H831458 – Trials@Home

Center of Excellence – Remote Decentralised Clinical Trials

WP2 - TECH

# D2.3 – Technology scan

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## Document History

| **Version** | **Date** | **Description** |
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| V0.8 | 28 Aug 2020 | First Draft |
| V0.9 | 21 Sept 2020 | Comments from BBB subgroups |
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| VX.X | dd Mmm YYYY | Final Version |

## Publishable Summary

This task involves the performing of a broad technology scan, based on a systematic review framework (i.e. according to PRISMA guidelines[1] for systematic literature review), in scientific literature (e.g., PubMed, CINAHL, Google Scholar, etc.), app stores (e.g., Google Play, Apple store, etc.), internet search, registers (e.g., ClinicalTrials.gov, patent registers) and other public sources. The technology scan will include all patient-facing, data collection, and supporting software services, include broader overarching technologies such as central research platforms, that are likely to be required. These solutions are classified per trial building block (Figure 1) and screened based on (pre-defined) eligibility criteria.

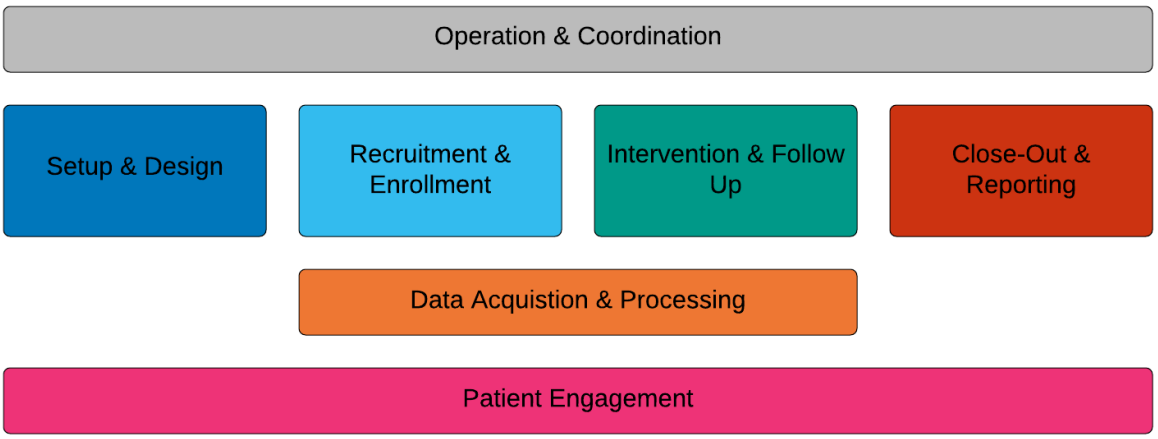


*Figure 1: Basic Building block overview*

To maximise the yield and efficiency of the search efforts, both 'snowballing' (reference tracking) and informal approaches ('asking around' and being alert to serendipitous discovery) will be used. Here we will leverage the results of the RADAR-AD literature and market review (see https://www.imi.europa.eu/projects-results/projectfactsheets/radar-cns). Both academic and industry partners will use their expert knowledge and experience to reach out to actors in the field, assess whether their technology is in principle suitable for RDCTs, even when not yet used and/or not yet validated for clinical research.

To streamline and focus these scanning efforts, a distinction will be made between "Core" technologies, i.e. technologies for RDCTs that are independent of the therapeutic area of a trial, and "Specific" technologies, that are dependent of the therapeutic area of the RDCT. In the beginning, most research will be concentrated on the search and assessment of the core technologies. After the choice for the therapeutic area for the WP3 pan-EU pilot has been made, the focus of the technology scan will be further narrowed to disease- and/or outcome- specific technologies.

A selection matrix for these technologies developed within this WP will involve (but is not limited to) the following questions:

1. What is the technology? How do we (Trials@Home) define it?
2. Is the technology now or in the future key to RDCT development?
3. Are there current suppliers or commercial entities with products or services in these technology areas? And if so, what is novel about the technology that would provide solutions to new areas of inquiry?
4. Is this technology immediately relevant, potentially relevant in the future, not directly relevant or modifying a current or future technology?
5. How does this RDCT technology address the capture of novel end points?

Given the rapid speed of technological innovation, new technologies that are not ready or available at the start of the WP3 pan-EU pilot will be further investigated and evaluated after month 12. The continued technology scan has a

synergetic relationship with WP1 BEST and other WPs: new technologies found in this wider technological scan may drive new best-practices, thus potentially influencing findings in WP1 BEST. In turn, new best-practices found in WP1 may drive the development of new technological solutions to support those practices, influencing the results of WP2 TECH. The same can be said about the relationships with WP4 EAGLE, where technology and legislation influence each other in a similar way. Results of the wider technology scan and interactions with other WPs will be included in the final recommendations.

Technology focus areas:

- Using cloud technologies in RDCTs
- Technologies for data retention and access by patient post study
- Technologies for (remoted) patient identification, screening and randomization
- Use of blockchain technologies in RDCTs. (IMI project on Blockchain Enabled Healthcare)

## Methods[3]

Scanning of software, hardware and technologies is primarily oriented towards the basic building blocks (provided as part of the project proposal. However, for these basic building blocks to provide guidance in the scanning of technologies suitable for remote decentralized clinical trials (RDCTs), first a definition needed to be provided for each basic building block, as well as definitions for activities that take place within each basic building block.

After the basic building blocks and their activities were defined, scanning for technologies suitable for RDCTs was performed using a variety of methods, such as the request for information and online scanning for technology.

### Basic building block definition

Definition of the basic building blocks proceeded in three stages. First, a workgroup dedicated to this task created a first draft of the basic building block and activity model and their definitions. This workgroup comprised members from all work packages of the Trials@Home project, to make use of a wide range of expertise and perspectives. During a series of weekly calls, a definition for each basic building block was constructed and discussed, as well as activities that would take place within respective basic building blocks, and definitions for these activities.

Apart from a workgroup for the definition of the basic building blocks and activities therein, specialty workgroups focussing on a single basic building block were also established. Part of their tasks was to create visions for each basic building block on how activities therein could be performed in an RDCT fashion, and what kind of systems would be able to support these activities. Furthermore, they were responsible for reviewing the results of the basic building block and activity definitions, the scanning activity, and the quality criteria established for the assessment of technologies in the respective basic building block.

