What could regulatory agencies do to facilitate increased adoption of appropriate DCT solutions in clinical trials?

- Publish clear guidances on the implementation of DCTs (long overdue!)
- Provide clear and consistent guidance
- Publish clear guidelines to adapt DCT
- Importance of Health Authorities issuing guidance
- Provide guidance on implementation of DCTs
- Guidance - clear and concise
- Publish guidance
- be positive & see the opportunities. But also make clear, what is acceptable and what not.
What could regulatory agencies do to facilitate increased adoption of appropriate DCT solutions in clinical trials?

<table>
<thead>
<tr>
<th>Action</th>
<th>Description</th>
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<tbody>
<tr>
<td>Reduce barriers of cross state, cross country regulatory differences e.g. licensure, differences in eConsent regs, etc.</td>
<td>Ensure that the regulatory approach is consistent across different departments and agencies.</td>
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<tr>
<td>Sponsor development of best practices/toolkits</td>
<td>Issue draft guidance and facilitate deep discussion of feedback with stakeholders.</td>
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<tr>
<td>Be realistic! DCTs are not &quot;stoppable&quot; anymore. Europe seems to be a little behind with DCTs, therefore more progress in Europe would be good. CTs are global projects!</td>
<td>Provide framework for agreements between sites/HHCP/sponsor.</td>
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<tr>
<td>Provide guidelines</td>
<td>clear guidance on what is needed.</td>
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<tr>
<td>flexibility beyond COVID</td>
<td>Provide guidelines.</td>
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</table>
What could regulatory agencies do to facilitate increased adoption of appropriate DCT solutions in clinical trials?

| Provide real time lists of accepted data collection devices and procedures |
| Road show? Continuous participation in these types of virtual conferences and sharing the messages of adoption, learning and doing. |
| Clear guidance |

ICH E6 is going to be key to the data aspects. The timelines for that are pretty long and that will hold up implication of DCTs today. How do we move forward?

Tackle eSource direct-data-capture head on

Global alignment - given the global nature of clinical trials, sponsors are only as innovative as the lowest common denominator country

Provide encouragement, guidelines, and alleviate regulatory barriers.

Clarification on what health authorities will and will not inspect when DCT features are employed
What could regulatory agencies do to facilitate increased adoption of appropriate DCT solutions in clinical trials?

- Provide guidance on verification/validation requirements for digital tools and the right balance between remote vs. onsite monitoring.
- Remove barriers (US) from State/local laws (e.g., Medical practicing across state lines, IMP prescriptions, etc.).
- Clarification on variability and what it means for analyses - i.e., are DCT features adding "more" selection bias or "different" selection bias?
- Emphasizing Diversity and Inclusion for clinical trial participation.
- Update public health educational material on clinical trials to say they may/may not include DCT features depending.
What can Industry and other stakeholders do to help build on the benefits of DCTs that we have seen during the pandemic?

Besides publishing DCT guidance, putting together globally harmonized guidance will be hugely beneficial.

We (industry) should remember that we also have a responsibility to openly share our experiences and learnings regarding DCT implementation.

DKMA's dialogue forum is providing a great opportunities to informally share DCT experiences - Other authorities could consider this kind of informal knowledge-sharing workshop.

Plan and prepare and involve stakeholders at the beginning of the trial prior to implementation.

Share lessons learned... what works and doesn't...

Sharing of case studies/lessons learned for others to learn from

Improve DCT tools
What can Industry and other stakeholders do to help build on the benefits of DCTs that we have seen during the pandemic?

paradigm shift to more of a sponsor/vendor partnership - Vendors working across sponsors will have more experience than any one sponsor. They need to be more than just a vendor, but a strong partner.

- Share experience, successes and failures to improve DCT practices
- IMI Trials@Home pilot trial (RADIAL) will generate large data volumes and will compare conventional, hybrid and virtual trial delivery.
- Sponsors should harmonize what they expect from sites --> use TransCelerate!
- Participate in CTTI, DIA and other working groups to propose feasible solutions
- Keep the education and public awareness of CTI ongoing to healthcare and patients alike
- Leverage technology to reach more diverse participants.

