PCMG - T he Future of Site Agreements – 10th Apr 2014

CLINICAL SITE CONTRACTING IN AN OUTSOURCING ENVIRONMENT - EFFICIENCIES AND TOOLS

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Agenda

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- MIDCRO positioning for balanced outsourcing in the site contract deliverables
  - Responsibility Breeds Delivery to Expectations
  - Balance for the Depth of Interaction
  - Visualisation of timelines and deliverable
  - Fast Decision Making and Flexibility
- Negotiation Guidelines and Legal Autonomy
  - General Principles
  - Tools (Knowledge Pool & Guidelines)
  - Controls and Implications
  - Regionalised Specialisation Model
- Deliverables, Reporting, Metrics and Performance Indicators
  - Tracking Types (Budget, Progress, Metrics)
  - Collection of Metrics and Benchmarking
  - Key Cycle Times & Quality

Responsibility - Delivery to Expectations

"You cannot mandate productivity, you must provide the tools to let people become their best"

– Steve Jobs

Responsibility - Delivery to Expectations

Given the Responsibility

- Those that feel valued for their contribution will contribute more and commit extra focus and resource.
- By giving the CRO the ownership of their own deliverable under the ethos of the true outsourced model, the CRO can own a sense of delivery under their process.
- No where to hide from any delivery failure.
- Needs very clear up-front planning and communication of expectations – less flexibility.
- Sense of Empowerment to contribute the added value of a service provider
- Risk Share Benefits.

Maintained Micro Management of Deliverable

- Trust to deliver is removed and CRO interaction is more in line with that you expect from those under your direct control.
- CRO will be looking towards Biotech/Pharma for guidance on the deliverable and will feel less empowered to make swift decisions.
- Can lead to a blame game scenario when timelines or deliverables miss target expectations.
- Clear understanding throughout life-cycle of expectations and meeting that need.

Balance for the Depth of Interaction

Macro

- Freed Resources to act as a true Project Manager for deliverables
- Use of CRO templates and procedures
- CRO will provide the legal support for all change request from sites -
- Clear understanding must be established for expectations upfront – more rigid due to upfront planning needed
- Greater autonomy to succeed which must be balanced against the higher risks associated with loss of control
- Top level reporting of status
  - Quick and efficient reviews
  - Lack of specific knowledge around any upcoming delays or pro-active planning of mitigation action from Sponsor
- Priorities are driven from the CRO's need to balance their various clients targets

Micro

- Higher Sponsor Resource Impact
- Sponsor Own template controls
  - Reduction of Exposure to Legal Risk, including loss of adequate protection
  - Consistency across different CROs
- Approval on all language changes
- Weekly in-depth meetings (resource implications)
- Communication pathways need to flow well through all levels of CRO through to Trial Site
- Detailed and frequent awareness of progress
- More Flexibility to react to Sponsor's internal changing project requirements
- Direct management and drive for your priorities for CRO team members

Balance for the Depth of Interaction

Midcro

- Freedom for Sponsor resources to act as both Project Manager and critical approval path for deliverables
- Benefit from local and centralised legal experience and skills of CRO
- Use of Sponsor templates, with CRO influence on changes for achievable nuances
- CRO will provide the legal support for all change request from sites on non-material clauses and autonomy to make decisions during negotiation
- Guidance and Tracking Tools are very important to establish a clear balance of interaction and decision making efficiencies
- Greater autonomy to succeed whilst maintaining appropriate levels of control over risk profile
- Weekly meetings to discuss only critical path matters, top level status reports
- Priorities are driven from both CRO and Sponsor through sharing your priorities in a team environment
- Capitalising on the value of the contracted service.

- True feeling of acting and delivering as a team with shared responsibilities and achievements
- Key aspects for this to work are to still maintain a clear balance of the relationship – Use of a Relationship Manager and Preferred Provider status
- Creation of consistency documents for the process of contracting with Trial Sites.