When first draft was specified, members of the basic building block specialty groups were asked to review the first draft of the basic building blocks. After reaching consensus on the basic building block and activity definitions in WP TECH, the workgroup dedicated to the definition of basic building blocks then proceeded to define what types of computer systems or technologies were relevant for each activity to support for query formulation for the scanning process.

Table 1 presents an overview of the final basic building blocks, as well as the activities therein. Moreover, a visual grouping of activities per basic building block can be found in Figure 2

*Table 1: Basic building blocks and activities*

| BASIC BUILDING BLOCK | ACTIVITIES IN BASIC BUILDING BLOCK |
|---|---|
| **SET UP & DESIGN** | Protocol development (includes , Trials registration, Creation of informed consent form); Regulatory and ethics approvals (includes EMA, country, local, and ethics committee submissions, query responses, and approvals); Study branding (includes, Create participant and investigational site education strategy using brand-specific materials); Operational feasibility assessment and selection (includes country and investigational site selection criteria, site feasibility assessments, and recruitment strategies); , Operational setup (includes all services and activities required to conduct the study such as CRO selection, home visit materials, technologies for telemedicine visits, IMP delivery, and study payments); Site start-up, (includes contracting, clinical trial budget, connectivity, rater training, site master file, and SIV);Technology setup (selection of devices and apps, provisioning and setup, access to key systems); and IMP (randomization, delivery and return, drug accountability). |
| **RECRUITMENT & ENROLMENT** | Participant outreach, Pre-screening, Participant education, Obtaining informed consent, Screening, Randomization, IMP Supply, Patient technology enablement. |
| **INTERVENTION AND FOLLOW UP** | Self-intervention and self-monitoring, Home Health visits, Telemedicine visits, Clinic visits, IMP supply & re-supply, IMP adherence monitoring |
| **CLOSE OUT AND REPORTING** | Decommissioning, Archiving, Producing study report, Publishing of clinical study results, Publishing of operational study results, Scientific dissemination of study results |
| **DATA ACQUISITION AND PROCESSING** | Management of study-generated data, Gathering and management of real-life data, Clinical data repository management, eCRF and system query design, Data reconciliation and Query management, Database lock, Data transformation & standardization, Data analysis |
| **OPERATION AND COORDINATION** | Clinical monitoring (CRA oversight, Clinician oversight, Medical Monitor oversight); Performance monitoring (dashboards for monitoring visits and issues and actions, study recruitment, data entry timeliness and participant visit assessment compliance); Inspection facilitation (audit prep); System approval facilitation (key systems |

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| | access, completion of training); Telemedicine visit management (audio-visual connectivity); Regulatory management (GDMS); Vendor management (vendor oversight plans); Safety management (SAE reporting, data review plans); Documentation management (trial master file, source document locator); Home Health Visit management; Operational analytics; Manage protocol and GCP Deviations (dashboard, monthly review, PD alert letters); Study oversight (qualification of current members across functional lines, recruitment timelines, operational oversight tools, medical oversight). |
| **PATIENT ENGAGEMENT** | Create patient engagement plan, Social listening and patient landscape analysis, Patient advocacy group mapping, Provide updates to patients throughout the trial, Provide patient recruitment and retention incentives, Patient concierge service or travel reimbursement, Introducing behavioural incentives, Provide patient satisfaction surveys, Consult participant and/or caregiver advisory board, Patient-HCP interaction and communication, Provide direct patient messaging, Patient social community establishment |

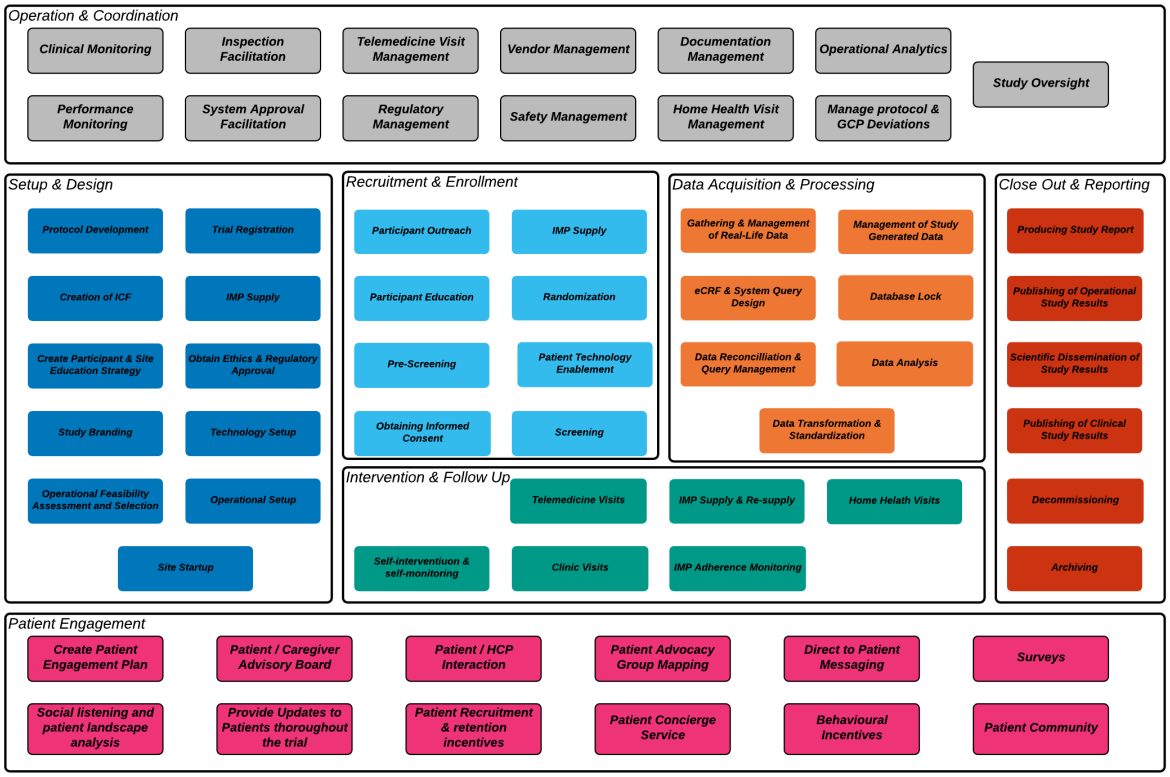


*Figure 2: Activities grouped per basic building block*

## Request for information

The first method to gather information on RDCT technologies currently available or in development is through a request for information (RFI). In this process, we asked project partners to submit (possible RDCT) technologies that they developed, and to inform other parties and vendors of our project and ask them to submit their technologies as well.

