Technology and Data Harmonization for Enabling Decentralized Clinical Trials
Industry Connections Activity Initiation Document (ICAID)

Version: 3.0, 10 November 2021

<mark>IC19-004-03 Approved by the IESS SMDC 13 December 2021</mark>

Instructions

1. Contact

Provide the name and contact information of the primary contact person for this IC activity. Affiliation is any entity that provides the person financial or other substantive support, for which the person may feel an obligation. If necessary, a second/alternate contact person's information may also be provided.

Name: Mathew E. Rose, MD MS (Co-Chair)
Email: mattrose@saavha.com
Affiliation: SAAVHA Inc.

Name: Walter De Brouwer (Co-Chair)
Email: Walter@Doc.ai
Affiliation: Sharecare

IEEE collects personal data on this form, which is made publicly available, to allow communication by materially interested parties and with Activity Oversight Committee and Activity officers who are responsible for IEEE work items.

2. Participation and Voting Model

Specify whether this activity will be entity-based (participants are entities, which may have multiple representatives, one-entity-one-vote), or individual-based (participants represent themselves, one-person-one-vote).

Entity-Based

3. Purpose

3.1 Motivation and Goal

Briefly explain the context and motivation for starting this IC activity, and the overall purpose or goal to be accomplished.

Describe the motivation and goal.

The global clinical trials market size was estimated at 44.2 billion in 20181. The traditional clinical trial model not only makes it inconvenient for patients to participate, but it creates a chaotic approach to collecting, managing, leveraging and tracking the data. The modernization of clinical trials through a multi-stakeholder approach where optimization of process and efficiencies are identified in protocol development, determination of digital end points, more inclusive and diverse patient population, and data interoperability and portability.

The cost of conducting clinical trials is rapidly rising due to complex manual processes intended to meet regulatory policy and inefficient methods of recruiting and maintaining qualified patients to meet enrollment requirements. Failure to recruit patients results in delay or sometimes termination of trials, more costs and ultimately depriving patients to access to potential life-saving or quality of life therapies.

Compliance obstacles associated with Covid-19 have driven awareness of the need for decentralized clinical trials. Building inclusive and diverse clinical trial protocols reflecting a diversity in patient population such as age, race, ethnicity, lifestyle, and other factors into account may impact drug efficacy and safety. Yet, less than 10% of the US patient population engages in clinical trials today. Among those, 18% of randomized trial patients will drop out due to compliance challenges or other reasons.

Major challenges:

1.   Sponsors of clinical trials remain hesitant to adopt decentralized clinical trials (DCT) early on to optimize efficiencies in all steps of clinical research
2.   Difficulty in recruiting qualified patients that match the trial design protocol. Challenges include lack of access to patients either through patients lack of awareness
3.   Inability for patients to conveniently and consistently access the trial site
4.   Inefficient data tracking and processing, creates unusable data and delays in filing for approval
5.   Interoperable and secure source of "truth" from patient informed consent through published results of the trial where participating sponsor and patient can obtain access and updates to the clinical trial's progress

A snapshot of clinical trials:

- **80% of trials fail to meet their enrollment timelines**[2]
- Patient recruitment services annually contribute over $5.9 billion in expenses to the pharmaceuticals industry and can take up 30% of clinical development time.[2]
- Approximately one-third (30%) of phase III study terminations are due to enrollment diffculties[2]
- A typical Phase III clinical trial takes nine months to complete enrollment and can cost up to $86 million[3]
- **Only 1 in 30 cancer patients participate in a trial**[4]
- Non-Hispanic white patients accounted for 82.9% of phase 3 study populations between 2001 and 2010, or seven times the combined percentage of black (6.2%), Asian (3.3%), Hispanic (2.2%) and Native American (0.1%) patients[4]

- **$1.89Bn** cost of patient recruitment per year[5]
- **30%** of investigator sites fail to recruit one single patient[5]

The Goal

To utilize and harmonize viable uses of novel technologies including but not limited to AI (artificial intelligence), distributed ledger technologies (DLTs), IoT/sensors, and VR/AR and existing technology systems and processes to conduct an optimized decentralized clinical trials (DCT). The initial phase of the work will review existing pilots and attempts, develop a workflow for these technologies, and finally build a test bed to validate the proof of workflow developed. The project will look at the use of open technologies, data ethics and governance, KPIs for optimization of time and cost for recruitment and auditing trials of patients, etc.

