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PER LA RICERCA FARMACOLOGICA
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December 10th, 2021
Virtual meeting

XIV FORESIGHT TRAINING COURSE
The health emergency: regulatory crash and future perspectives

Decentralized Clinical Trials: strengths and weakness of safety management

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OUTLINE

- How clinical trials changed during the pandemics
- Overview on Decentralised Clinical Trials
- Safety monitoring in DCT
- Conclusions

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A tsunami overwhelmed us …

31 Dec-2019: A new Coronavirus was identified in Wuhan (China)

21 Feb-2020: First confirmed case of SARS-CoV-2 in Italy

11 Mar-2020: the WHO declared a global pandemic

20-Mar-2020: Guidance to sponsors on how to manage clinical trials during the COVID-19 pandemic (4 February 2021 v4)

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"Behind every problem there is an opportunity"

(Galileo Galilei)

Pandemic experience has accelerated the use of innovative technologies in the clinical research

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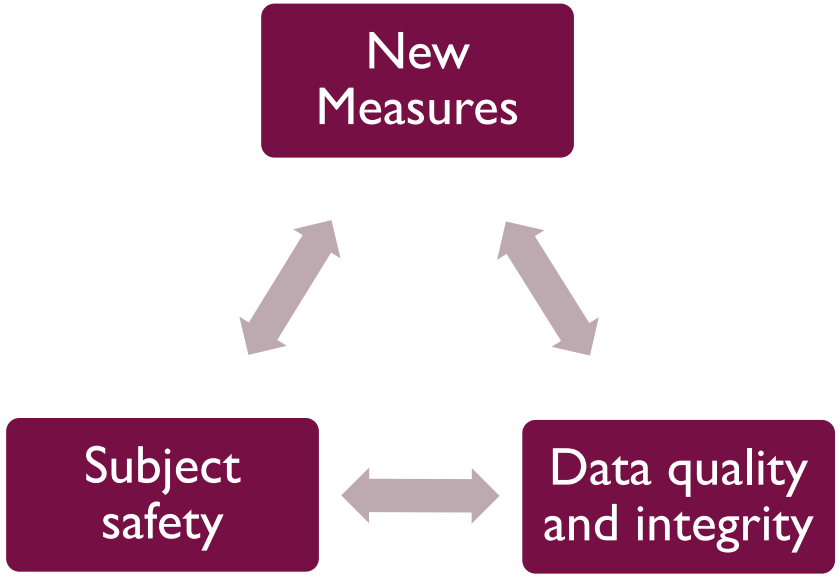
EMA Guidance to sponsors on how to manage clinical trials during the COVID-19 pandemic



- *Where a trial participant is unable to attend the site,* ***other measures may be required.***
- *However, the* ***limitations and risks of such methods*** *should be taken into account.*

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Clinical trial activities during the pandemic according the EMA Guidance

Increased use of digital technologies

Start-up

- EC and CA study evaluation sessions

Recruitment and treatment

- Procedure for Informed Consent
- IMP management
- Clinical tests

Monitoring

- Centralized monitoring
- Remote Source Data Verification

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The pandemic has highlighted the possibility of decentralizing specific elements of clinical research that can work even in a "non-pandemic" situation and could become the "standard" moving forward

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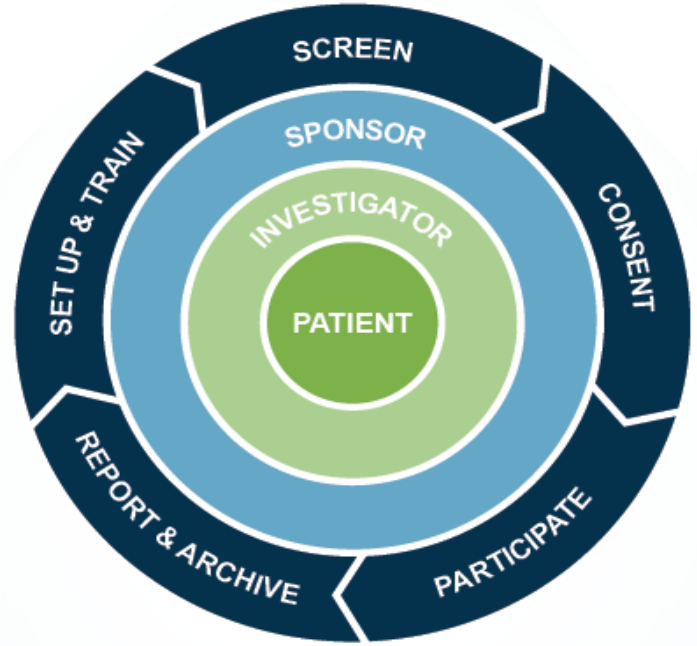
Decentralized Clinical Trial