The RFI process comprised three phases, which were evaluated internally by the project's Executive Board and externally by IMI. In the first phase, the data entry form for the RFI was conceptualized, developed, and refined. A series of discussions led by the UMCU were held between involved members of WP2 on what information elements should be captured, and how RDCT-specific the technologies should be. Table 2 provides an overview of the types of information elements included in the form, and specific elements belonging to those types.

*Table 2: Information elements in the Request for information*

| INFORMATION TYPE | INFORMATION ELEMENTS |
|---|---|
| **SUBMITTER INFORMATION** | Email Address*, First Name*, Last Name*, Company*, Job Title*, Telephone. Address |
| **SOLUTION INFORMATION** | Name of solution*, Basic building blocks supported by the information*, Technology Readiness Level* (ranging from 1-9), Brief description of the solution, Link to information, Upload a file (pdf, gif, png, jpg only) |

Fields marked with a * were mandatory

In the second phase, project partners were invited to submit their technical solutions relevant to RDCTs using the RFI form. Submission of solutions was done by filling out a word document containing the information described in Table 2, and sending it to the project management office via email. The project management office then forwarded the email to the party responsible for evaluating the solution, i.e., the technology scanning team leader.

For the third phase, in which the RFI was disseminated online, a web submission form was created from the word document, and amended in order to provide more information on the Trials@Home project, as well was more information on the project's basic building block model. Furthermore, the form was amended again after the project's therapeutic area was decided on, at which point the request was extended to include the exploration and mapping of "specific diabetes-oriented technologies, that can be deployed in RDCT approaches". The final form was published on the Trials@Home website: https://trialsathome.com/request-for-information/. Again, submissions were sent to the project management office and forwarded from there to the technology scanning team leader

## Scanning

Apart from gathering submissions from vendors and partners, an active search for new technologies that support RDCTs was also undertaken. To this end, a workgroup was formed from public an EFPIA project members with an interest and experience in technology research.

The scanning task was divided into a sequence of subtasks, whereby each sequence was started for each basic building block. Table 3 contains this sequence of tasks in chronological order and provides a small description for each subtask.

*Table 3: Methodology for the scanning task*

| Subtask name | Description |
|---|---|
| **Draft methodology** | Creation of an initial generic technology scanning methodology, to be further specified individually for each basic building block where needed. This draft was then reviewed and improved on by management staff from WP TECH |
| **Methodology review** | Discussion with the workgroup for each basic building block on the draft methodology. Here, details are discussed and fixed for each activity in the basic building block with respect to the core technology search strategies, which sources can be searched in, what data should be |

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| | captured, and what technological focus points and novelties should initially be looked for. Infrastructural details are also discussed here, e.g., what programs to use to manage references and results. |
| **Infrastructural setup** | Based on the results from the methodology review, software is setup and user accounts are provided where needed. Documentation on how to use infrastructural resources is provided as well. Ideally, the infrastructure is uniform across all the scanning activities in the WP. |
| **Task assignment** | Final task assignments are provided to each workgroup participants for core technology scanning, together with documentation that clearly state how results should be collected as agreed upon in the finalized methodology. |
| **Scan review** | Review of the first results, adaptions of the search strategies and refinement of the queries and technology focus. |
| **Expert review** | Second review of the scan results by the basic building block expert groups. Further adaptions of the search strategies and refinement of the queries and technology focus |
| **Deliverable preparation** | Preparation of the methodology description for the core technology scan, as well as preliminary results. |

Using the process outlined in Table 3, scanning proceeded on a per-basic-building-block basis. Each member of the scanning team was assigned to scan for software in the respective basic building block, thereby focussing on a specific activity within this basic building block; per activity, at least 2 members were assigned for scanning.

## Results[3]

In this section we present the results of the RFI and scanning processes, whereby we do not indicate through which process a technology was found. Results are presented per basic building block, and for each result we present the solution name, the vendor or institution offering the technology, and which basic building block activities these solutions seem to support. A more complete report on the solutions including a short description will be presented in Appendix A.

### Setup & design

For setup & design, a total of 129 solutions were found that matched the search criteria (see Table 4). Most of the activities in this basic building block (see Table 1) were supported by at least one technology, except for the creation of ICF and Study branding, for which no specific technologies were found. Most technologies were found for protocol setup (30), as well as supply chain management (20). The type of feature most often mentioned in this basic building block is interactive response technology.

*Table 4: Technologies found for the basic building block "Setup & design"*

| Name | Vendor/Institution | Supported Activities |
|---|---|---|
| ADDIS | IMI GetReal project | Protocol Development (Data Collection, Data Management, Data Analysis) |
| AdvancedClinical | AdvancedGroup | Site Startup (Insourcing / Staffing) (Patient recruitment) |
| AG's Cumulocity IoT platform | Software AG | Technology Setup (IoT Platform) |
| AiCure | AiCure | Patient compliance |

