1. Your Company Type (Check One)
   1. Sponsor
   2. Service Provider (CRO)
   3. Other (Specify)
2. Your Company Size – Number of Concurrent Trials (Check One)
   1. Large (>200 Phase I-III clinical trials ongoing)
   2. Medium (>100 & ≤ 200 Phase I-III clinical trials ongoing)
   3. Small (≤100 Phase I-III clinical trials ongoing)
3. Which Functional Area(s) are involved in trial level Risk-Based Approaches to Quality1 (Please check all that apply)
   1. Clinical Operations
   2. Data Management
   3. Biostatistics
   4. Clinical Science
   5. Safety Science
   6. Quality Functions
   7. Other (Please Specify)

1 Please see ICH E6 (R2) section 5.0 and ICH e8 (R1)

1. Which Functional Area leads trial level Risk-Based Approaches to Quality (Please check only one)
   1. Clinical Operations
   2. Data Management
   3. Biostatistics
   4. Clinical Science
   5. Safety Science
   6. Quality Functions
   7. Other (Please Specify)
2. Are there any trial types where your company does not apply Risk-Based Approaches to Quality, (Please select all that apply, and provide comments as to why this is the case)?
   1. Phase I
   2. Phase 2
   3. Complex Designs (e.g Platform, Basket, Cohort designs)
   4. Post-marketing approval (interventional)
   5. Other (Registry, non-interventional)
   6. Comment Why:
3. Which aspects of Risk-Based Approaches to Quality does your company apply to the following Trial Types (Please check all that apply)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Trial Type** | **Critical to Quality Factors (CTQ**1**)** | **Quality by Design Processes (QbD**2**)** | **QTL’s** | **Alignment of QTL’s with CTQ’s** | **Other Risk-Based Approaches** |
| FIH |  |  |  |  | Yes/No |
| Phase I Non-FIH |  |  |  |  |  |
| II |  |  |  |  |  |
| III – Regulatory Submission |  |  |  |  |  |
| III – Follow up |  |  |  |  |  |
| IV |  |  |  |  |  |

1 CtQ (Critical to Quality) is “…[a] basic set of factors relevant to ensuring study quality… attributes of a study whose integrity is fundamental to the protection of study participants, the reliability and interpretability of the study results, and the decisions made based on the study results… considered to be critical because, if their integrity were to be undermined by errors of design or conduct, the reliability or ethics of decision-making based on the results of the study would also be undermined.” ICH E8 (R1) Section 3.2.

2 QbD (Quality by Design) is the “…use of a prospective, multidisciplinary approach to promote the quality of protocol and process design in a manner proportionate to the risks involved, and clear communication of how this will be achieved.” ICH E8 (R1) Section 2.2. For this activity it is recognized that not all elements of QbD may have been / are in the process of being implemented at any one organization. Please provide your response based on your current state of QbD implementation.

1. If you answered Yes to Other Risk Based Approaches used in Question 6, please identify those used (Check all that apply)
   1. KRI’s
   2. KPI’s
   3. Team Tracking risk items
   4. Other
2. Is your company’s Risk Based Approach to quality applied differently depending on the following trial attributes?

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Activity** | **Trial Attributes** | | |  |  |  |
| **Trial Design** | **Trial Phase** | **Trial Size** | **Not Utilized** | **Mixed Response4** | **Unable to Answer** |
| Identification of CTQ’s1 | YES/NO? |  |  |  |  |  |
| Overall Implementation of QbD2 |  |  |  |  |  |  |
| QTL’s Utilized |  |  |  |  |  |  |
| QTL’s Aligned with CtQ’s |  |  |  |  |  |  |
| QTL Review Processes |  |  |  |  |  |  |
| Frequency of QTL Review |  |  |  |  |  |  |
| Communication of QTL Breaches |  |  |  |  |  |  |
| Implementation of Corrective Actions |  |  |  |  |  |  |
| Reporting Significant QTL Deviations in CSR |  |  |  |  |  |  |

4 Some organizations may have more than one activity that is tightly integrated across multiple elements (e.g., Trial size and Phase). Please utilize the Mixed Response for these situations.