General Principles – Legal Autonomy

CRO's Templates and Guidance – Total Autonomy (Macro)

- Reliance entirely on governance through the Master Agreement terms and other contractual controls for the maintenance of legal protection, obligations and adherence to regulations and legal principles;
- Indemnification of Sponsor by CRO – does not entirely relieve Sponsor of their responsibility and potential penalties;
- CRO enters into contract with Trial Site, without Sponsor;
- Lack of direct legal relationship with Trial Site (IP, Indemnity for patient injury etc…)

Sponsor's Templates and Sponsor Approval – Restricted Autonomy (Micro)

- Reliance entirely on the Sponsor for the approval of all changes to the contract;
- Entire responsibility and control for all legal aspects accepted by Sponsor;
- Sponsor enters into contract with Trial Site, without CRO;
- Agreement with Trial Site signed by the Sponsor;
- Direct legal relationship with Trial Site (IP, Indemnity for patient injury etc…)

Sponsor's Templates and Guidance Tools – Granted Autonomy (Midcro)

- Reliance on the experience and skills of CRO with support of Pre-approved Guidance;
- Control of Sponsor only for key legal aspects that entail highest risk profile;
- Sponsor party to contract, although signed by CRO (PoA).

Legal Autonomy (Key Clauses)

- Non-Key Clauses:
  - Sponsor **does not** need to review changes to **non-key clauses** where new obligations are not imposed on Sponsor.
- Key Clauses:

  All Sponsor companies have different concepts of what they consider as Key to their Legal protection and risk profiling, the following are some potential considerations:
  - **Intellectual property**
  - **Publication**
  - **Indemnification**
  - **Confidentiality**
  - **Termination**
  - **Other:** Any change that imposes a new obligation on Sponsor (such as reporting drug delivery example)

  - Adequate Control should be maintained to review any proposed changes to the key clauses that are not covered by an improved negotiation guidelines

Ultimately you must remember that the level of autonomy should be balanced against the risk that the Sponsor Company is responsible for the CRO's decisions that impact the performance of the trial.

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Negotiation Guidelines

- A Document that is structured to give our outsourced partners the ability to apply pre-approved language and guidance:
  - Changes to current template contractual language;
  - Explanations on inclusion of certain contract terms;
  - Preferences;
  - Guidance on application of Legal Principles;
  - key questions to ensure Sponsor Company have the full background to understand intent in order to propose a final position;
  - Country Specific Changes and Guidance.

- BIIB and preferred CROs recently participated in a Kaizen event aimed at improving and streamlining our site contracting process.

- The creation of Negotiation Guidelines with an intention of…
  - recognizing efficiencies in the negotiation of key clauses, or where a site requests a change that creates a new obligation to Sponsor
  - limiting the back and forth communications that occur between Sponsor and the CRO teams and between the site and Sponsor/ CRO.
  - ensuring consistency of approach and resolution to sites across CROs

GOAL: To ensure our preferred CROs are equipped with as much guidance as possible on Sponsor's position in order to limit the number of reviewers and approvers of any contractual language changes.

The revised guidelines should limit the number of escalation to Sponsor for key clauses and ensure that any escalations that are submitted include the relevant background. If successful, this will provide you with a **reduction in overall CTA cycle time**.

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Negotiation Guidelines

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Negotiation Guidelines

- Example: Confidentiality and Data Protection

Request for Change / Site Query	Acceptable Resolution/Alternative Language
Removal of any confidentiality obligations for Ethics Committee.	The clause relating to the Ethics Committee obligation of confidentiality… Or The following alternative text can be inserted: "Confidential Information and Independent Ethics Committees…."

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Knowledge Pool Tool

What is the Knowledge Pool Concept?

- Knowledge Pool **(*KP*)** is a tool in which contractual and legal knowledge and experience of the Biotech/Pharma company is banked for future application in contract negotiations.
- The tool captures information not already contained in the established guidance documents and negotiation guidelines provided by Biotech/Pharma.
- KP content is maintained by the Site Contract Manager team and fully supported by the company's legal counsel function

What benefits KP provides?

- access previous successful approaches and knowledge base;
- ensure a consistent approach / position when providing guidance to CROs;
- leverage previous legal guidance (internal & external) and approved changes;
- ascertain trends in repeated contractual language to provide substantive evidence of agreeable alternative terms.