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| ARENA | Rockwell Automation | Protocol Development (Data Management, Data Analysis) |
| Best Clinical Trial Management Software | Capterra | Protocol Development Software |
| CastorEDC | Castor | Protocol Development (Data Collection, Data Management) |
| CIRT2 | Cenduit | Interactive Response Technology (IRT), Randomization and Trial Supply Management, Supply Chain Management |
| Click Health´s Regulatory Approval Systems | | Ethics&Regulatory Approval |
| ClickUp | ClickUp | Technology Setup (Task Management) |
| Clinical Conductor CTMS | Bio-optronics | Protocol Development (Financial Management, Patient & Visit Management, Recruitment, Reporting, System Integration) |
| Clinical One RTSM | Oracle | Interactive Response Technology (IRT), Randomization and Trial Supply Management, Supply Chain Management |
| Clinical Trial Budget Costing Tool | NSW Public Health Organisations | Site Startup (budget planning) |
| Clinical6 | PRA Health Sciences | Site startup (Clinical Trial Management Platform. Recruitment, reporting, eConsent, patient engagement, EDC, workflow management) |
| ClinicalTrials.gov | U.S National Library of Medicine | Trial registration |
| ClinPhone | Parexel | Interactive Response Technology (IRT), Randomization and Trial Supply Management, Supply Chain Management |
| ClinSite | Phesi | Operational feasibility assessment & selection (Site Selection) |
| ComplyDocs | ComplyDocs (McDougall Scientific) | Site Startup (collection of essential documents) |
| CTTI Implementation Tools | Clinical Trials Transformation Initiative (CTTI) | Tools for nearly all activities |
| CTTI Prioritization Tool for Sponsors and Patient Groups | Clinical Trials Transformation Initiative (CTTI) | Operational feasibility assessment & Patient selection |
| DFNet | DFNet | Protocol development (EDC, coding, queries, CDISC, stats/biostats support) |
| Downloadable Templates and Tools for Clinical Research | Global Health Trials | Tools for nearly all activities |
| Dr. Explain | Dr. Explain | Technology Setup (Manual Creation) |
| DrugDev Spark | DrugDev | Operational setup, (Site Activation, Learning Management, Site Engagement, Document Exchange, Consent Creation, eConcent Delivery, Consent Tracking) |

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| DupCheck | IMI Project NEWMEDS | Operational feasibility assessment & selection (Patient recruitment). Site Start-up |
| eConsent | DatStat | Protocol Development / Site Startup (Contracting / permission for data access) |
| EDGE | University of Southampton | Protocol Development (Patient Management, Document management, Project Site workflows) |
| eTMF connect | Montrium | Site Startup (collection of essential documents) |
| EU Clinical Trials Register | European Medicines Agency | Trial registration |
| Eudra CT | EMA | Trial registration |
| FireCrest | ICON | Create participant and site education strategy (Training Site & Study Staff, Medical Animation, Patient Education - eConsent Viewer - Enhanced informed consent) |
| Firecrest | Icon | Ethics&Regulatory(ICF) |
| goBalto Activate | goBalto / Oracle | |
| Harvest | The Children's Hospital of Philadelphia (CHOP) | Protocol Development (Data Management, Data Analysis, Data Transformation, Clinical data repository management) |
| Hawthorne Effect | Hawthorne Effect | Operational setup (Home Health Visit management) |
| HOMA2 Calculator | University of Oxford - Diabetes Trials Unit | Protocol Development (Data Analysis) |
| IBM Watson Clinical Trial matching | IBM Watson | Operational feasibility assessment and selection (Patient recruitment) |
| iConnect | WCG Clinical | Operational feasibility assessment & selection (Patient Recruitment) |
| imarc | IMARC RESEARCH, INC. | Site Startup (training) |
| InSite | Custodix NV (IMI Project EHR4CR) | Operational feasibility assessment & selection (Patient Recruitment). Site Start-up |
| Interactive Selection tool | CTTI | Operational feasibility assessment and selection (Patient selection) |
| International Clinical Trials Registry Platform (ICTRP) | WHO | Trial registration |
| INVESTIGATORSPACE | Trifecta | Site startup, (Standardized Training (GCP), Protocol , specific Training.<br>Amendment Training<br>Therapeutic Area/Compound Specific Training<br>Rater Training<br>CRA/Monitor Training) |
| IRT - IXRS 3 | ALMAC | Interactive Response Technology (IRT), Randomization and Trial Supply Management, Supply Chain Management |
| iSpring | iSpringSolutions | Technology Setup (Training) |
| ISRCTN registry | BMC | Trial registration |
| Jinkō | Novadiscovery | Trial simulation |
| KCE_Trials_Budgeting_tool_V4.0 | KCE belgian Healthcare Knowledge Center | Site Startup (budget planning) |
| Maelstrom Research | The Research Institute of | Protocol development |

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| cataloguing toolkit | the McGill University Health Centre (RI MUHC), Montreal General Hospital | (Data Collection, Data Management, Data Analysis) |
| MAFEIP: Monitoring and Assessment Framework for the European Innovation Partnership on Active and Healthy Ageing | European Union | Protocol Development (Operational feasibility assessment & selection) |
| Marken Allegro | MARKEN a UPS Healthcare division subsidiary | interactive online scheduling tool |
| Marken FastTrack | MARKEN a UPS Healthcare division subsidiary | Shipment Tracking System |
| Marken Maestro | MARKEN a UPS Healthcare division subsidiary | Shipment Tracking System (online, cloud-based booking and tracking system) |
| Marken Sentry | MARKEN a UPS Healthcare division subsidiary | Shipment Tracking System (GPS technology for real-time, track and trace of drug shipments.) |
| Marken Solo | MARKEN a UPS Healthcare division subsidiary | Site-startup (state-of-the-art system to manage all information and inventory for clinical trials throughout the life cycle) |
| Marken Viseo | MARKEN a UPS Healthcare division subsidiary | Technology setup (allows patients and sites to track their home deliveries of clinical trial materials and the pickup of their biological specimens via their mobile device or personal computer.) |
| MasterControl Clinical Excellence | Master Control | Protocol Development (Data Collection, Data Management) |
| MasterControl ClinicalExcellence | MasterControl | Site Startup (collection of essential documents) |
| MasterControl eTMF Manager | MasterControl | Site Startup (collection of essential documents) |
| MasterControl eTMF Manager | MasterControl | Site Startup (collection of essential documents) |
| MAXQDA | | Protocol Development (Data Analysis) |
| MediXine Suite | MediXine | Operational setup (Telemedicine Visit Management) |
| MEIRxRS | MEIRxRS | Site Startup (Insourcing / Staffing) |
| NIHR Mental Health BRC online recruitment portal | NIHR | Operational feasibility assessment & selection (Patient Recruitment) |
| nrollmed - Online Patient Recruitment & Retention | nRollmed | Operational feasibility assessment & selection (Patient Recruitment and Site Selection) |
| NVivo | QSR International | Protocol Development (Data Import) |
| OpenBUGS | Started in MRC Biostatistics Unit, Cambridge, and developed jointly with the | Protocol Development (Data Analysis) |