1. Does your company have a process in place with regard to completing a Feedback Loop?
   1. Yes
   2. No

1. How does your company document your Risk-Based Approaches to Quality? The goal of this question (and others that follow with similar activities regarding CTQ’s & QBD) is to understand what and how your company makes links, if any, from these activities to QTL’s. Please check all that apply.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Activity** | **Via Technology Solution(s)** | **Separate, Protocol- Level Plans (for example,** **Risk Mgmt Strategy Plan, Monitoring Plan, etc.)** | **Part of a Protocol- Level Plan (e.g., part of a Risk Mgmt Strategy Plan)** | **Not Utilized** | **Other** |
| Identification of CTQ’s 1 |  |  |  |  |  |
| Implementation of QbD2 |  |  |  |  |  |
| Implementation of a Risk Strategy3 |  |  |  |  |  |
| QTL’s Utilized |  |  |  |  |  |
| QTL Review Processes |  |  |  |  |  |
| QTL’s Aligned with CtQ’s |  |  |  |  |  |
| Frequency of QTL Review |  |  |  |  |  |
| Communication of QTL Breaches |  |  |  |  |  |
| Implementation of Corrective Actions |  |  |  |  |  |
| Reporting Significant QTL Deviations in CSR |  |  |  |  |  |

1 See Note below Question 6 for additional information

2 See Note below Question 6 for additional information

3 See ICH E6 (R2) Sections 5.1.1-5.1.3

1. How would you characterize the success of the deployment of all Risk-Based Approaches to Quality in your company? Please provide one response per characteristic:

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Characteristic** | **Highly Successful** | **Moderately Successful** | **Somewhat Successful** | **Unsuccessful to Date** | **Not Applicable** | **Not Involved** |
| Senior Leadership | Strong alignment, active participation / messaging / communication / celebrate successes | Alignment, aware, support messaging / communication / successes | Not all are aligned, aware during issue escalations | No alignment, do not view as critical |  |  |
| Functional Leaders | All accountable | Most accountable | Some accountable | Deprioritize implementation |  |  |
| Functional Leaders | All Visibly Driving implementation | Most Visibly Driving implementation | Some Visibly Driving implementation | Not Driving implementation |  |  |
| Change Management | Significant presence, impact | Strong presence, moderate impact | Some presence, limited impact | Not considered, or if in place no impact |  |  |
| Continuous Improvement  (Formal Feedback Loop Process) | Strong approach and process impact | Strong approach and moderate process impact | Limited impact | Not considered, or if in place no impact |  |  |
| Study Teams | Vast majority of impacted teams actively engaged | Moderate engagement, teams participate in processes | Limited engagement, some refusing to participate | No engagement |  |  |
| Mandatory Study Performance Objectives | Not required | Required for lagging functions / study teams | Required for majority of impacted functions / study teams | Not prioritized |  |  |

1. For trials that are outsourced to service providers, how are your Risk-Based Approaches to Quality managed? Please provide one response per activity:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Activity** | **Fully Outsourced** | **Hybrid** | **Retained Internally** | **Activity Not Utilized** | **Comments** |
| Identification of CTQ’s 1 |  |  |  |  |  |
| Implementation of QbD2 |  |  |  |  |  |
| Definition of QTL’s |  |  |  |  |  |
| Management of QTL Review |  |  |  |  |  |
| Communication of QTL Breaches to Sponsor |  |  |  |  |  |
| Implementation of Corrective Actions |  |  |  |  |  |
| Reporting Significant QTL Deviations in CSR |  |  |  |  |  |

1. For trials that are outsourced to service providers, whose Risk-Based Approaches to the following Quality processes are utilized? Please provide one response per activity:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Activity** | **Sponsor Only** | **Service Provider Only** | **Hybrid (Mix of Sponsor & Service Provider)** | **Not Utilized** | **Comments** |
| Identification of CTQ’s 1 |  |  |  |  |  |
| Implementation of QbD2 |  |  |  |  |  |
| Definition of QTL’s |  |  |  |  |  |
| Management of QTL Review |  |  |  |  |  |
| Communication of QTL Breaches to Sponsor |  |  |  |  |  |
| Implementation of Corrective Actions |  |  |  |  |  |
| Reporting Significant QTL Deviations in CSR |  |  |  |  |  |