*"Bring the trials to the patient by utilizing local healthcare providers, optimizing **digital health technologies**, and enabling the voice of the patient in order to accelerate medical product development, speed delivery of therapies to patients, and create efficiencies across clinical research processes"*

Decentralized Clinical Trials Working Party (ACRO DCT WP)

They are characterized by the use of telemedicine and digital technologies that allow some or all of the testing activities take place outside traditional testing sites

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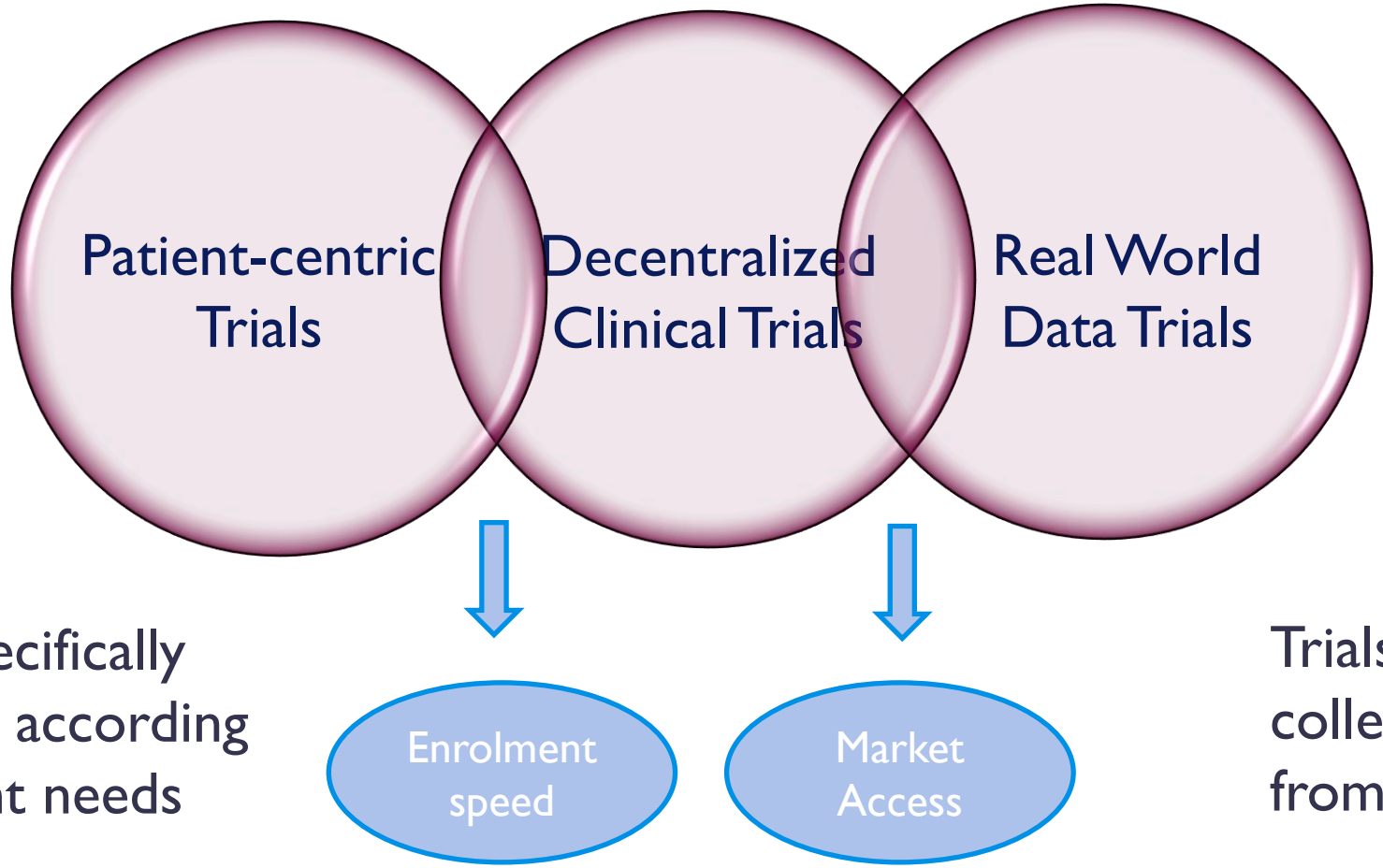
Patient-centric Trials and **Real-world data Trials**