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| | Imperial College School of Medicine at St Mary's, London | |
| OpenClinica | OpenClinica | Protocol Development (Data Collection, Data Management) |
| PragMagic tool | IMI GetReal project | Protocol Development (Operational feasibility assessment & selection, obtain ethics & regulatory approval, Study oversight) |
| Prancer RTSM | 4G Clinical | Interactive Response Technology (IRT), Randomization and Trial Supply Management, Supply Chain Management |
| Project Baseline Platform | Verily Life Sciences | Documentation management |
| PROSPERO | Centre for Reviews and Dissemination, University of York | Protocol Development (Key protocol features - Systematic review) |
| Protocol Software & Web Development | Protosoft | Protocol Development |
| Protocol Templates & Guidelines - Protocol Development | National Institute of Health | Protocol Development |
| PULSE | Endpoint Clinical | Interactive Response Technology (IRT), Randomization and Trial Supply Management, Supply Chain Management |
| qmsWrapper | qmsWrapper | Technology Setup (Quality Management) |
| Q-Pulse | Ideagen | Technology Setup (Quality Management) |
| QT9 Quality Management | QT9 | Quality Management Software |
| QuiteT Recruitment Intervention (QRI) | University of Bristol | Operational feasibility assessment & selection (Patient Recruitment) |
| R | R is an official part of the Free Software Foundation's GNU project | Protocol Development (Data Analysis) |
| RADAR-BASE | KCL, The Hyve | Technology Setup (Open-Source Platform) |
| Rave eConsent | Medidata | Ethics&Regulatory(ICF) |
| REDCap | Harvard University | Protocol Development (Data Collection) |
| RMH Clinical Trial Recruitment Predictor Tool | The Royal Melbourne Hospital | Operational feasibility assessment & Patient selection |
| RTSM & CUBE | Signant Health | Interactive Response Technology (IRT), Randomization and Trial Supply Management, Supply Chain Management |
| RTSM FLEX ADVANTAGE | ICON | Interactive Response Technology (IRT), Randomization and Trial Supply Management, Supply Chain Management |
| SAAM II | The Epsilon Group | Protocol Development (Data Analysis) |
| SAS | developed at North Carolina State University | Protocol Development (Data Management, Data Analysis) |
| Science37 | Science37 | Virtual trial management |
| SecureConsent | IQVIA company | Ethics&Regulatory(ICF) |
| Site Contracting | WCG | Data-Driven Negotiation |

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| | | Global Contract Templates<br>Contract Progress Monitoring |
| Snappii | Snappii Apps | Protocol Development (Data Collection, Data Management) |
| StarLink | Space Exploration Corporation (Space X) | Operational setup<br>(Telemedicine Visit management; Home Health Visit management) |
| Stata | Initially authored by William Gould & developed by Stata Corp. | Protocol Development (Data Management, Data Analysis) |
| Sure-Real tool | Collaboration between NICE and the MIT NEWDIGS program | Protocol Development (Operational Setup, Randomization, Data Collection, Data Management, Data analysis) |
| Suvoda IRT | Suvoda | Interactive Response Technology (IRT), Randomization and Trial Supply Management, Supply Chain Management |
| Talent Source | CROMSOURCE | Site Startup (Insourcing / Staffing) |
| Templates for informed consent forms | WHO | Ethics&Regulatory(ICF) |
| Trial initiation Process Map | Global Health Network | Site Startup |
| TrialHub | FindMeCure Ltd. | Feasibility, patient recruitment |
| TrialValue | RHIEOS-VENTURES Ltd. | Site Startup (budget planning) |
| Trident | BioClinica | Interactive Response Technology (IRT), Randomization and Trial Supply Management, Supply Chain Management |
| UKPDS Outcomes Model | University of Oxford - Diabetes Trials Unit | Protocol Development (Data Analysis) |
| UKPDS Risk Engine | University of Oxford - Diabetes Trials Unit | Protocol Development (Data Analysis) |
| VelocityEHS | EHS | Technology Setup (Quality Management) |
| WCG Site Feasibility Application | WCG Clinical | Operational feasibility assessment & selection (Site Selection) |

### Recruitment & Enrolment

A total of 17 systems were found that matched the search criteria (see Table 5). Most of the activities in this basic building block (see Table 1) were supported by at least one technology, except for patient technology enablement, which was never explicitly mentioned. Most technologies were found for IMP supply (7), as well as patient education (5). Interestingly, features like devices and wearables are most often mentioned in these kinds of technologies.

*Table 5: Technologies found for the basic building block "Recruitment & Enrolment"*

| Name | Vendor/Institution | Supported Activities |
|---|---|---|
| 4C Supply(TM) | 4G Clinical | IMP Supply |
| ActiGraph | ActiGraph | IMP Supply, Wearables/Devices |
| CENDUIT | IQVIA | Recruitment & Enrolment, eConsent, Education |
| Clinical6 | PRA Health Sciences | Recruitment/enrolment, engagement |
| Clinical Supplies | SignantHealth | IMP Supply, Wearables/Devices |
| CLINPAL | eClinicalHealth | Recruitement & Enrollement, Education |

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| CubixxCT | CubixxSolutions | IMP Supply, Refrigeration at home |
| Digital Trial Platform | Medable | Screening, Engagement, Education |
| Direct-to-Patient Services | World Courier | IMP Supply |
| EmpiraMed | EmpiraMed | Education, pre-screening |
| Equipment Sourcing, Rental, & Asset Management | MESM | IMP Supply, Wearables/Devices |
| FindMeCure | FindMeCure Ltd. | Education, Recruitment |
| iConnect | WCG Clinical | Participant Outreach |
| Mondosano | Mondosano GmbH | Recruitment |
| Prancer RTSM™ | 4G Clinical | Randomization |
| Slope | Slope | IMP Supply |
| SubjectWell | SubjectWell | Patient registries / databases |

### Intervention & Follow-up

We found 11 systems that matched the search criteria (see Table 6). All of the activities in this basic building block (see Table 1) were supported by at least one technology. Most technologies were found for clinical visits (4) and remote monitoring (3).

