AstraZeneca

DCT Through the Lens of QA

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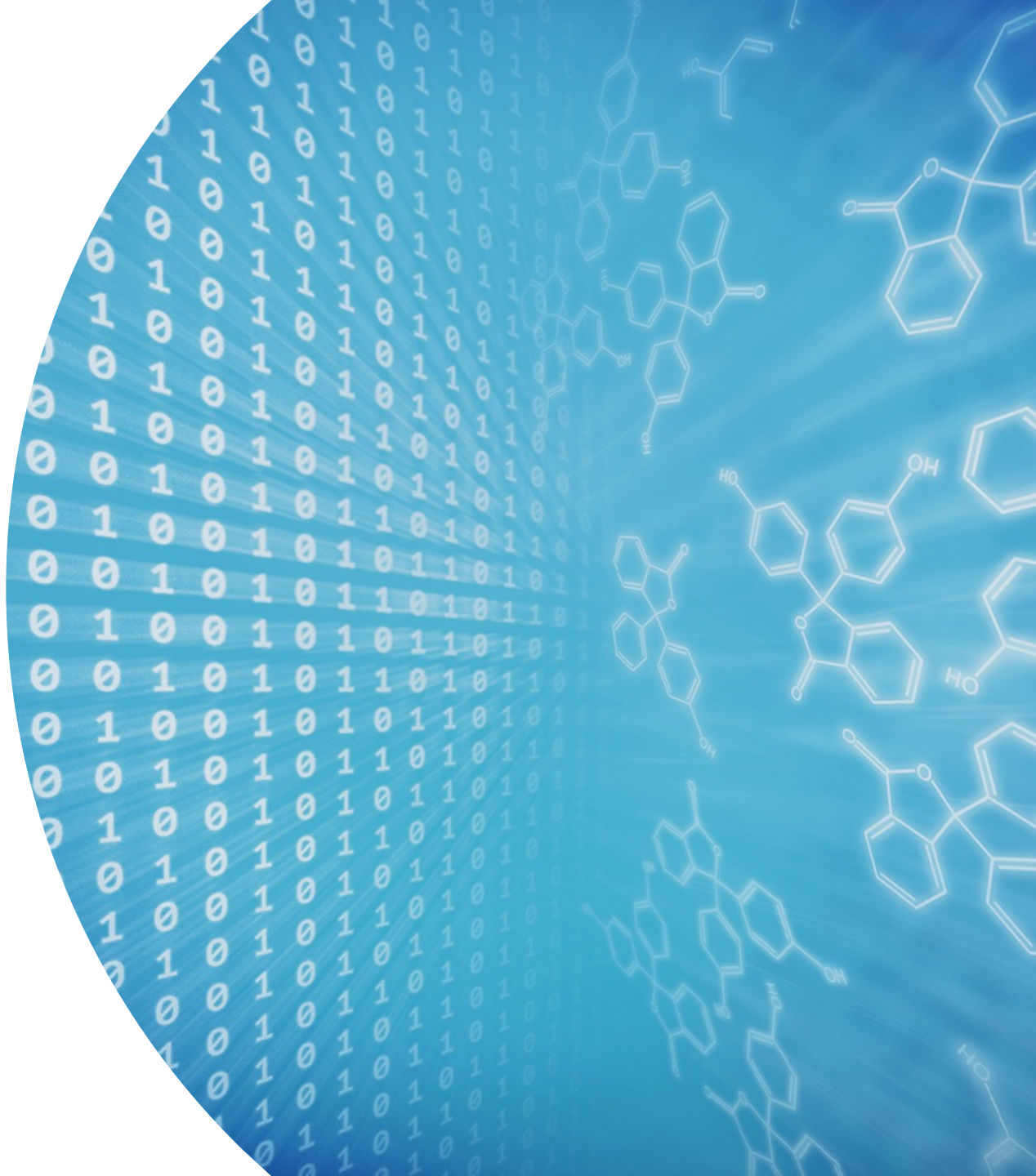


Fatemeh Jami PhD, MPharmSci.

- 18+ years in Clinical research , Quality & Compliance
- PhD in Organic Medicinal Chemistry University of Surrey
- Started Career at Janssen after graduating.
- In 2019 joined Medical Research Network as Director of Quality specializing in Quality framework for Decentralized trials.
- Joined AstraZeneca as Director, Strategic Advice QA in March 2021
- Member of RQA GCP Committee, and Trials@Home consortium
- Married and mother to a 5 y/o girl and 8 y/o boy

Focus for Today

We would like to explore the following thoughts:

- Is the traditional QMS too rigid? Is there an opportunity to be more “nimble” allowing the growth and evolution of clinical trials?
- Is there a role for QA, in driving innovations?
- Are QA a foe or friend, when it comes to change and disruption?
  - Share experiences/ challenges

Discussion Topics

1. Review of what we mean by Decentralised Clinical Trials (DCTs) in the context of Quality
   - Definitions
   - Regulatory challenges with the current DCT set-up

2. Current regulatory landscape
   - ICH GCP Renovation

3. QA Focus Areas
   - PI/ Sponsor oversight
   - E-Systems
   - Supply management

Are we equipped to manage the changing landscape of clinical trials ?