Trials specifically designed according to patient needs

Trials that collect data from real life

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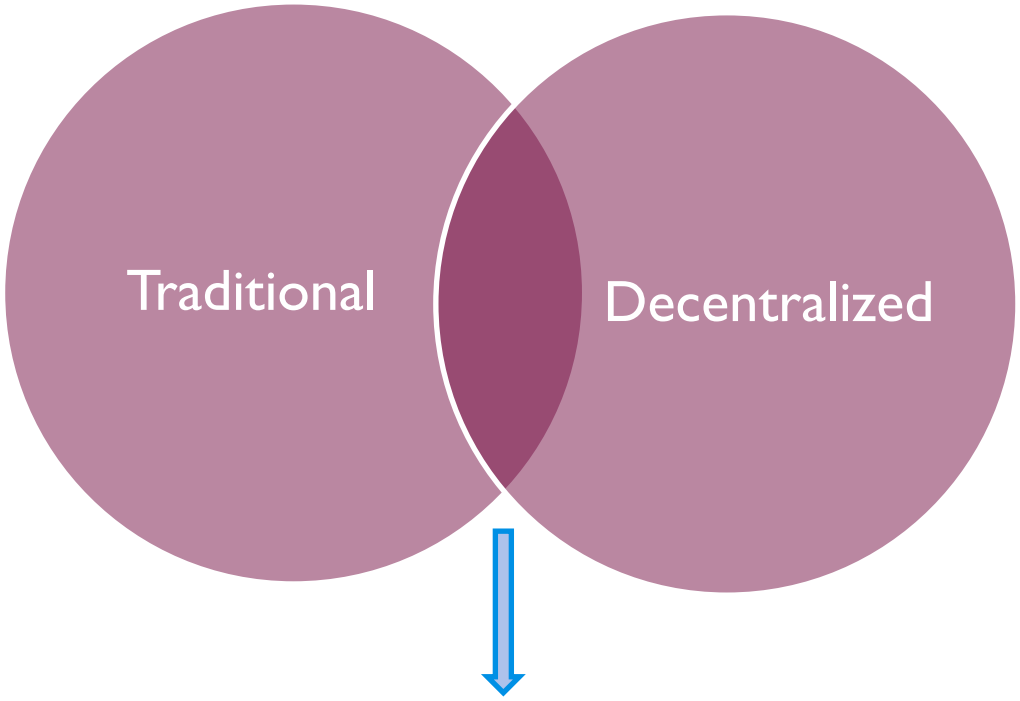
Partially Decentralized/Hybrid Approaches



Hybrid solutions

- a designated trial site at which specific trial-related activities occur (e.g., chest X-rays) while allowing other procedures (e.g., blood draws, treatment administration) to be completed elsewhere,
- data collection both within and outside of the clinical setting using mobile technologies, and/or
- trial participants and investigative site personnel interacting both at a clinical site and via video or teleconferencing.