Sharing lessons learned and key decisions made to mitigate any issues.

Expand recruitment and education to ensure diverse participants.
What can Industry and other stakeholders do to help build on the benefits of DCTs that we have seen during the pandemic?

<table>
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<th>Share best practices</th>
<th>Propose and publish reasonable methods for maintaining data integrity, how to analyze data from trials that incorporate optionality</th>
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<td>Advocating for keeping regs established during emergency as permanent.</td>
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<tr>
<td>Vendors have a lot of good tech capabilities. They have an opportunity to become stronger in the regulatory requirements and in project management capabilities.</td>
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<tr>
<td>Industry members to find forums to share information (e.g. Clubhouse, virtual conferences, etc)</td>
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<td>Would like to hear more from patients, do they like DCT features? Is there a way stakeholders can survey patients? Are we at that point where we can get this information?</td>
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<td>Stakeholders can work on developing the value proposition - are we at the point where actual benefits can be calculated?</td>
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<tr>
<td>Strong senior leadership and middle leadership within companies to support project teams doing DCT approaches is essential</td>
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EDUCATE / Learning / Training on DCTs for the industry.
What can Industry and other stakeholders do to help build on the benefits of DCTs that we have seen during the pandemic?

DCT studies are global. Share how to handle the protocol where there will be disparity between countries on which elements will be used. How do we avoid having country-specific protocols?

Be mindful of costs to conduct DCTs -- don't increase exponentially, unnecessarily.
What are the greatest challenges or unresolved questions about PI oversight in decentralized trials?

- Data integrity
- Comfort with not seeing patient in person
- Data quality and bias
- Data quality and consistency of care / touchpoint with the participants
- Loss of communication
- How to handle delegation of responsibilities and 1572 requirements
- Which responsibilities fall to local PI vs centralized PI?
- How can PI provide oversight of home health vendors, if they have not trained and met individual care providers
What are the greatest challenges or unresolved questions about PI oversight in decentralized trials?

- Making sure that actions are standardized
- How to oversee the data collection and standardization.
- Data integrity and completeness
- Data quality. Patient reported data.
- Lack of in-person contact
- Involving the patient's PCP - what responsibilities can they take
- Ensure that the patient completes the task as requested, at the time requested and done correctly.
- Determining when individuals are on 1572 and Delegation of Authority Log (e.g. what is considered clinical care)
- I think the "business model" doesn't currently support optimal oversight.
What are the greatest challenges or unresolved questions about PI oversight in decentralized trials?

- Who will be responsible for adverse event attribution?
- timelier data capture and reporting
- Cross state and country differences when overseeing multiple remote sites
- How would our PI actually provide true oversight of care provided by outside providers he has never met: this is a huge challenge when he perceives oversight as his responsibility on the #1572
- an SAE that occurs, how is PI involved, managing the event
- Data privacy regulations and ability to implement digital tools (eConsent, eSource, remote monitoring) globally
- In a fully virtual trial, how to ensure the required oversight? If the PI “never” sees the patient in person, can we really say that the oversight is given?
- IMP accountability and compliance by patient with no technology to track

Pls do not feel comfortable putting mobile healthcare provider on DOA which means they have direct oversight for them. Sites have told us that some sponsors don’t require site to list mobile healthcare on DOA - is that possible?
**What are the greatest challenges or unresolved questions about PI oversight in decentralized trials?**

<table>
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<tr>
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<tr>
<td>If a DCT includes a mobile phlebotomist drawing blood at a participant’s home, what level of oversight does the PI need have on the mobile phlebotomist, and what does that look like in terms of training, availability, safety events, etc.?</td>
<td>How can we demonstrate this aspect has been fully considered in the protocol when it's the PI's responsibility to demonstrate it during a clinical trial.</td>
</tr>
<tr>
<td>missed visits that impact data collection or Patient Safety. What is the PI's responsibility from an oversight perspective.</td>
<td>What oversight, if any, is expected if PI collects data from local HCP if data collection does not require protocol training.</td>
</tr>
<tr>
<td>How to bring in local labs or imaging (if), etc., to ensure PI oversight on the patient continuous participation in the CT is appropriate.</td>
<td>How can you consistently document PI oversight of external vendors that PI has not met and confidently provide oversight for a patient care where the PI doesn't not meet the patient.</td>
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<tr>
<td>Publish clear guidance documents on DCTs (long overdue!)</td>
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What needs to change in sponsor interactions with investigative sites, patients, and vendors to successfully implement DCT solutions?