*Table 6: Technologies found for the basic building block "Intervention & Follow-up"*

| Name | Vendor/Institution | Supported Activities |
|---|---|---|
| AICURE | AICURE | Compliance checking; IMP adherence monitoring |
| Achievement | Evidation | Remote monitoring |
| Castor ePRO | Castor | ePRO |
| DIABEO System | SANOFI | Clinical data repository management, clinical visits |
| Impact | Validic | Remote monitoring; specific diabetes functionality |
| Kareo Telemedicine | Kareo | Clinical visits |
| Longboat | Longboat | Clinical data repository management, clinical visits |
| Medable | Medable | Data capture, virtual visit technology, remote monitoring |
| Medrio ePRO | Medrio | ePRO |
| Rave eCOA | Medidata | eCOA |
| Skiplino | Skiplino | Clinical visits |

### Close-out and reporting

We found 53 systems that matched the search criteria (see Table :7). All of the activities in this basic building block (see Table 1) were supported by at least one technology. Most technologies were found for the publishing of clinical study results (17) and operational study results (13).

*Table :7 Technologies found for the basic building block " Close-out and reporting"*

| Name | Vendor/Institution | Supported Activities |
|---|---|---|
| ARPHA | Pensoft | Scientific dissemination of study results - (scientific) writing tool, dissemination, and |

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| | | publication |
| Australian New Zealand Clinical Trials Registry | AU Gov & HRC, NCRIS | Publishing of clinical study results |
| Bibtex | Oren Patashnik | Scientific dissemination of study results - reference management tool |
| Brazilian Clinical Trials Registry | Oswaldo Cruz Foundation | Publishing of clinical study results |
| Cancer Trials Victoria | Cancer Council Victoria | Publishing of clinical study results |
| CHES | ESD | nearly every BBB |
| Chinese Clinical Trial Register (ChiCTR) | Ministry of Health of China | Publishing of clinical study results |
| Citavi | Swiss Academic Software | Scientific dissemination of study results - reference management tool |
| Clinical Trials Toolkit | NHS | Scientific dissemination of study results |
| clinicaltrials.gov | U.S. National Library of Medicine | Publishing of clinical study results |
| Docear | group of students, postdocs, and professors around the globe | Scientific dissemination of study results - reference management tool |
| eB4CAST | West Virginia University | Publishing of operational study results, Scientific dissemination of study results |
| EU Clinical Trials register | EU | Publishing of clinical study results |
| EudraCT | EMA | Publishing of clinical study results |
| EVAL | Forte Research | Publishing of operational study results |
| German Clinical Trials Register | Federal Ministry of Education and Research (BMBF) | Publishing of clinical study results |
| Google Docs | Google | Scientific dissemination of study results - (scientific) writing tool |
| Grammarly | Grammarly | Scientific dissemination of study results - plagiarism checker, grammar checker |
| Health Canada Clinical Trial Database | Government of Canada | Publishing of clinical study results |
| InDesign | Adobe | Scientific dissemination of study results - (scientific) writing tool, creating publications, papers, posters |
| International Clinical Trials Registry Platform (ICTRP) | WHO | Publishing of clinical study results |
| ISRCTN | WHO & ICMJE | Publishing of clinical study results |
| iThenticate Similarity Check | Turnitin LLC | Scientific dissemination of study results - plagiarism checker |
| JabRef | The JabRef team | Scientific dissemination of study results - reference management tool |
| LabKey | LabKey Corporation | Publishing of operational study results |
| LaTeX | The LaTeX Project | Scientific dissemination of study results - |

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|---|---|---|
| | | (scientific) writing tool |
| Libre Office | The Document Foundation | Scientific dissemination of study results - (scientific) writing tool |
| marvin | xclinical | Publishing of operational study results |
| Mendeley | Elsevier Inc. | Scientific dissemination of study results - reference management tool |
| MS Office | Microsoft | Scientific dissemination of study results - (scientific) writing tool |
| Netherlands Trial Register (NTR) | Dutch Cochrane Centre, | Publishing of clinical study results |
| ODM Data Analysis (?) | "Institute of Medical Informatics (IMI), University of Münster" | Publishing of operational study results |
| OpenOffice | Apache | Scientific dissemination of study results - (scientific) writing tool |
| Overleaf | Overleaf c/o Digital Science | Scientific dissemination of study results - (scientific) writing tool |
| Pagination | Pagination.com | Publishing of operational study results |
| PharmNet.Bund Clinical Trials | German ministry of Health | Publishing of clinical study results |
| PUBSTRAT | Anju Life Sciences Software | Publishing of operational study results, Scientific dissemination of study results |
| Radar-Base | KCL | Publishing of operational study results |
| Recording and reporting clinical trial results | EUPATI | Scientific dissemination of study results |
| REF-N-WRITE | Astute Digital Solutions Ltd | Scientific dissemination of study results - (scientific) writing tool |
| Research Manager | My Research Manager | Publishing of operational study results |
| Rethinking Clinical trials | NIH | Publishing of operational study results, Scientific dissemination of study results |
| Scribbar Plagiarism Checker | Scribbar | Scientific dissemination of study results - plagiarism checker |
| Scrivener | Literature & Latte | Scientific dissemination of study results - (scientific) writing tool |
| SDMX | SDMX | Publishing of operational study results, Scientific dissemination of study results |
| Smartsheet | Smartsheet | Publishing of operational study results |
| Swiss National Clinical Trials Portal (SNCTP) | Swiss Federal Office of Public Health | Publishing of clinical study results |
| System for Active Knowledge Management (SAKM) | Polytechnic University of Catalonia | Publishing of operational study results, Scientific dissemination of study results |
| Typeset | PUBGENIUS, INC. | Scientific dissemination of study results - (scientific) writing tool |
| Ulysses | ulysses | Scientific dissemination of study results - (scientific) writing tool |
| Virtual Trials Archive | Collaborative | Publishing of clinical study results |
| Yale University Open Data Access | Yale University | Publishing of clinical study results |

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| (YODA) | | |
| Zotero | Corporation for Digital Scholarship | Scientific dissemination of study results - reference management tool |

### Patient engagement

We found 49 systems that matched the search criteria (see Table 8). All of the activities in this basic building block (see Table 1) were supported by at least one technology. Most technologies were found for providing patient satisfaction surveys (16) direct patient messaging (13).