Structure highly Dependant on levels of autonomy that the company is happy to release.

- Preferred Relationship;
- Flow-down of obligations and protection through contents of the Master CRO Agreement

Non-key clauses are free for CRO to negotiate on behalf of Biotech/Pharma.

Invite each CRO Site Contracting Function to assist in the banking of further knowledge.

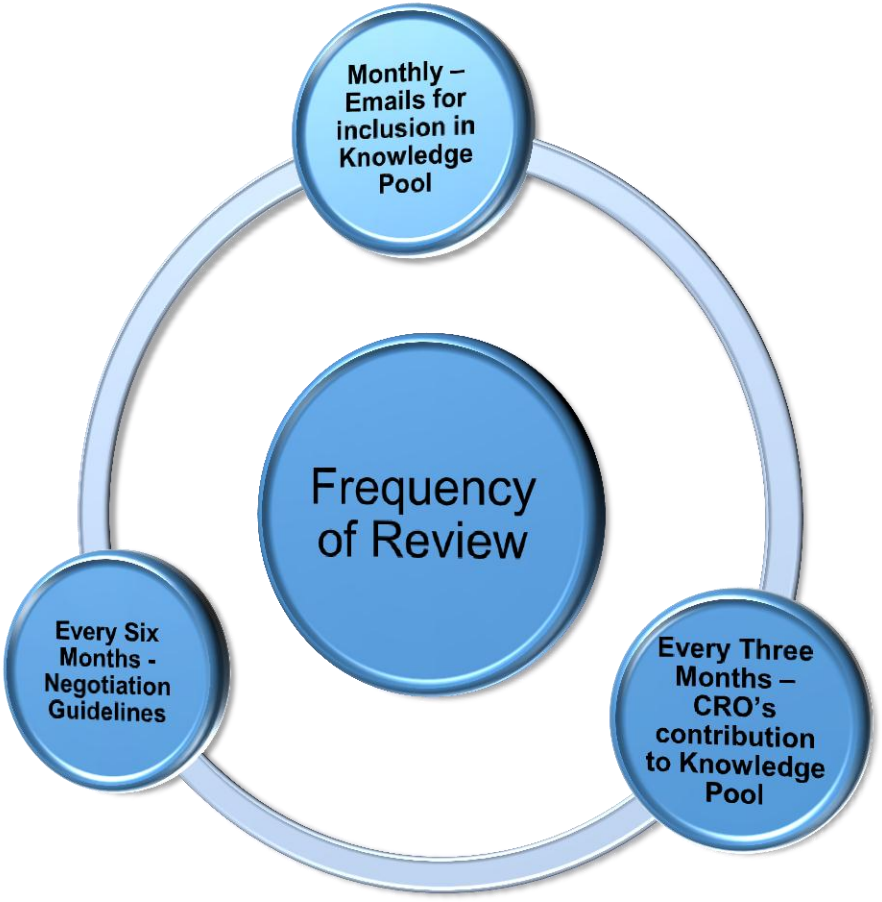
- Gives a share of the success and future extended autonomy;
- Gain from the experiences of other CROs;
- Reinforces benefit of a Macro environment

Knowledge Pool Tool

Additional Aspects that may Help:

- Set up and Email address for convenience and efficient filing;
- A consistent naming convention to structure the subject line will give benefits of quick referencing and delineation..

“SUBJECT MATTER / DOCUMENT TYPE / TYPE OF APPROVAL”



Regionalised Specialisation Model

SME Role

"The Site Outsourcing Lead" Regional Specialist Hub shall serve as the resident "expert" for legal aspects of site contracting in a designated country, maintaining current information and working to ensure a consistent approach across all studies in such country…"