1. Does your company currently utilize QTL’s (Yes/No)
2. **If you checked No to Question 14 please proceed to Question 21.**  **If you checked Yes** **to Question 14** indicate the year your company implemented QTL’s: \_\_\_\_\_\_\_\_\_.

|  |  |
| --- | --- |
| **Year** | **Implemented** |
| 2017 |  |
| 2018 |  |
| 2019 |  |
| 2020 |  |
| 2021 |  |
| 2022 |  |
| 2023 |  |

1. Has your company implemented QTL’s for trials that started prior to the release of E6 (R2) step 4 (Y/N/Unknown)
2. What are the top 3 drivers for choosing a QTL parameter at your company?

1. Key Safety Objectives
2. Key Efficacy Objectives
3. Standard Parameters preset by organization
4. Easy to Measure
5. Easy to Control
6. Previous experience with the parameter in another study
7. Choice guided by Subject Matter Experts and Study Team
8. How are QTL’s governed / utilized at your company? Please check all that apply:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Characteristic** | **In Use** | **Planned** | **Not In Use and Not Planned** | **Not Known** | **Comments** |
| Formally Integrated in QMS – Health Authority Inspection |  |  |  |  |  |
| Formally Integrated in QMS – Continuous Improvement (e.g., future protocol development / process improvement activities) |  |  |  |  |  |
| Formally Integrated in QMS - Submissions |  |  |  |  |  |
| Formally Integrated in QMS – Senior Management Review |  |  |  |  |  |
| Formally Integrated in QMS – Quality Management Oversight (e.g., GCP / Quality Councils / Committees) |  |  |  |  |  |
| Formally Integrated with Quality by Design Processes |  |  |  |  |  |
| Formally Integrated with Critical to Quality Processes |  |  |  |  |  |
| Other (Please specify) |  |  |  |  |  |

1. What types of actions has your company typically taken, or plan to take, in response to a QTL breach? Provide one response per possible action:

|  |  |  |  |
| --- | --- | --- | --- |
| **Possible Action** | **For Primary Breach** | **For Secondary Breach** | **Not Applicable**  **(e.g do not use this action)** |
| Protocol Amendment |  |  |  |
| Change in QTL threshold(s) (resetting) |  |  |  |
| Change in QTL parameter metric |  |  |  |
| Change in QTL statistical distribution |  |  |  |
| Change in QTL statistical methodology |  |  |  |
| Change to trial monitoring strategy |  |  |  |
| Instruction(s) provided to sites |  |  |  |
| Instruction(s) provided to vendors (service providers or otherwise) |  |  |  |
| Other (specify) |  |  |  |

1. Regarding reporting of a Primary Limit Breach of the QTLs in the CSR (per ICH E6 R2 Section 5.1.7)

|  |  |
| --- | --- |
| **Possible Action** | **Response** |
| Following a Primary Limit Breach, are QTL’s assessed for Importance? | Yes / No (all considered Important) |
| If QTL Primary Limit Breaches are NOT evaluated for importance, has your organization considered implementing this process as part of QTL reporting in the CSR? | Yes/No |
| If QTL Primary Limit Breaches are NOT evaluated for importance, and your organization has discussed implementing this process as part of QTL reporting in the CSR, what considerations have been made in determining if this would be implemented or not? | *Free text* |
| If QTL Primary Limit Breaches are evaluated for importance, how do you determine as to whether they should be reported in the CSR | Pick List: Against pre-defined criteria; via statistical methodology; by study team; other?*add free text box* |
| If QTL Primary Limit Breaches are evaluated for importance, is this evaluation process consistent across your studies/organization | Yes / No |
| Do you treat this QTL evaluation process similar to that for Important Protocol Deviations | Yes / No |
| Do you treat this reporting requirement similar to that for Important Protocol Deviations (content, e.g. level of detail provided) | Yes / No |
| Has your organization finalized a CSR with a subset of deviations/excursions excluded because they were determined not important and so not reported? | Yes / No |
| If yes to prior question, please provide details on what was considered not important. | Free text |