The goals of this activity is to identify through the workflow and testing process if conducting DCTs would result in or enhance the following:

a. Reduce delay and cost of recruiting qualified patients to enable more diversity and inclusion with DCTs for patients who are unable to travel to sites, excluded due to lack of awareness or living in remote areas in the US and around the world
b. Creating a more sustainable approach and efficient method to recruit, engage and retain qualified patients during the trial
c. Increase patient participation and completion rates and recruit more diverse patient populations
d. <u>Validate and verify selected decentralized heath technologies (DHT)/tool kits prior to changing or modernizing standard procedures, to be certain there is consistency, mitigation of source or data variability, mitigation of data interruption, mitigation of malfunctions, irregularity, bugs etc., in transfer of data</u>
e. End-to-end security of a DHT data platform ensuring interoperability and encryption to information
f. Optimize the integrity of management, tracking and collection of patient data from informed consent through to publishing results of trial
g. Enhance the patient consent process with the use of one original record to track from consent through to end of trials.
h. Reduce time in the auditing and verification of trial data and submission for FDA approval
i. Endeavor to demonstrate an overall cost reduction in identifying and training at sites to conduct trials including the need for less transportation and housing patients at designated sites.

3.2 Related Work
Provide a brief comparison of this activity to existing, related efforts or standards of which you are aware (industry associations, consortia, standardization activities, etc.).

Describe the related work.

The following organizations are addressing the regulatory, data and technical challenges throughout the clinical trials process inclusive of patient recruitment, engagement and retention for trials and managing the data transactions across the multiple partners in the clinical trials operations process:

- The Clinical Trials Transformative Initiative (CTTI) seeks to overcome barriers of patients participating in trials.

- Clinical Data Interchange Standards Consortium (CDISC) creates clarity in clinical research by bringing together a global community of experts to develop and advance data standards of the highest quality.

- Alliance for Clinical Research Excellence and Safety (ACRES) is a multi-stakeholder collaboration building a global system for excellence in clinical research and a global network to connect sponsors, regulators, service providers, ethics committees, research sites and patient subjects with an ability to use information seamlessly and securely to benefit all stakeholders.
- ATA (American Telemedicine Association) – Establishing best practice guides in the space of telehealth – inclusiveness and diversity in the application of remote patient monitoring from clinical research to bedside practice.
- IEEE-SA standards activities with relevance to this topical area:
    - IEEE P2418.6 – Blockchain for Healthcare and Life Sciences
    - IEEE P2733 – TIPPS & Clinical IOTs
    - IEEE 2791- Standard for Bioinformatics Analyses Generated by High-Throughput Sequencing (HTS) to Facilitate Communication
    - IEEE P1752 – Open Source Standard for Mobile Health Data
    - IEEE P2721 Healthcare Device Security Assurance Working Group

3.3 Previously Published Material

Provide a list of any known previously published material intended for inclusion in the proposed deliverables of this activity.

List the previously published material, if any.

3.4 Potential Markets Served

Indicate the main beneficiaries of this work, and what the potential impact might be.

Describe the potential markets.

Bio/Pharmaceutical Industry:

- Pharmaceutical and biopharmaceutical manufacturers (sponsors of trials)
- Research hospitals (sponsors of trials)
- Service Providers to Clinical Trials Operations (Laboratories, Contract Research Organizations [CROs], Informed Consent Providers, Sites [Hospitals]

Patients

Regulatory (FDA)

Technology Companies

- Artificial Intelligence (AI), Machine Learning, Augmented Reality, Blockchain/DLTs, IoMTs/Sensors

The development of a technical and ethical workflow to enable complete remote patient trials for certain therapeutic conditions will create a more inclusive patient recruitment process, create a more bilateral data communication protocol between patients and clinical trials operations ecosystem, and reduce the time and delays in the clinical trial thereby optimizing the development of medicine to market.

3.5 How will the activity benefit the IEEE, society, or humanity?

There are expected technical and data governance standards to be extracted from the workflow developed from this activity.
Published white papers and industry recommendations to provide guidance
Recruitment of new entities as corporate members from the pharmaceutical industry and tech start-ups
Development of workshops, specific-building work streams, and educational webinars to amplify the program's mission, objectives and participation
Conformity Assessment Project on the created, tested and consensus-developed workflow.