Regionalised Specialisation Model

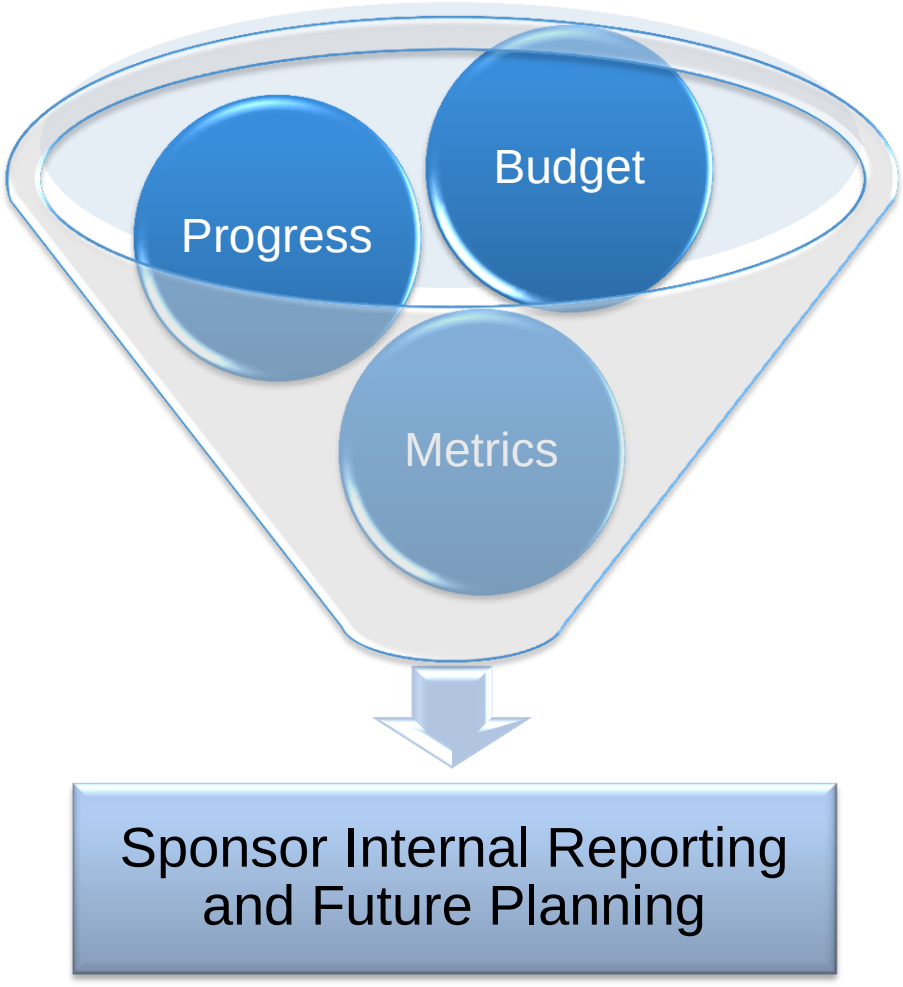
Program & Study Oversight

- Providing a consistent site contract strategy, oversight and support to GCO and CRO at both the program and study level…
  - Up-front and ongoing strategic planning specific to program / study needs
  - Oversight in the development of and approval of global investigative site budgets (GrantPlan)
  - Monitoring of KPIs including cycle time and SIV targets to ensure agreed study timelines remain on track
  - Agenda driven SMT attendance (i.e. Where strategic decisions are to be made that impact site contracts at a study or country level)
  - Risk Management…
    - Single point of contact for GCO in dealing with broader study related site contract challenges
    - Management of investigative site budget escalations

Contract Strategy & Oversight Hub

- Providing portfolio level contracts strategy and support to GCO and CRO…
  - Regional SMEs establishing country level strategy, monitoring trends and refinement of guidance, tools and templates to enable increased autonomy of CRO
  - Direct management of all key clause / new BIIB obligation negotiations escalated by CRO to expedite the delivery of a pragmatic solution

Tracking Types



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Site Contract Progress Tracking

