Stakeholder Involvement – Tools and Methods; Barriers

Responding companies largely use multidisciplinary team meetings and technology enabled methods for internal stakeholder involvement.

Tools and methods to engage internal stakeholders

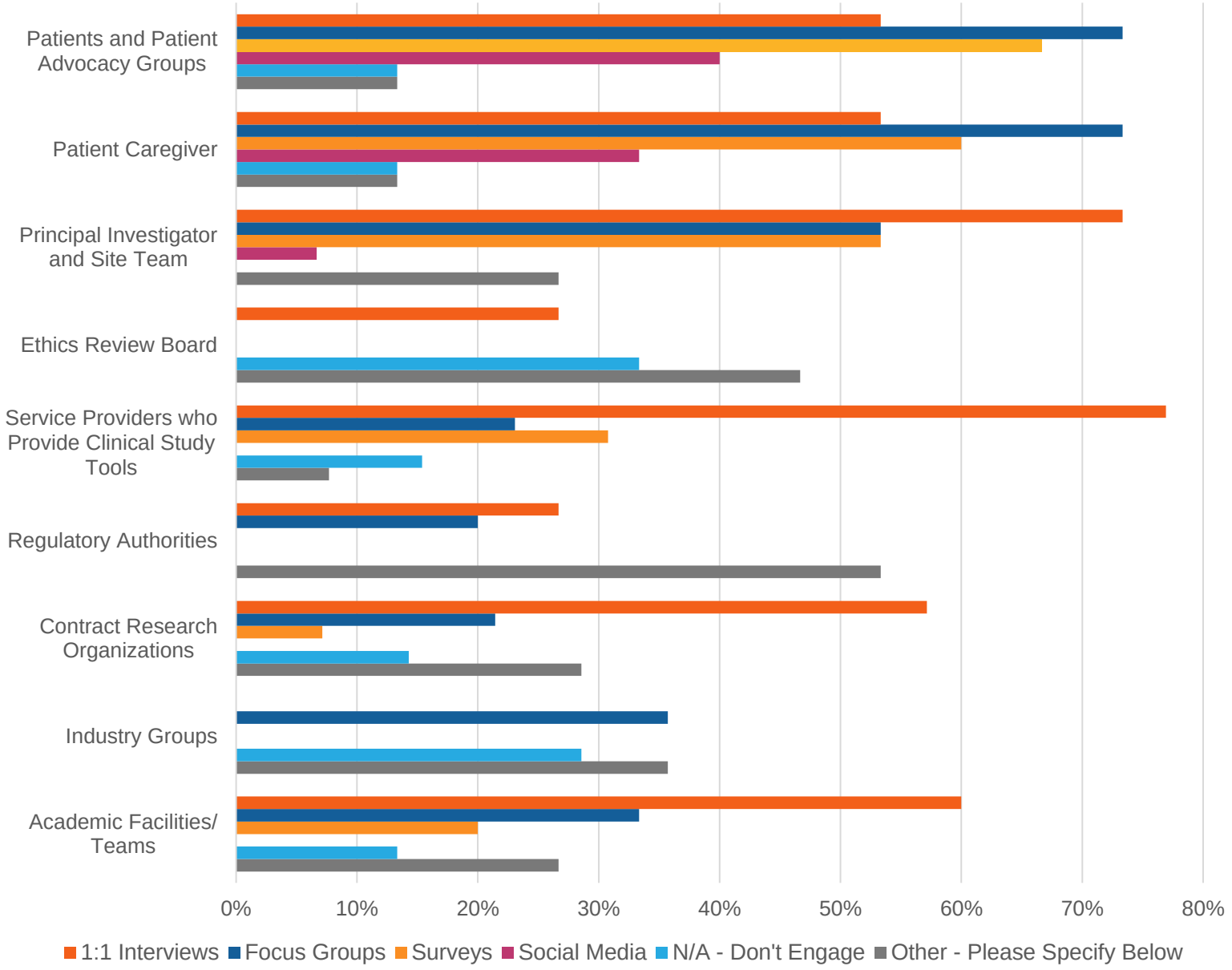


Potential barriers to internal cross-functional engagement



Methods Responding Companies are using to Engage External Stakeholder Groups

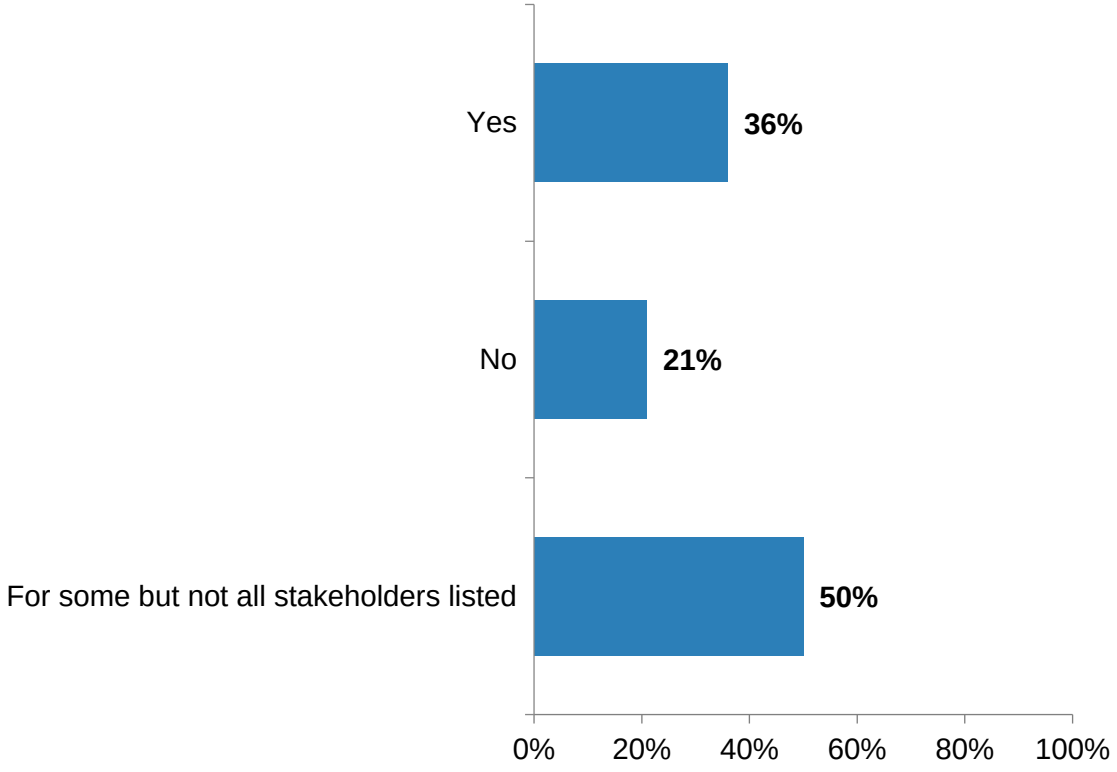
- Most external stakeholders are involved via 1:1 interviews, focus groups, and surveys.
- Many groups wrote in “other” methods inclusive of:
  - consultations and direct connections such as email/phone
  - advisory boards
  - disease area patient councils
  - patient/caregiver simulation workshops
  - embedded patient advocate on study team
  - patients/caregivers and principal investigators on steering committees
  - scientific advisory meetings
  - regulatory Type B or C meeting requests
  - collaboration forums
  - formal meetings.



External Engagement Formalization and Potential Barriers

Most responding companies have formalized in policies and procedures some external stakeholder interactions, but not all.

External engagement formalized in policies and procedures



Potential barriers to external stakeholder engagement

Examples of When Responding Companies are Engaging External Stakeholder Groups

Patients, patient advocacy, caregivers, as well as regulators, generally consulted during early stages of clinical development.

Principle investigator and site team engaged, as well as CROs and service providers, at all stages of study design and implementation, but not typically during integrated development planning.

Many groups reported variation, external stakeholders were not consulted systemically.

Other stakeholders included: Informed consent review, during the course of a study, support initiatives with patient organizations to advance R&D.