- Listen
- Earlier interactions with Patients and Sites to obtain their input into CTPs
- greater degree of collaboration between all the players
- Transparency & education for patients! Patients need to understand
- more investment of time and planning with all stakeholders
- engage with stakeholders in protocol development early on
- flexibility based on patient need
- solicit more feedback earlier on in the drug development plan
- should be a partnership, not a transactional relationship. Input from all stakeholders
What needs to change in sponsor interactions with investigative sites, patients, and vendors to successfully implement DCT solutions?

- Clearly defined operational plans— at a level of detail not seen or required for traditional clinical trials.
- Solid protocol design.
- Involvement in trial design and planning.
- What are the benefits for a patient compared to a conventional trial?
- Providing options to patients without adding too much logistical burden to the study team.
- Include them in the development of the protocol.
- Paradigm shift to more of a sponsor/vendor partnership - Vendors working across sponsors will have more experience than any one sponsor. They need to be more than just a vendor, but a strong partner.
- Open and honest discussions and appropriate training/education.
- Standardization within and between sponsors - requirements, communications, etc.
What needs to change in sponsor interactions with investigative sites, patients, and vendors to successfully implement DCT solutions?

- Less complexity and more streamlined ways of working and interactions
- More transparency from Vendors regarding what their systems currently do and don't do and what their actual experience is in this space
- More thorough interaction during protocol design of the different parties
- Clear evidence for a decreased burden!
- Embed DCT in protocol design and proactively engage sites in the process during site selection to ensure alignment on remote visits
- Centralization to facilitate exchange of information/communication
- Patient AND caregiver education
- Trial design and planning.
- EDUCATE
What needs to change in sponsor interactions with investigative sites, patients, and vendors to successfully implement DCT solutions?

- Thinking - having all stakeholders think a bit more creatively as to how to get the essential aspects of a trial completed.
- Active partnerships with sites
- There needs to be more holistic collaboration involving ALL stakeholders with stakeholders not only coming to the table with their ideas in hand but with open ears and minds to consider the feedback of others.
- We as the sponsor need to implement well defined processes and procedures for DCT solutions so we can have consistency and control. DCT is so new and we don't have established processes.
- More sharing of Lessons Learned from all parties involved in DCTs
- Vendors have a lot of good tech capabilities. They have an opportunity to be stronger in knowledge of regulatory requirements and in project management.
- Easy administration
- Flexibility!
- Practice/Testing of protocols with sites and sample patients
<table>
<thead>
<tr>
<th>Improved communications with patients, especially the underserved.</th>
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<tr>
<td>Investigators need to separate their own discomfort with DCTs from valid reasons to oppose DCT features</td>
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<tr>
<td>More oversight of CROs to ensure they are not adding undue burden on sites and patients.</td>
</tr>
<tr>
<td>HCPs learn how to reach and explain clinical trials and encourage their patients to enroll.</td>
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<tr>
<td>Education / training needed so sites, patients, etc aren't left to figure DCT aspects on their own</td>
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<tr>
<td>More fit for purpose designs based on specific patient population</td>
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<tr>
<td>Sponsor brings investigators and patients to the table in the design phase</td>
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<tr>
<td>SURVEY engines that are targeting stakeholders (site, patients, etc) for Protocol development in accommodating DCT elements</td>
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<td>More willingness to try and be open to failure (before reassessing and trying again). We won't get it right first time and if we have, then we're probably kidding ourselves</td>
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What needs to change in sponsor interactions with investigative sites, patients, and vendors to successfully implement DCT solutions?

- Would like to hear more from patients, do they like DCT features? Is there a way to survey patients? Are we at that point where we can get this information?
- Perhaps getting all the previous information out of what works and doesn't work. Keep constant feedback in the planning and intervention.
- Value proposition - Are we at the point where actual benefits of DCT approaches can be calculated?