Protocol #	Site #	Site Name	Site Country	PI Name	Description	Needed for Submission	Contract Tracking Status	Planned Ethics/Reg Submission	Planned SIV
218MS205	1	AZ Hospital	Belgium	Dr V	Ancillary agreement (Pharmacy)	Draft	In Review (IR)	end Aug	31-Oct-2012
218MS205	1	AZ Hospital	Belgium	Dr V	Ancillary agreement(LAB)	Draft	In Review (IR)	end Aug	31-Oct-2012
218MS205	1	AZ Hospital	Belgium	Dr V	PI & Institution	Draft	In Review (IR)	end Aug	31-Oct-2012
218MS205	1	AZ Hospital	Belgium	Dr V	PI & Institution (Indemnity)	Draft	In Review (IR)	end Aug	31-Oct-2012
218MS205	2	CHU	Belgium	Dr L	PI & Institution	Draft	Final Signed by All (S)	June 15	13-Sep-12

Site Contract Progress Tracking

Draft sent to site	Negotiations Concluded	Final Sent to Site	Signed Received From Site	Signed at CRO	Signed Received from CRO (Signatory)	Fully Executed	Days b/n Contract Draft Sent to Site to Fully Executed	Date of comments	Comments
14-Aug-12								23-Aug	
14-Aug-12								23-Aug	
14-Aug-12								23-Aug	
14-Aug-12								23-Aug	
14-May-12	18-May-12	14-Jun-12		13-Jun-12	14-Jun-12	22-Jun-12	46		FE

Tracking Types (Metrics)

Collection of Metrics and Benchmarking gives you team and other stakeholders a good measure for use during early stage planning and setting/reviewing expectations for the outsourcing provider:

- Improvement Insights
- Achievability Discussion (Robust support for internal and external timeline discussions)
- Measures for Benchmarking Performance – Positive & Negative
- Industry Indicators – CROs' (Macro), Sponsor's (Micro), Consulting work groups (KMR)