4. Estimated Timeframe
Indicate approximately how long you expect this activity to operate to achieve its proposed results (e.g., time to completion of all deliverables).

Expected Completion Date: 12/2023

IC activities are chartered for two years at a time. Activities are eligible for extension upon request and review by ICCom and the responsible committee of the IEEE SA Board of Governors. Should an extension be required, please notify the ICCom Administrator prior to the two-year mark.

5. Proposed Deliverables
Outline the anticipated deliverables and output from this IC activity, such as documents (e.g., white papers, reports), proposals for standards, conferences and workshops, databases, computer code, etc., and indicate the expected timeframe for each.

Specify the deliverables for this IC activity, please be specific.

- Hold subject focused industry educational talks four or more times per year to educate and build industry support.
- Consensus-driven and tested process workflow for decentralized clinical trials
- Elevation of pre-standards activities to technical and data standards working groups for applications of decentralized health technologies (DHTs) and toolkits for remote patient monitoring   **– 18 months**
- Exploration of standards for patient data governance, security and portability for decentralized clinical trials **– 18 months**
- Industry guidance (i.e. industry behavior changes) for regulatory and industry behavioral changes, approach on digital end point validation with autonomous data collection and portability   **– 12 months**
- Patient Value and PHR Empowerment Proposition Report **– 12 months**

- ROI Case Study Analysis Report on simulated trial using working new Remote Patient workflow **– 24 months**
- Conformity Assessment for Remote Patient Trial Workflow (conformity to regulatory, industry clinical standards and technical standards) **– 36 months**

5.1 Open Source Software Development

Indicate whether this IC Activity will develop or incorporate open source software in the deliverables. All contributions of open source software for use in Industry Connections activities shall be accompanied by an approved IEEE Contributor License Agreement (CLA) appropriate for the open source license under which the Work Product will be made available. CLAs, once accepted, are irrevocable. Industry Connections Activities shall comply with the IEEE SA open source policies and procedures and use the IEEE SA open source platform for development of open source software. Information on IEEE SA Open can be found at https://saopen.ieee.org/.

Will the activity develop or incorporate open source software (either normatively or informatively) in the deliverables?: No

6. Funding Requirements

Outline any contracted services or other expenses that are currently anticipated, beyond the basic support services provided to all IC activities. Indicate how those funds are expected to be obtained (e.g., through participant fees, sponsorships, government or other grants, etc.). Activities needing substantial funding may require additional reviews and approvals beyond ICCom.

Specify funding requirements and sources, if any.

All participating members will be contributing their valuable time, effort, & resources as volunteers toward this effort. Therefore to ensure a diverse community of properly represented entities are participating, no participation fee will be charged. Should additional funds be required we will submit requests for additional reviews and approvals.

7. Management and Procedures

7.1 Activity Oversight Committee

Indicate whether an IEEE Standards Committee or Standards Development Working Group has agreed to oversee this activity and its procedures.

Has an IEEE Standards Committee or Standards Development Working Group agreed to oversee this activity?: No.

If yes, indicate the IEEE committee's name and its chair's contact information.

IEEE Committee Name: Committee Name
Chair's Name: Full Name
Chair's Email Address: who@where

Additional IEEE committee information, if any. Please indicate if you are including a letter of support from the IEEE Committee that will oversee this activity.

IEEE collects personal data on this form, which is made publicly available, to allow communication by materially interested parties and with Activity Oversight Committee and Activity officers who are responsible for IEEE work items.

7.2 Activity Management
If no Activity Oversight Committee has been identified in 7.1 above, indicate how this activity will manage itself on a day-to-day basis (e.g., executive committee, officers, etc).

Briefly outline activity management structure.

The Activity will be managed by an Executive Committee as described in the Activity's Policies and Procedures.

7.3 Procedures
Indicate what documented procedures will be used to guide the operations of this activity; either (a) modified baseline *Industry Connections Activity Policies and Procedures,* (b) Standards Committee policies and procedures accepted by the IEEE SA Standards

Board, or (c) Working Group policies and procedures accepted by the Working Group's Standards Committee. If option (a) is chosen, then ICCom review and approval of the P&P is required. If option (b) or (c) is chosen, then ICCom approval of the use of the P&P is required.