*Table 8: Technologies found for the basic building block "Patient Engagement"*

| Name | Vendor/Institution | Supported Activities |
|---|---|---|
| Clinical Communication Center | within3 | Patient Engagement |
| ConvergeHEALTH Patient Connect | Deloitte | Patient engagement, provide direct patient messaging |
| Direct Messaging | Secure Exchange Solutions | Provide direct patient messaging (share messages / information / content with one or more patients) |
| DrChrono OnPatient Portal | DrChrono | Provide direct patient messaging |
| Google Forms | Google LLC | Provide patient satisfaction surveys |
| Habitu | Habitu | Patient engagement |
| Healthblocks | Healthblocks | Patient engagement |
| Hivebrite | Hivebrite | event management; data management; communications; collaborations& opportunities |
| iPlato | iPlato | Provide direct patient messaging |
| MD Message | MDTech | Provide direct patient messaging |
| Medeo Virtual Care | MedeoHealth | Provide direct patient messaging |
| Medixine | Medixine | Provide patient satisfaction surveys, Provide direct patient messaging |
| Medixine Suite | Medixine | Patient Engagement, direct patient messaging, Patient-HCP-interaction |
| MTBC CareConnector | MTBC | Patient Engagement, Patient-HCP interaction and communication |
| myMedidata | Medidata | |
| NelumBox | Tec4Med Lifescience GmbH | Patient engagement |
| Nfield Online | NIPO | Provide patient satisfaction surveys |
| ngSurvey | Data Illusion Zumbrunn | Provide patient satisfaction surveys |
| NowGP | Now Healthcare Group Ltd | Patient-HCP interaction and communication |
| OptimizeRx Platform | OptimizeRx Corporation | Provide direct patient messaging (share messages / information / content with one or more patients) |
| Patient Care | RippleCare | Patient Engagement, direct patient messaging, Patient-HCP-interaction |
| Patient Engagement | admedicum Business for Patients | Patient engagement |
| Patientjourney app | Interactive Studios | Patient Engagement, Patient Direct Messaging |
| PatienTrials | PatienTrials Inc | Patient engagement |
| Popit platform to increase adherence and track medication use | Popit | Patient engagement |
| ProofPilot | ProofPilot | recruitment |
| Q1.6 | Q1.6 | Patient engagement |
| Qualtrics CoreXM | Qualtrics | Provide patient satisfaction surveys |

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|---|---|---|
| Rauno Saarnio | SE Innovations Oy | Patient engagement |
| Sharedoc | Agnitio | Provide direct patient messaging (share messages / information / content with one or more patients) |
| SimpleVisit | SimpleVisit | Patient Engagement, Patient-HCP interaction and communication |
| SmartSurvey | SmartSurvey | Provide patient satisfaction surveys |
| SmartXP | UbiCare | Provide direct patient messaging (share messages / information / content with one or more patients) |
| SoGoSurvey | SoGoSurvey | Provide patient satisfaction surveys |
| Solo by InTouch | InTouch Health | Provide direct patient messaging |
| SurveyAnyplace | SurveyAnyplace | Provide patient satisfaction surveys |
| SurveyGizmo | SurveyGizmo | Provide patient satisfaction surveys |
| SurveyLab | SurveyLab | Provide patient satisfaction surveys |
| SurveyLegend | SurveyLegend AB | Provide patient satisfaction surveys |
| SurveyMethods | Methods Groups LLC | Provide patient satisfaction surveys |
| SurveyMonkey | SurveyMonkey | Provide patient satisfaction surveys |
| SurveySparrow | SurveySparrow Inc. | Provide patient satisfaction surveys |
| TriNetX Live | TriNetX | patient recruitment |
| Typeform | Typeform | Provide patient satisfaction surveys |
| updox Engagement | updox | Provide direct patient messaging (share messages / information / content with one or more patients) |
| VirTrial | VirTrial | Provide direct patient messaging |
| WCG Patient Engagement | WCG clinical | Enhancing site resources and capabilities, connecting patients with trials; Improving study data quality |
| Within3 | Within3 | online advisory board; online steering committee; Publication Developement center; Speaker communication center;Clinical communication center; Custom collaboration solution |
| ZohoSurvey | Zoho Corporation Pvt. Ltd. | Provide patient satisfaction surveys |

### Operations & Coordination

We found 14 systems that matched the search criteria(see Table 9). A substantial number of the activities in this basic building block (see Table 1) were supported by at least one technology, except for the monitoring and various clinical and home health visit management activities, which were not explicitly mentioned but are expected to be part of the technologies that actually track and perform these activities. Most technologies were found safety data management (6) and for study oversight (4).

*Table 9: Technologies found for the basic building block "Operation & Coordination"*

| Name | Vendor/Institution | Supported Activities |
|---|---|---|
| Business Intelligence platform | Bioclinica | operational oversight; |
| ClinDAP | thought sphere | Study oversight, operational analytics, (Also, possible end-to-end clinical trial processes, from site activation to study closeout) |
| Clinical Conductor CTMS | Bio-optronics | Safety data management |
| Continuouscare for Health | Continuouscare | Study Oversight |
| Data Quality Monitoring | Signant Health | Safety data management |
| eQgest | eQgest | Safety data management |

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|---|---|---|
| Longboat integrated platform | Longboat | Study Oversight (real-time) |
| OpenClinica | OpenClinica | Safety data management |
| Rave RCM | Medidata Solutions | Inspection facilitation |
| Saama clinical analytics | Saama | Operational insights; clinical insights; (also RBM) |
| Signalpath | Signalpath | Study Oversight |
| SurveyCTO | SurveyCTO | Safety data management |
| Veeva Vault Clinical Operations Suite | Veeva | Study Oversight; Operational Analytics; Protcocol deviations; (Also, possible end-to-end clinical trial processes, from site activation to study closeout) |
| VirTrial | VirTrial | Safety data management |

### Data collection and processing

We found 69 systems that matched the search criteria (see Table 10). Most of the activities in this basic building block (see Table 1) were supported by at least one technology, except for Data reconciliation & Query management and Database lock activities, which were not explicitly mentioned. Most technologies were found were Clinical data repository management (24) and for Management of study-generated data (20).