Tracking Types (Metrics) – BIIB/CRO 2011

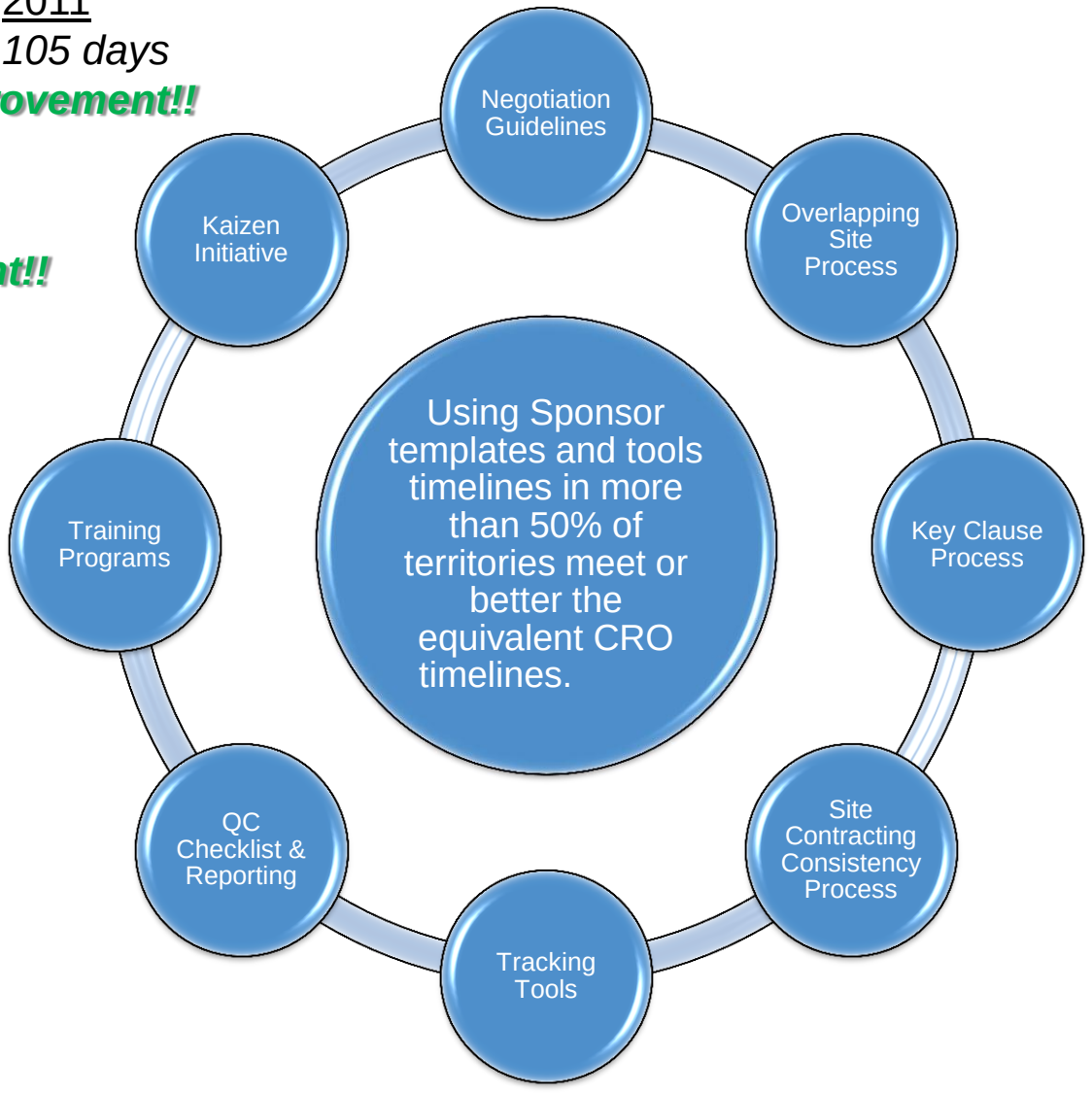
Global Average: 2010 2011

136 days 105 days

23% Improvement!!

Global Average: 2013

~40% Improvement!!



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Key Cycle Times & Quality

What is clear from the various aspects of the Macro, Micro or anywhere in between management styles, is that one key goal is to be able to gain efficiencies in the start-up phase for clinical trial outsourcing, whilst balancing the legal risk.

The ability to measure this performance is an important element of developing a clear understanding and direction for any plan for improvement or measurement of delivering the expectations.

The Main ‘macro’ measured cycle time to capture and analyse is the median per country of:

- Final Protocol – Full Execution Date
- 1st Draft to Full Execution Date

The Main ‘micro’ measured cycle times that should be captured, as these can give a hint into the area that are:

- 1st Draft to Response from Site
- Site Response to Sponsor/CRO Response (1st Negotiation Cycle)
- Number of Negotiation Cycles
- Signature Process

There are also considerations of subjective variants that can skew the data:

- Regulatory impact on contract negotiations: draft for submission; FE CTA for submission; negotiate terms in parallel; or only negotiate terms after regulatory/ethics approvals.

Key Cycle Times & Quality

Reduction of Cycle times may impact the achievement of quality of performance, which can add concern from a legal risk and compliance/audit perspective.

Quality is difficult to measure due to its subjective nature.

Number of Amendments due to QC Checks by Sponsor

Penalty clause or the cost implications of any quality issues based on Material or Non Material resolution – this is an important consideration when operating under a Macro environment. There is increased risk of exposure to the Sponsor of claims, penalties and audit findings