Such hybrid approaches can increase trial flexibility

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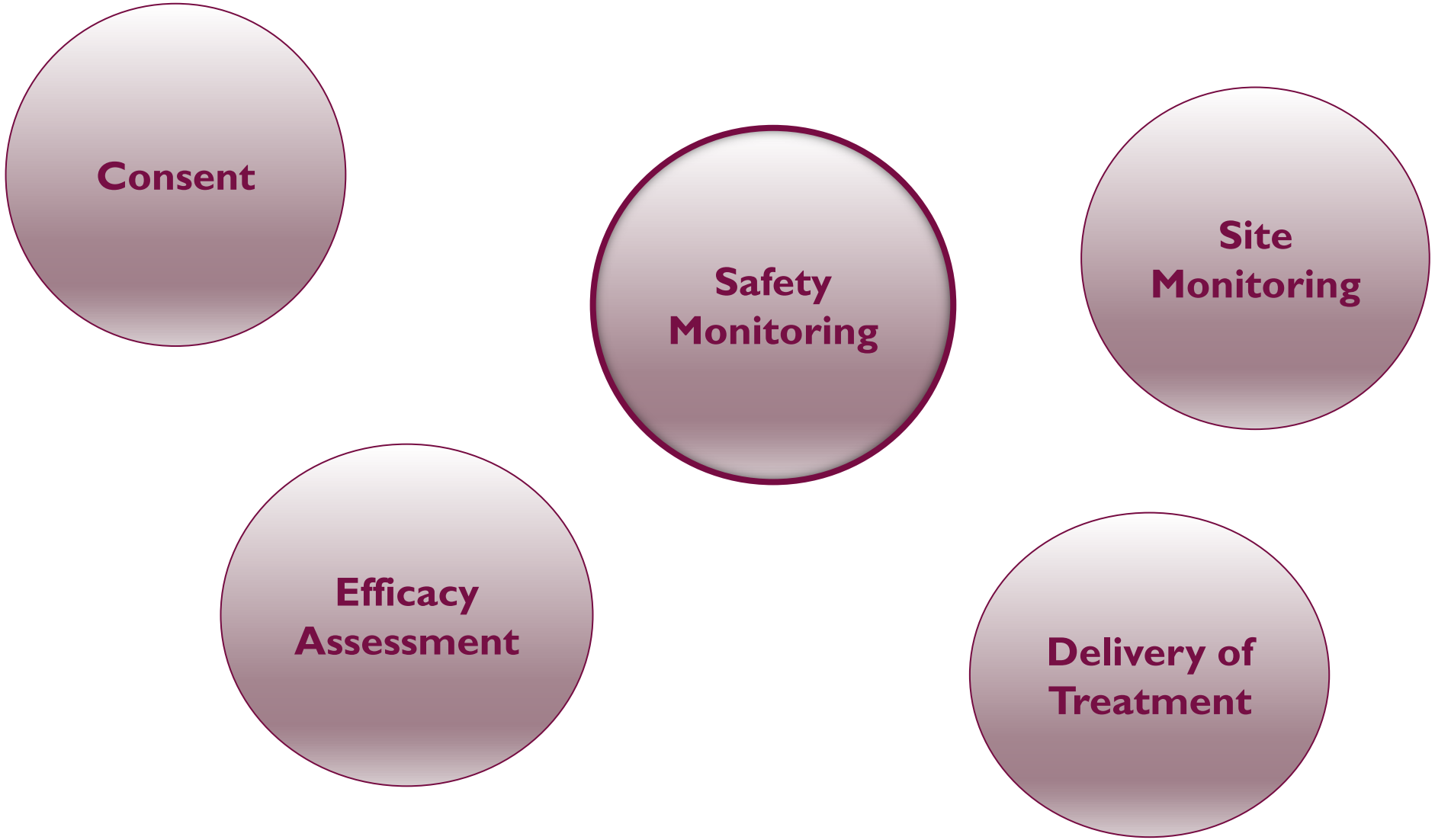
Impact of decentralization on several domains



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Safety Monitoring

- Procedures well documented
- Staff well trained
- Escalation plan for safety communication
- Review safety data in timely manner
- Contracts in place to react over distance

- Training and education
- Technological skills

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Safety management in DCT

DCT are less suitable for early phase trial or any study using an IMP that does not have an established safety profile

RISK ASSESSMENT → PATIENT SAFETY → TRIAL SUCCESS

Developing a risk assessment plan should be considered at the beginning of a project's lifecycle, and intermittent project level risk reviews should continue for the course of the trial

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ACRO

DCTs initiatives

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DCT WP provides a set of operational best practices for the implementation of decentralized clinical trials that will be helpful sponsors and research organizations