What are Challenges from a QA perspective?

Decentralised elements are typically placed into the following categories*

- Recruitment
- Direct-to-patient services (D2P/DtP)*
- Digital technologies
- Remote monitoring of trial participants' safety
- Adverse events reporting
- Validation of endpoints
- Remote access to source data
- IT systems
- Data Privacy
- Electronic collection, handling and storage of data

Recent Survey Results

We recently conducted a coffee morning discussion about DCTS,

The audience comprised of 60 Quality professionals who were interested in DCTs.

Here are the key take aways.

Poll# 1 (with answers)

- How are you currently managing the adoption of Decentralised Clinical Trials in your organisations?
  - 1. We have already assessed our processes against the regulatory expectations to ensure appropriate Quality Oversight of DCTs.
  - 2. We are currently discussing whether QA need to get involved.
  - 3. We have not thought about it yet.
  - 4. What are Decentralised trials and why is it important for QA to get involved?
-

Recap | DCTs

***A** multitude of elements which reduce, or in some cases even eliminate, the need for the trial participants to go to the clinical trial sites.*

(DKMA – Sep 2021)

***By** optimizing digital health technologies and enabling the voice of the patient in accelerating medicinal product development speed of delivery of therapy to patients and creating efficiencies across clinical research processes.*

(ACRO)

Poll#3 (with Answers)

- Which area in your opinion is highest priority and needs consolidated regulatory guidance:

- Direct- to-Patient services
- PI oversight of 3rd parties conducting clinical activities
- Sponsor oversight of 3rd Parties
- Data Integrity/ security
- Monitoring activities

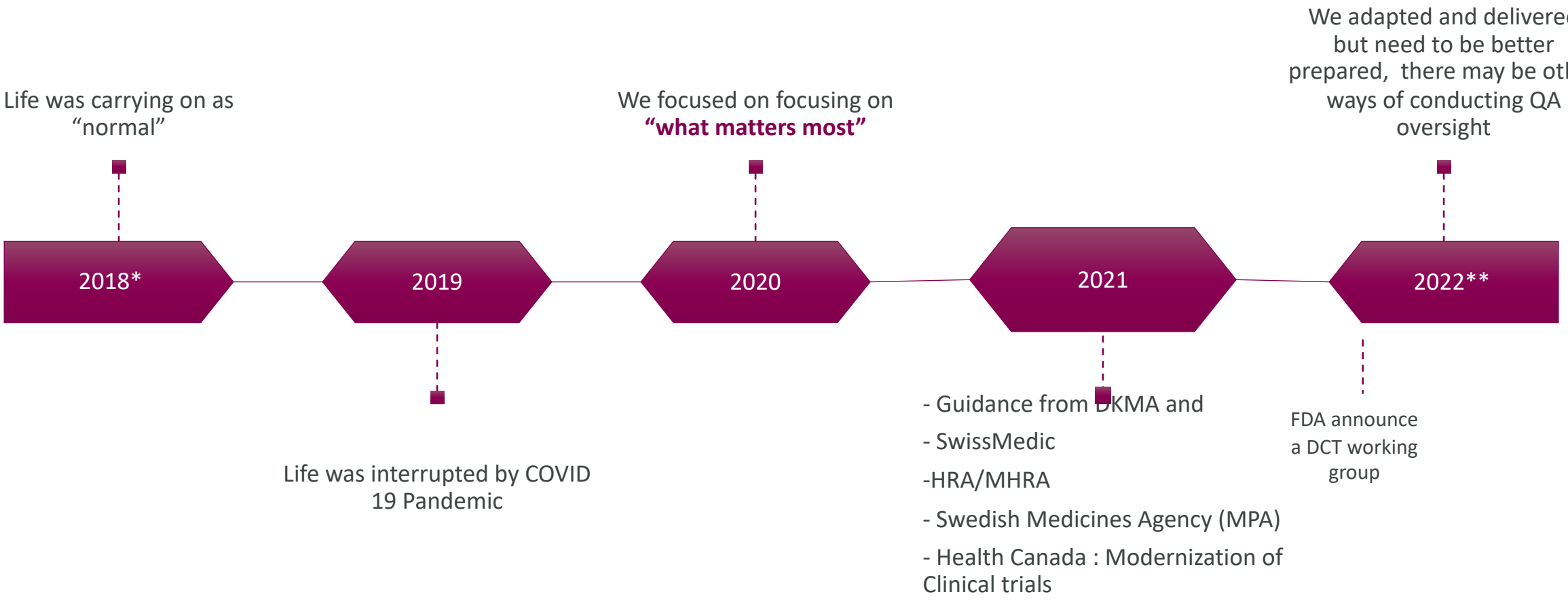
Poll# 2

- What is your top QA priority when assessing DCT needs:

1. Data Privacy
2. Impact on Audit programmes
3. Qualification of 3rd parties
4. PI oversight
5. Validation of digital technologies

Does ICH GCP apply to DCTs ?