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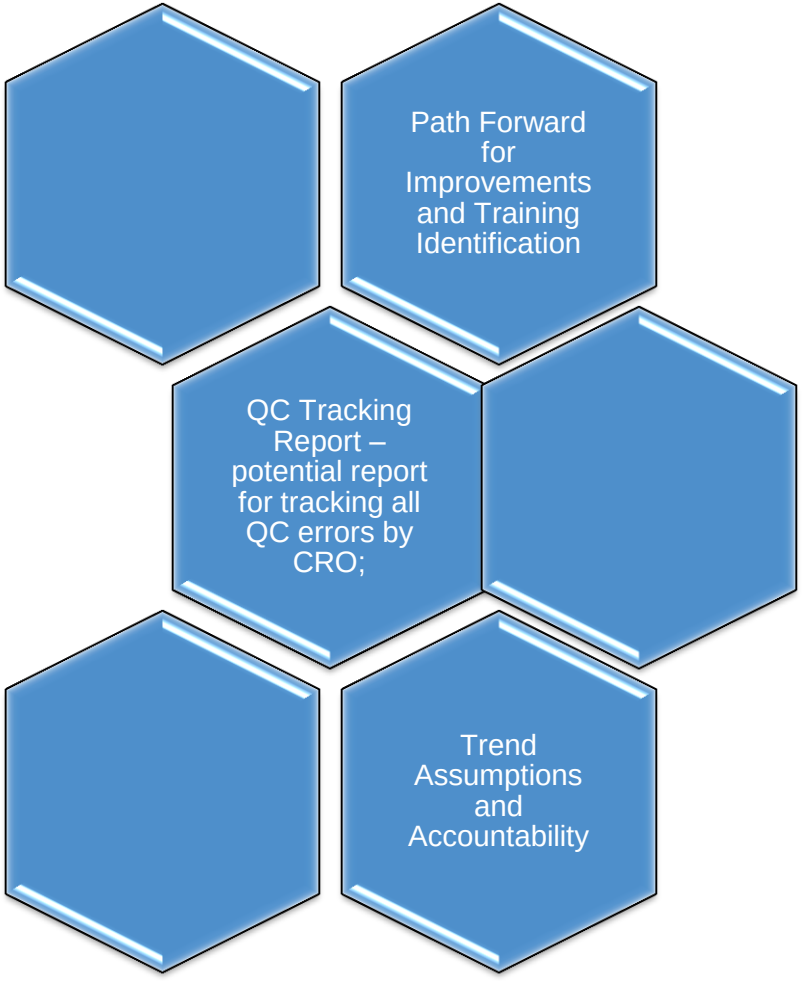
Key Cycle Times & Quality



QC Checklist Template Should be considered as a valuable tool

Key Cycle Times & Quality

Formal escalation to Sponsor RM?	Date Escalated to Sponsor RM	Escalated to Sponsor RM By	Issue Key Area	Study/Protocol	Issue Description
Date Escalated to CRO	Proposed Plan for Resolution	Target Resolution Date	Resolution Date	Current Status	Recent comment

QC Checklist Template
Should be considered as a valuable tool

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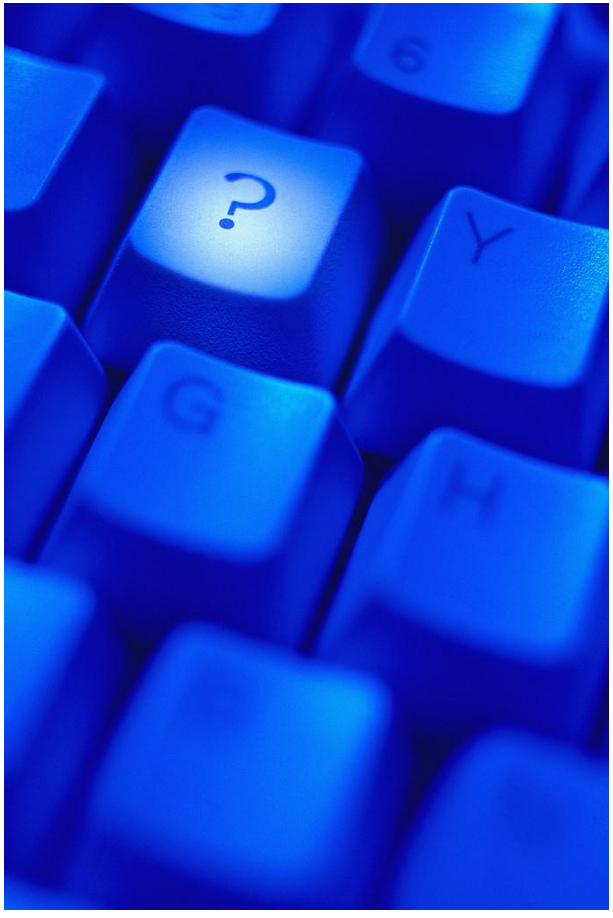
Questions & Answers



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