*Table 10: Technologies found for the basic building block "Data collection & processing"*

| Name | Vendor/Institution | Supported Activities |
|---|---|---|
| CliniPro | Numedics | Clinical data repository management |
| Accu-Chek Connect | Roche Diabetes Care | Clinical data repository management |
| Castor CDMS | Castor | Clinical data repository management |
| Clinical Data Management | Clinipace | Clinical data repository management |
| Clinical Trial Management | Smartsheet | Clinical data repository management |
| DiabetEASE | DiabetEASE | Clinical data repository management |
| Diabetes - Diario de glucosa | Klimaszewski Szymon | Clinical data repository management |
| Diabetes Partner PC | Numedics | Clinical data repository management |
| d-Nav® Insulin Guidance Service | Hygieia | Clinical data repository management |
| Esysta | Emperra | Clinical data repository management |
| Full scope Medical Device CRO | Qserve | Clinical data repository management |
| Lifebringer | Lifebringer | Clinical data repository management |
| mySugr - App Diario de Diabetes | mysugr | Clinical data repository management |
| Nightscout | Open Source | Clinical data repository management |
| Research Manager | Research Manager | Clinical data repository management |
| SiDiary | SiDiary | Clinical data repository management |
| SMART-TIRAL | SMART-TRIAL | Clinical data repository management |
| SocialDiabetes. Toma el control de tu diabetes | Social Diabetes | Clinical data repository management |
| Viedoc Clinic | Viedoc | Clinical data repository management |
| Longboat | Longboat | Clinical data repository management, clinical visits |

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|---|---|---|
| glooko+diasend | Glooko | Clinical data repository management, Management of study-generated data |
| Insights | encapsia | Clinical data repository management, Management of study-generated data |
| Acuity Analytics | Anju life sciences software | Data Analysis |
| Atlas | OHDSI | Data Analysis |
| Biostatistics Services | Scientific toolbox Consulting | Data Analysis |
| Dexcom CLARITY software | Dexcom | Data Analysis |
| JMP ® Clinical | SAS Institute Inc. | Data Analysis |
| MaxisIT® | Maxist | Data Analysis |
| MyStar Connect® | Sanofi diabetes | Data Analysis |
| MapForce | ALTOVA | data integration |
| AdClin Clinical Study Standardization Solution™ | AdClin | Data standardization |
| Oracle DMW | Oracle | Data standardization |
| CONFORM™ | Edetek | Data transformation and standardization |
| Data Programming Services | Scientific toolbox Consulting | Data transformation and standardization |
| MaxisIT® | Maxist | Data transformation and standardization |
| elluminate® | eClinical Solutions | Data transformation and standardization, Data analysis |
| eCRF design guide | OpenClinica | eCRF and system query design |
| ShareCRF | ShareCRF | eCRF and system query design |
| Viedoc Designer | Viedoc | eCRF and system query design |
| Marvin | XClinical | ecRF and system query design, Clinical data repository management |
| Studymate | raffeiner | ecRF and system query design, Clinical data repository management |
| Clinical Research Data Warehouse | center for research informatics | Gathering RealWorldData |
| Diabetes collaborative registry | NCDR | Gathering RealWorldData |
| PatientsLikeMe | Patients Like Me | Gathering RealWorldData |
| RealWorld Data Service | Parexel | Gathering RealWorldData |
| RealWorldDataAndInsights | IQVIA | Gathering RealWorldData |
| Studiomed+ | studio.201 software GmbH | Gathering RealWorldData |
| OpenClinica3 | OpenClinica | Management of data |
| trialmaster | anju | Management of data |
| Talend DataFabric | Talend | Management of data, data integration |
| Anju Big Data Platform | Anju Software | Management of study-generated data |
| Artem Andrianov | Cyntegrity Germany GmbH | Management of study-generated data |
| Clinical | Oracle | Management of study-generated data |

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|---|---|---|
| DM | encapsia | Management of study-generated data |
| EDC | encapsia | Management of study-generated data |
| EDC | OpenClinica | Management of study-generated data |
| Electronic Data Capture System | Castor | Management of study-generated data |
| FeetMe Evaluation | FeetMe | Management of study-generated data |
| Medidata Rave Clinical Cloud | Dassault Systems | Management of study-generated data |
| Medisanté ELIOT a unique direct to cloud medical IoT platform | Medisanté | Management of study-generated data |
| Medixine Suite | Medixine Oy | Management of study-generated data |
| myHeartSentinel | Sentinhealth SAS | Management of study-generated data |
| Pryv.io | PRYV SA | Management of study-generated data |
| RealWorld4Clinic | Profil Institute for metabolic research | Management of study-generated data |
| Testing 3 | DW Cre8tive | Management of study-generated data |
| Viedoc Admin | Viedoc | Management of study-generated data |
| Zana | Zana Technologies GmbH | Management of study-generated data |
| ThirdPartyData | encapsia | Management of study-generated data; Management of Real World Data |
| PCORnet DataDriven | PCORnet | RealWorldData |

## Discussion[3]

In this document we presented the results of our search for software systems that support activities in (remote decentralized) clinical trials. As a methodological guideline, we used a partitioning of clinical trial processes in what we call basic building blocks, whereby each basic building block contains several related activities. Using this partitioning, we present the results per basic building block, to indicate for which activities ample systems exist, and for which activities less systems are available.

One striking result is the variety of available systems and tasks and the difference between these basic building blocks Whereas for most basic building blocks, a multitude of systems were available, intervention and follow-up, as well as operations and coordination, distinctly lacked the availability of systems that supported electronic handling. Of course, this information was derived from the descriptions of the systems found online, and system demos might prove that certain activities are indeed present.

## Conclusion[3]

The breadth of systems and solutions offered across the BBBs provides opportunity to ensure end-to-end coverage of every aspect of clinical trial, clinically and operationally. From Figure 2, which summarizes the remits of the BBBs, the end-to-end technology requirements need to span the tasks of all BBBs, whilst minimizing overlap and potential duplication. Independent Medical Quality Assurance (MQA) shall utilize systems and technology for ongoing assessment of protocol and operational compliance, to ensure regulatory compliance and inspection readiness.

## Repository for primary data[3]

3: These are only suggested headings