CRISI

Proposal and Implementation Guide

Revision History

Date	Version	Description	Author
Sep 5, 2024	0.1	Initial Outline	Jay Smith
Sep 20, 2024	0.2	Added Study fields	Jay Smith

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1 Abstract

The Clinical Research Interoperability Standards Initiative (CRISI) proposes a standardized framework to facilitate seamless management and operational metadata and, in the future, document exchange, across clinical research systems. This proposal addresses the current inefficiencies in interoperability between Electronic Data Capture (EDC), Clinical Trial Management Systems (CTMS), electronic Trial Master File (eTMF), Institutional Review Boards (IRB/EC), IXRS, Site Portals/eISF, CROs, and investigative sites. CRISI aims to reduce study initiation times, eliminate redundant data entry, and allow for flexible software application choices by standardizing operational data elements and leveraging FHIR as the foundational standard.

2 Background and Rationale

2.1 Problem Statement

When it comes to management and operational clinical trial metadata, the current landscape of clinical research is marred by significant inefficiencies due to the lack of standardized interoperability between core clinical research systems. Custom API integrations are often required when initiating new studies, leading to increased time and costs. Documents and evidence are most often sent without metadata or identification, leaving multiple parties responsible to re-classify and re-verify information. This lack of standardization also results in redundant data entry, error-prone document handling, and limited flexibility in software application choices.

2.2 Need for the Standard

CRISI addresses the urgent need for a standardized approach that enables efficient and secure data exchange across clinical research systems. By establishing a common framework based on FHIR, CRISI will streamline operations, reduce redundancy, and enhance flexibility in system and application selection. This initiative is crucial for advancing the efficiency of clinical trials and ensuring that data management practices align with evolving industry and regulatory standards.

3 Objectives

3.1 Scope

The CRISI standard focuses on operational and management data exchanged between core clinical research systems, including EDC, CTMS, eTMF, IRB/EC, IXRS, Site Portals, CROs, and investigative sites. The standard will cover key data elements related to studies, sites, investigators, participants, and documents. It does not address clinical data directly related to patient outcomes or other clinical trial results, as these are currently handled with standards such as ODM.

3.2 Goals

- Standardize Management and Operational Metadata Elements: Define and implement a set of standard data elements for study, site, and participant management.
- Improve Interoperability: Facilitate seamless data exchange across diverse clinical research systems using FHIR.
- Reduce Redundancy: Eliminate redundant data entry and document uploads by standardizing data sharing protocols.
- Enhance Flexibility: Enable study sponsors and sites to use their preferred software applications while ensuring interoperability.
- Accelerate Study Initiation: Reduce the time required to start new studies by streamlining data sharing processes.
- Future: Allow Sites, CROs, Sponsors, and Vendors to easily exchange document content required during study startup and trial execution.

4 Technical Specifications

4.1 Description

The Clinical Research Interoperability Standards Initiative (CRISI) aims to standardize the exchange of operational and management data across clinical research systems by leveraging FHIR (Fast Healthcare Interoperability Resources). CRISI focuses on the core entities and their respective data points that are critical for the smooth operation and management of clinical trials. These entities include studies, sites, contacts, participants, and potentially documents. Each entity is associated with specific FHIR resources and is modeled to ensure comprehensive data capture, interoperability, and future scalability. Key components include:

- Study Object (ResearchStudy): Captures essential metadata and operational aspects of clinical trials.
- Site Object (Location): Models study sites, including physical and organizational data.
- Contact Object (Practitioner and PractitionerRole): Represents individual professionals and their roles within studies.
- Participant Object (ResearchSubject): Manages participant data, including enrollment and status.
- (FUTURE) Trial Document Object (DocumentReference): Standardizes the management and exchange of clinical trial documents.

4.1.1 Study Object (ResearchStudy)

Purpose: Represents a clinical trial or research study, capturing all necessary metadata.

Key Data Points:

- identifier: Unique identifiers for the study. Each identifier is an instance of the Identifier data type, which includes the following key elements:
    - use: Defines the purpose of the identifier (e.g., official, temporary, secondary).
    - system: Specifies the namespace or system that issued the identifier (e.g., ClinicalTrials.gov or an internal system URL).
    - value: The actual unique identifier assigned to the study.
    - assigner: The entity or organization that assigned the identifier.
    - type: A code representing the type of identifier (e.g., protocol number, registry number).
- title: Title of the study.
- description: A brief description of the study's objectives and scope.