1. Has you ever had a Health Authority inspection that focused at least in part on your use of QTLs (Yes/No)
2. **If you checked No to Question 21 please proceed to Question 23.** Can you share which of the Activities below were discussed with the HA representative? Check all that apply:

|  |  |
| --- | --- |
| **Activity** | **Discussed with HA** |
| QTL Governance |  |
| QTL Threshold(s) |  |
| QTL Parameter Metric |  |
| QTL Statistical Methodology |  |
| QTL Review Process |  |
| QTL Documentation Process |  |
| QTL Communication Process |  |
| QTL Corrective Action Process / Outcome |  |
| Other (specify) |  |

.

1. Please indicate below the possible/potential Parameters for QTLs **(as defined by TransCelerate)** that are currently in use or are planned to be used (check all that apply, one response per Parameter). For those that are Currently in Use, please rate on a scale of 1 (Low), 2 (Medium), or 3 (High) the perceived value of the Parameter. (DISCLAIMER: This is not considered a definitive list of potential parameters, and may be interpreted differently between responders).

| **Parameter** | **Currently in Use** | **Planned to Use** | **Perceived Value** | **Not Considered a QTL** |
| --- | --- | --- | --- | --- |
| Protocol Deviation – Inclusion / Exclusion Criteria |  |  |  |  |
| Protocol Deviation – Study Conduct |  |  |  |  |
| Protocol Deviation - Other |  |  |  |  |
| Primary Endpoint Assessment |  |  |  |  |
| Secondary Endpoint Assessment |  |  |  |  |
| Investigational Product – Compliance |  |  |  |  |
| Investigational Product - Other |  |  |  |  |
| Randomization Failure |  |  |  |  |
| Lost to Follow Up |  |  |  |  |
| Informed Consent |  |  |  |  |
| AE / SAE - Reporting |  |  |  |  |
| Censored Data – Trial participants censored for primary objective statistical analysis |  |  |  |  |
| Disposition – Early Termination from Study Drug |  |  |  |  |
| Repeated Measures Timepoints for FIH / Early Phase trials |  |  |  |  |
| Stratification |  |  |  |  |
| Other (Specify) |  |  |  |  |
| Other (Specify) |  |  |  |  |
| Other (Specify) |  |  |  |  |

1. Please indicate if any of the below **additional** Parameters are also considered as Parameters for QTLs, whether they are currently in use or are planned to be used (check all that apply, one response per Parameter). For those that are Currently in Use, please rate on a scale of 1 (Low), 2 (Medium), or 3 (High) the perceived value of the Parameter. (DISCLAIMER: This is not considered a definitive list of potential parameters, and may be interpreted differently between responders).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **~~QTL~~ Parameter** | **Currently in Use** | **Planned to Use** | **Perceived Value** | **Not Considered a QTL** |
| CRF Transcription Errors |  |  |  |  |
| TMF – Completeness |  |  |  |  |
| TMF – Quality |  |  |  |  |
| Vendor Oversight |  |  |  |  |
| AE / SAE – Management |  |  |  |  |
| Data Entry Timeliness |  |  |  |  |
| Data Processing – Querying |  |  |  |  |
| Asset / Compound Specific |  |  |  |  |
| Therapeutic Area Specific |  |  |  |  |
| Indication Specific |  |  |  |  |
| Protocol Specific |  |  |  |  |
| Other (Specify) |  |  |  |  |
| Other (Specify) |  |  |  |  |
| Other (Specify) |  |  |  |  |

1. ICH E3 QTL language may evolve to become “acceptable ranges”. Will your company potentially change their approach as a result?

No / Yes / Not Applicable

If Yes or No, can you provide specifics?

1. Approximately what proportion of excursions that your organization have investigated, have surfaced an underlying systemic issue? ALWAYS

MOST OF THE TIME

RARELY

NEVER

1. How often did the application of QTLs successfully control the intended risk/Critical Quality Factor

ALWAYS

MOST OF THE TIME

RARELY

NEVER

1. Are you open to industry level collaborations and standardizations in areas such as a) Opensource Software Development for QTL's b) Core definitions of QTLs? Y/N