Specify the policies and procedures document to be used. Attach a copy of chosen policies and procedures.

Modified Baseline Industry Connections Activity and Policies and Procedures

8. Participants

8.1 Stakeholder Communities
Indicate the stakeholder communities (the types of companies or other entities, or the different groups of individuals) that are expected to be interested in this IC activity, and will be invited to participate.

Specify types of entities or groups of individuals.

- New Technology Companies - (AI, Blockchain, VR/AR, Sensors/IoTs, etc)
- Existing Technology Systems – (informed consent providers, EDI, ERPs etc)
- Sponsors of trials – Bio/Pharmaceutical companies, university research hospitals
- Sites (Hospitals)
- Investigators
- CROs (Contract Research Organizations)
- Regulatory
- Patient Advocacy
- Academic researchers in clinical studies

8.2 Expected Number of Participants

Indicate the approximate number of entities (if entity-based) or individuals (if individual-based) expected to be actively involved in this activity.

Number of entities or number of individuals.

50 entity participants

8.3 Initial Participants

Provide a number of the entities or individuals that will be participating from the outset. It is recommended there be at least three initial participants for an entity-based activity, or five initial participants (each with a different affiliation) for an individual-based activity.

Use the following table for an entity-based activity:

Entity	Primary Contact	Additional Representatives
Saavha	Mathew Rose	
Sharecare	Walter De Brouwer	
ICON plc	Isaac R. Rodriguez-Chavez	
Sanofi	Dany DeGraves	
Pfizer	Craig Lipset	
Accenture	Sri Bindiganavile	
Florene Healthcare	Andres Garcia	
Bristol Myers Squibb	Basker Gummadi	
Cognizant	Darpan Ahuja	
Consilx	Dr. Rajesh Jain	
Parexel	Kieran Connolly	
ERT	James Carrigan	
Embleema	Robert Chu	
FDA CDER	Elizabeth Kunkoski	
DiME	Jennifer Goldsack	
Acoer	Jim Nasr	
PRA	Dr. Greg Nicholai	
Novartis	Adama Ibrahim	
UCB Pharma	Shelly Barnes	
Walmart Pharmacy	Melissa Swoope	

Use the following table for an individual-based activity:

Individual		Employer	Affiliation
Name			

Appendix: Data Sources

1. Clinical Trials Market Size, Share & Trends Analysis Report By Phase (I/II/III/IV), By Study Design
   (Interventional, Expanded Access), By Indication (Oncology, Diabetes, Obesity), And Segment Forecasts, 2019 – 2026; Grandview Research, Feb 2019
   https://www.grandviewresearch.com/industry-analysis/global-clinical-trials-market
2. Patients Recruitment Forecast in Clinical Trials, Cognizant 20-20 Insights, August 2015
   https://www.cognizant.com/whitepapers/patients-recruitment-forecast-in-clinical-trialscodex1382.pdf

3. Bring Down The Cost Of Clinical Trials With Improved Site Selection; Clinical Leader, December 2013 https://www.clinicalleader.com/doc/bring-down-the-cost-of-clinical-trials-with-improvedsite-selection-0001
4. Effort to recruit more minorities for clinical trials becoming 'national priority'; HemOnc Today; June 2017 https://www.healio.com/hematology-oncology/practice-management/news/print/hemonctoday/%7B0763da89-b3d3-4074-beec-bbfe32d900d6%7D/effort-to-recruit-more-minorities-forclinical-trials-becoming-national-priority
5. Legal and Ethical Issues Associated with Patient Recruitment in Clinical Trials: The Case of Competitive Enrolment; Timothy Caulfield;
   https://pdfs.semanticscholar.org/a4b2/fe0c8c19fc65686c6c69475ebe3172ecff9b.pdf

8.4 Activity Supporter/Partner
Indicate whether an IEEE committee (including IEEE Societies and Technical Councils) has agreed to participate or support this activity. Support may include, but is not limited to, financial support, marketing support and other ways to help the Activity complete its deliverables.

Has an IEEE Committee agreed to support this activity?: Yes

If yes, indicate the IEEE committee's name and its chair's contact information.

IEEE Committee Name: Engineering in Medicine and Biology Society
Chair's Name: Carole Carey
Chair's Email Address: c.carey@ieee.org

Please indicate if you are including a letter of support from the IEEE Committee.