- status: Current status of the study (e.g., active, completed, terminated).
    - planned:
    - in-review: The study is under review, pending approval or disapproval.
    - approved: The study is approved but has not yet started.
    - disapproved: The study has been disapproved.
    - protocol-final
    - feasibility
    - start-up
    - recruiting
    - postponed
    - active: The study is currently ongoing and recruiting or treating patients.
    - on-hold:
    - randomizing
    - enrolling
    - maintenance
    - closeout
    - administratively-completed: The study has been stopped for administrative reasons.
    - closed-to-accrual: The study is closed to new participant enrollment.
    - closed-to-accrual-and-intervention: Closed to new enrollment and interventions are no longer being applied to participants.
    - completed: The study has ended normally, and all participants have completed their interventions.
    - withdrawn: The study was withdrawn before starting.
- protocol: Reference to the study's protocol, including detailed descriptions of the study's phases, interventions, therapeutic area, indication, study design, and eligibility criteria.
    - Primary Purpose Type
    - Study Design

    - Therapeutic Area
    - Condition: Indication using ICD-11, ICD-10, or SNOMED
    - Keyword
    - Region
    - Eligibility Criteria: Provides the eligibility criteria for the trial.
    - Phase: The phase of the clinical trial (e.g., Phase I, II, III, IV).
- site: References to sites involved in the study, using the Location resource.
- principalInvestigator: Reference to the Practitioner who is the primary investigator for the study.
- regulatoryApprovals: Extension that tracks the Country Regulatory approval dates for the trial.
- ethicsApprovals: Extension that tracks the Country Ethics approval dates for the trial.
- siteIRBApproval: Extension that tracks the IRB Ethics approval dates for each site.
- milestones: Tracks Milestones that occur during the trial, including their name, status, date, and description.
- subjectVisitInfo: Provides subject visit information at the study level, including subject ID, visit name, visit date, and visit status.
- enrollmentDetail: Provides subject enrollment information at the study level, including subject ID, visit name, visit date, and visit status.
- protocolDeviations: Provides protocol deviations at the study level, including the subject ID, description, date, and status.
- relatedArtifacts: Links to related documents such as informed consent forms, IRB approvals, and study amendments.