Decentralized Clinical Trials

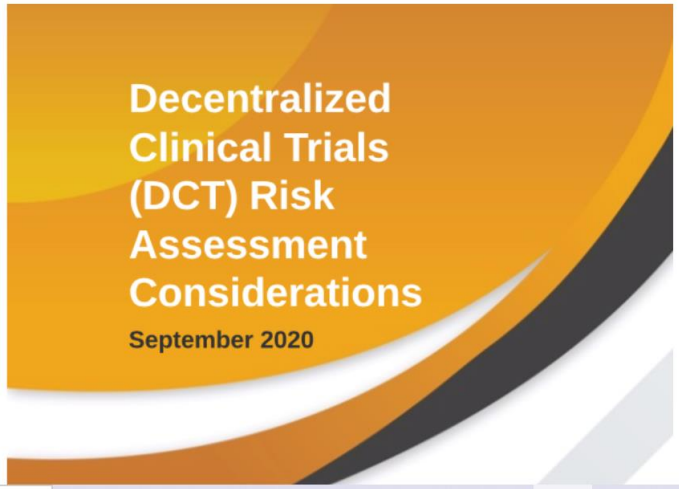
In October 2019, ACRO established the Decentralized Clinical Trials Working Party to examine the barriers to adoption of DCTs and create quality-based principles and tools to facilitate implementation of decentralized clinical trials.

Thought Leadership on DCTs

ACRO's DCT Toolkit includes four resources: (1) a detailed QbD Manual for DCTs; (2) an accessible, quick-reference QbD Manual; (3) a Risk Assessment Considerations template; and (4) DCT Data Flow Maps. In addition to the DCT Toolkit, ACRO's White Paper provides an overview of key issues in the decentralization of clinical trials

- **ACRO DCT White Paper: A New Quality-by-Design, Risk-Based Framework**
- **Bringing the Trial to the Patient: A Quality-by-Design Manual for Decentralized Clinical Trials**
- **QbD Manual for Decentralized Clinical Trials: The Quick Reference Guide**
- **Decentralized Clinical Trials Risk Assessment Considerations**
- **Decentralized Clinical Trials Data Flow Maps**

Click Here to Download the Full Template



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DCT Risk Assessment Tool

DCT Risk Assessment Considerations workbook was inspired by TransCelerate Biopharma INC. Risk Assessment Catagorization Tool (RACT)

					Overall Risk Score			#VALORE!		
Assessment #	**Category**	**Objective**	**Assessment Criteria / Questions for Discussion**	**Considerations**	**Impact**	**Probability**	**Detectability**	**Total Score**	**Category Weighting 0.1 - 1.0 (summary rating only 1.0 is default)**	**Mitigation Strategies**
1	General IT and Systems Consideration	Consider connectivity and robust infrastructure of the DCT network			*Medium (2)*	*Medium (2)*	*Medium to detect (2)*	8	1,0	
1,1			Is there a mechanism in place to inform and educate trial participants on a DCT and the process?	Need to evaluate if there is additional burden on the participant for the trial design using technology. How will participants be educated on the use of technology to ensure compliance? What are the training requirements?						Paper back up option for if a device fails
1,2			Is there a mechanism in place to inform and educate site staff on a DCT and the process?	Training requirement, consideration to be made due to the nature of the trial and site performing activities remotely.						
1,3			Is there a mechanism in place to inform and ethics and IRBs on a DCT and the process?	Determine the timing of submissions and what documentation is needed for submissions as this will vary per country.						
1,4			Have all the stakeholders been identified to allow for adequate time to create the appropriate training materials prior to key milestones?	Have Trial participants, sites, sponsors, vendors, ethics committees, couriers, CROs etc been identified and training available for all relevant users pertinent to the process, role and systems being used.						
1,5			Is the an appropriate infrastructure in place to support the DCT based on geography?	Is there an architectural/infrastructural document that provides an overview of the DCT design? Is there appropriate infrastructure to support the DCT based on geography? This could cover on premise, on site, or						
1,6			Is there appropriate documentation that provides an overview of the DCT data flow, collection and overall data strategy?	Requirement for a overall data strategy to support oversight. Requirement for a data flow diagram, considering who owns the data, who can query the data, how investigator retains control and access during and after study conclusion						
1,7			Will there be connectivity issues for the participants and the site?	When might the trial participant need to access the applications, at home, at work or external to the home i.e. need for Wi-Fi and roaming 4G/5G, foreign places.						
1,8			Does the site have sufficient bandwidth and connectively to manage data and interactions and engagement via remote means for all user?	May need to update bandwidth and connectively capabilities to manage multiple participants and geographies. Are the systems scalable.						