Review | DCT Regulatory Milestones



T@H pilot DTRA/ ACRO DCT Activities**

EMA Q&A published**

FDA/ Health Canada and MHRA GCP Symposium presents om DCTs

GCP and DCTs

The ICH is planning to develop an Annex 2 on the topic of **“Additional considerations for non-traditional interventional clinical trials”** as part of the modernisation of the global GCP Guideline ICH GCP E6 (R2).

The new guidelines explain the opportunities of the new trial setting and challenges while ensuring patient safety and data integrity.

QA Areas of Interest
Do we need to re-think these areas for DCTs?

PI Oversight

- *The term 'Investigator Site' to mean the activities (regardless of their location) with effective oversight by one Principal Investigator (HRA / MHRA)
- Contracts & agreements
- Training of 3rd parties
- Documentation of delegation
- Insurance and Indemnity

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E-Systems

- Validation and testing responsibilities
- Contractual Obligations / Outsourcing
- Data Security/ Integrity
- Access to medical health records
- Real time access to data
- Technical Knowledge and skills
- Interoperability requirements

Sponsor Oversight Activities

- Audit Strategy – focus areas?
- Monitoring Strategy – focus areas?
- Frequency of Audits
- Suitability of traditional Audits
- Potential for real-time oversight
- Qualification of DCT vendors
- Direct-to Patient Services

PI Oversight
EMA Q&A- recap from 2018- lets dig a little further

- 10. According to the ICH-GCP and applicable EU laws, is it allowed that the Sponsor contracts third parties to conduct trial-related duties and functions that are clearly responsibility of the investigator?

  Dec 2018

- 11. According to the ICH-GCP and applicable EU laws, is it allowed that the Sponsor contracts third parties to conduct trial-related duties and functions that are clearly responsibility of the investigator? Rev. March 2022

ICH-GCP R2

The GCP-IWG recognises that a clarification about this practice is required to avoid misinterpretation of the requirements and non-compliance and in order to guarantee clear separation of roles and responsibilities between investigator and Sponsor and ensure their independence, in accordance with ICH-GCP principles.

How will this be conducted in reality?

In the revision of ICH-GCP (R2) the following points were added regarding this practice:

4.2.5 *The investigator is responsible for supervising any individual or party to whom the investigator delegates trial-related duties and functions conducted at the trial site.*

4.2.6 *If the investigator/institution retains the services of any individual or party to perform trial-related duties and functions, the investigator/institution should ensure this individual or party is qualified to perform those trial-related duties and functions and should implement procedures to ensure the integrity of the trial-related duties and functions performed and any data generated.*

"Although the Sponsor can contract directly some activities belonging to the Institution/Hospital e.g centralized analysis, archiving or central reading of images, the Sponsor cannot delegate tasks related to the medical care of the subjects that are specific of the Investigator (e.g. IMP dispensing/administration, AE/SAE evaluation), because the Investigator is responsible for all the trial medical activities. For this type of tasks, even if the Sponsor may need to be involved in the process of selection of the organization providing services and/or personnel (e.g. because the Institution and the clinical investigator site do nothave resources for third parties selection), the contractual arrangements should not be made directly between the organization and the Sponsor.