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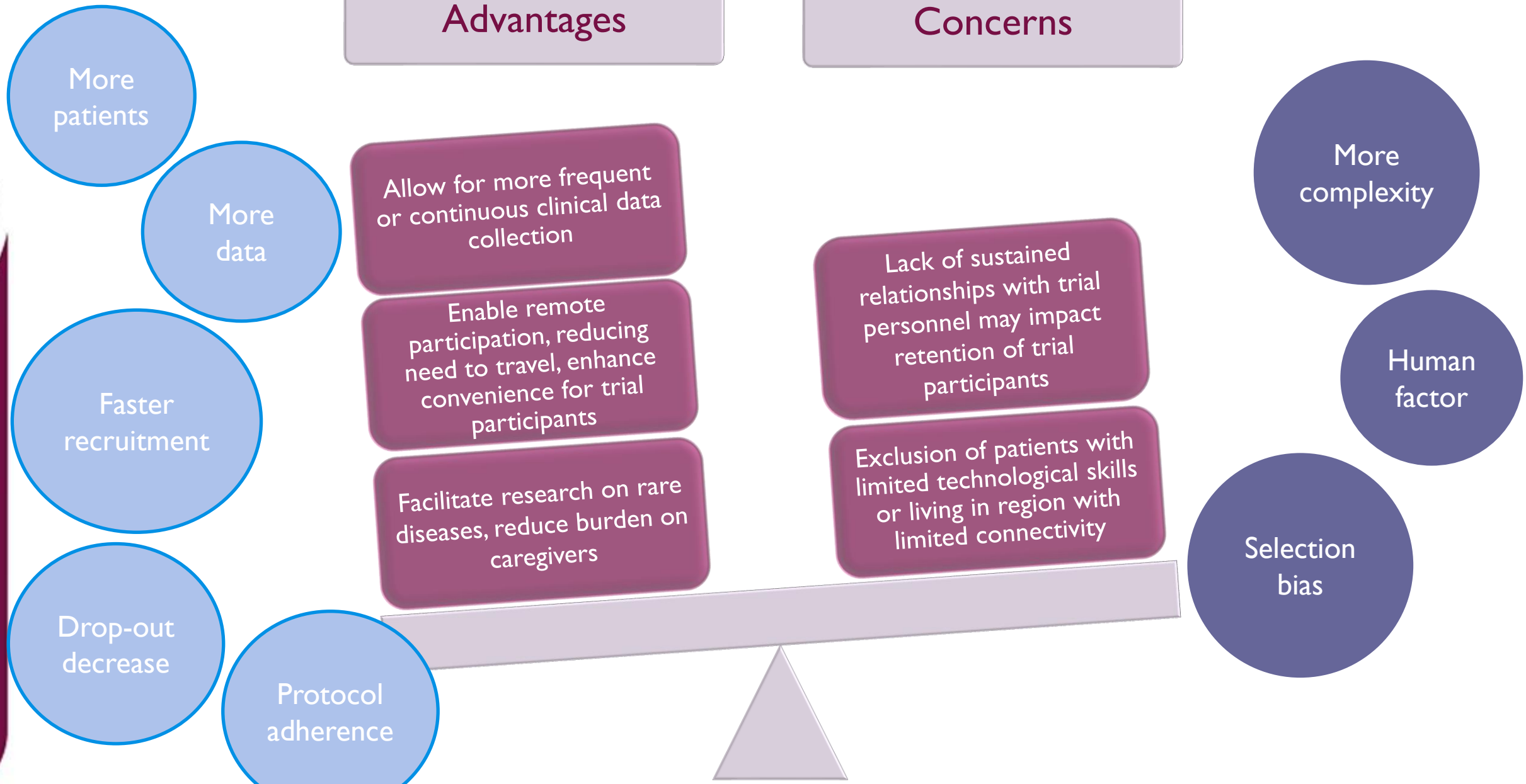
Advantages

- Allow for more frequent or continuous clinical data collection
- Enable remote participation, reducing need to travel, enhance convenience for trial participants
- Facilitate research on rare diseases, reduce burden on caregivers

Concerns

- Lack of sustained relationships with trial personnel may impact retention of trial participants
- Exclusion of patients with limited technological skills or living in region with limited connectivity



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Conclusions

- We are facing a progressive shift of the various clinical research activities around the patient
- Innovation allows to accelerate the development of a product, speeding up the delivery of therapies to the patient and making clinical research processes more efficient

in the respect of the rights,
safety and well-being of trial subjects

⇩

- Hold to the same standard as traditional trials
- Clearly articulate remote safety monitoring procedures and train investigative staff
- Develop protocol-specific safety monitoring and communication escalation plans