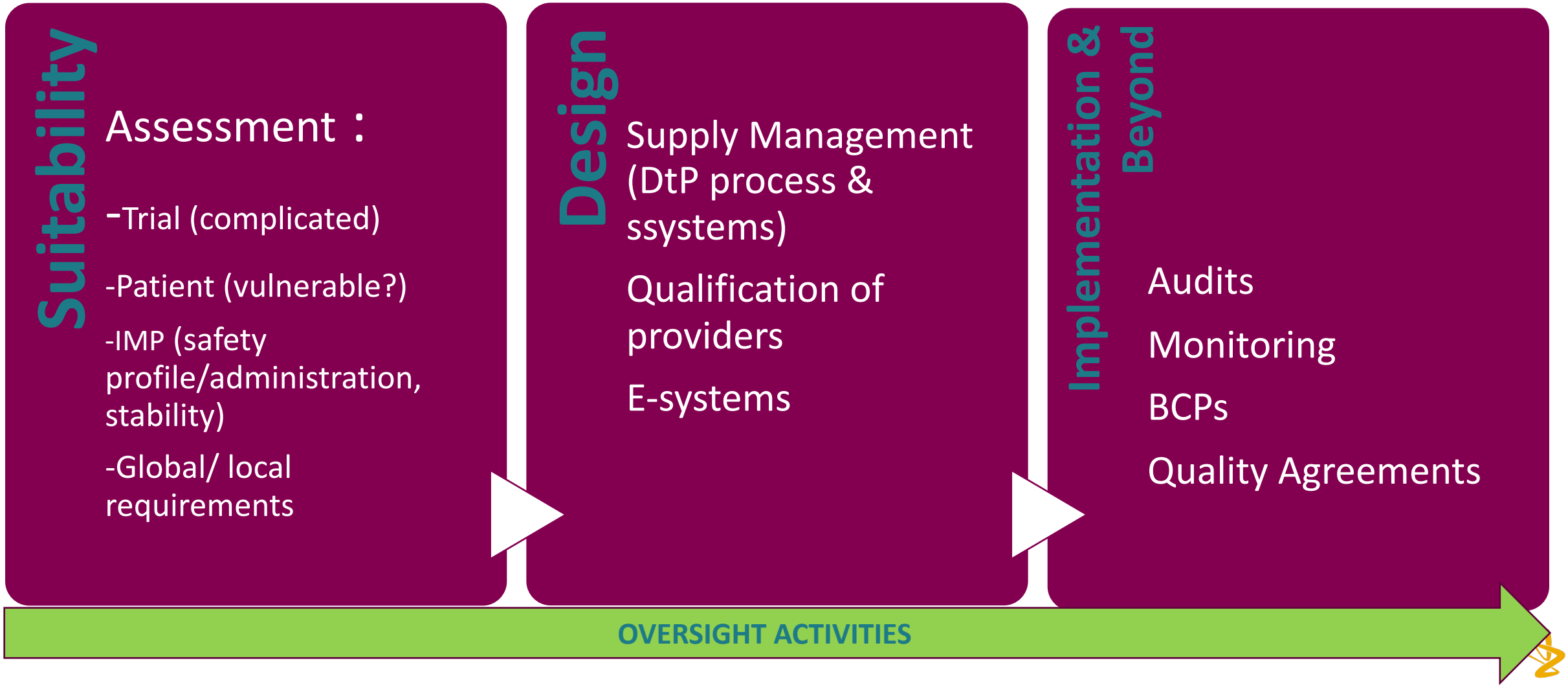
A contract/written agreement should be in place between the Institution/Hospital/Investigator and the single individual(s) or the organization which will provide the service/personnel. The contract between the Sponsor and the Institution/Hospital/Investigator should mention the involvement of this external organization or personnel. The contract should specify that the investigator is responsible for the oversight of the personnel of the external organisation."

The involvement of external parties should be submitted to and approved by the Ethics Committee before the start of the activities of "contracted personnel", as required by local regulations.

An individual or party to perform trial-related duties and functions the following points should be fulfilled:

- Considerations should be made about the protection of subject confidentiality and the Informed Consent Form should reflect this point.
- The personnel appointed for the procedure should be identified and its tasks should be documented on the contract/delegation log.
- In general, relationship and communications between Principal Investigator and organization or personnel should be independent from the Sponsor and should not go through the Sponsor in order to guarantee the independence of clinical trial conduct

Where/ When should QA get involved



Deeper Dive into the Regulatory Landscape

- Understanding and Application of ICH GCP guidelines
- ICH (E8) Revision/ Quality by design Thinking
  - Framework for designing quality in clinical trials, stakeholder engagement, trial design, proportionate trial management , critical to quality factors (CtQs)
- ICH (6) R2) Renovation leading to ICH E6 (R3)
  - Diverse trial types and data/quality and source
  - Centralised testing facilities
  - Flexibility in use of digital solutions
  - Clarity in roles and responsibilities
- EMA guidance regarding electronic system validations
- CFR part 11

Key takeaway

We can't solve problems by using the same kind of thinking we used when we created them.

Albert Einstein

& Challenges

Opportunities

- Engagement of QA earlier in the planning and adoption phase
- Getting “a QA seat on the table”
- Building a flexible QMS
- Working with the regulators proactively
- Being generous with knowledge

- Fast “hurried” adoption.
- Desire to be a part of the revolution.
- Moving too fast with rushed “onboarding” of technologies.
- Onboarding of providers who have limited regulatory/ GCP knowledge and experience
- Applying traditional thinking to non-traditional solutions.
- Data security expectations