4.1.1.1 Study Object (ResearchStudy) JSON Example


```
{
  "resourceType": "ResearchStudy",
  "id": "study-001",
  "identifier": [
    {
      "use": "official",
      "system": "https://clinicaltrials.gov",
      "value": "NCT01234567",
      "type": {
        "coding": [
          {
```

```
            "system": "http://terminology.hl7.org/CodeSystem/v2-0203",
            "code": "CT",
            "display": "Clinical Trial Number"
          }
        ]
      },
      "assigner": {
        "display": "ClinicalTrials.gov"
      }
    }
  ],
  "title": "A Phase III Randomized Study of Drug Y",
  "status": "active",
  "description": "This study aims to evaluate the efficacy and safety of Drug Y in treating
hypertension.",
  "primaryPurposeType": {
    "coding": [
      {
        "system": "http://terminology.hl7.org/CodeSystem/research-study-primary-purpose",
        "code": "treatment",
        "display": "Treatment"
      }
    ]
  },
  "protocol": [
    {
      "reference": "PlanDefinition/protocol-001"
    }
  ],
  "studyDesign": {
    "coding": [
      {
        "system": "http://terminology.hl7.org/CodeSystem/study-design",
        "code": "randomized",
        "display": "Randomized"
      },
      {
        "system": "http://terminology.hl7.org/CodeSystem/study-design",
        "code": "double-blind",
        "display": "Double-Blind"
      }
    ]
  },
  "condition": [
    {
      "coding": [
        {
          "system": "http://snomed.info/sct",
          "code": "123456",
          "display": "Hypertension"
        },
        {
          "system": "http://hl7.org/fhir/sid/icd-10",
          "code": "I10",
          "display": "Essential (primary) hypertension"
        },
        {
          "system": " http://id.who.int/icd/release/11/mms",
          "code": "BA00",
          "display": "Essential hypertension"
        }
      ]
    }
  ],
  "keyword": [
    {
```

```
      "text": "Hypertension"
    },
    {
      "text": "Phase III"
    }
  ],
  "therapeuticArea": {
    "coding": [
      {
        "system": "http://snomed.info/sct",
        "code": "C0011847",
        "display": "Cardiology"
      }
    ]
  }
  "region": [
    {
      "coding": [
        {
          "system": "http://iso.org/iso-3166",
          "code": "US",
          "display": "United States"
        }
      ]
    }
  ],
  "phase": {
    "coding": [
      {
        "system": "http://terminology.hl7.org/CodeSystem/research-study-phase",
        "code": "phase-3",
        "display": "Phase 3"
      }
    ]
  },
  "eligibilityCriteria": [
    {
      "type": "inclusion",
      "description": "Subjects with hypertension",
      "status": "met"
    },
    {
      "type": "exclusion",
      "description": "Subjects with diabetes",
      "status": "not met"
    }
  ],
  "site": [
    {
      "reference": "Location/site-001",
      "display": "Clinical Research Facility A"
    },
    {
      "reference": "Location/site-002",
      "display": "Clinical Research Facility B"
    }
  ],
  "principalInvestigator": {
    "reference": "Practitioner/practitioner-001"
  },
  "associatedParty": [
    {
      "name": "Study Sponsor ABC",
      "role": {
        "coding": [
          {
```

```
            "system": "http://terminology.hl7.org/CodeSystem/role-type",
            "code": "sponsor",
            "display": "Sponsor"
          }
        ]
      },
      "period": {
        "start": "2022-01-01",
        "end": "2024-12-31"
      },
      "party": {
        "reference": "Organization/org-001",
        "display": "Sponsor Organization"
      }
    }
  ],
  "progressStatus": [
    {
      "state": {
        "coding": [
          {
            "system": "http://terminology.hl7.org/CodeSystem/research-study-status",
            "code": "active",
            "display": "Active"
          }
        ]
      },
      "actual": true,
      "period": {
        "start": "2022-05-01",
        "end": "2024-05-01"
      }
    }
  ],
  "milestones": [
    {
      "id": "milestone-001",
      "name": "First Patient Enrolled",
      "status": "complete",
      "dateTime": "2023-08-01T00:00:00Z",
      "description": "First patient enrolled in the study."
    },
    {
      "id": "milestone-002",
      "name": "Last Patient Visit",
      "status": "draft",
      "dateTime": "2024-06-30T00:00:00Z"
    }
  ],
  "recruitment": {
    "targetNumber": 200,
    "actualNumber": 180,
    "eligibility": {
      "reference": "Group/group-001",
      "display": "Inclusion/Exclusion Criteria"
    },
    "actualGroup": [
      {
        "reference": "Group/group-002",
        "display": "Control Group"
      }
    ]
  },
  "enrollmentDetail": {
    "targetNumber": 100,
    "actualNumber": 2,
```

```
    "subjectStatusHistory": [
      {
        "subjectId": "participant-001",
        "status": "enrolled",
        "date": "2023-06-01"
      },
      {
        "subjectId": "participant-002",
        "status": "randomized",
        "date": "2023-06-15"
      }
    ]
  },
  "subjectVisitInfo": {
    "screenedSubjects": 2,
    "visitDates": [
      {
        "subjectId": "participant-001",
        "visitName": "screening",
        "visitDate": "2023-07-10",
        "visitStatus": "completed"
      },
      {
        "subjectId": "participant-002",
        "visitName": "screening",
        "visitDate": "2023-07-15",
        "visitStatus": "completed"
      }
    ]
  },
  "protocolDeviations": [
    {
      "subjectId": "participant-001",
      "description": "Missed visit",
      "date": "2023-08-01",
      "status": "resolved"
    }
  ].
  "objective": [
    {
      "name": "Primary Endpoint",
      "type": {
        "coding": [
          {
            "system": "http://terminology.hl7.org/CodeSystem/research-study-objective-type",
            "code": "primary",
            "display": "Primary"
          }
        ]
      },
      "description": "Evaluate the efficacy of Drug Y in reducing blood pressure."
    }
  ],
  "regulatoryApproval": [
    {
      "type": {
        "coding": [
          {
            "system": "http://terminology.hl7.org/CodeSystem/regulatory-approvals",
            "code": "FDA",
            "display": "Food and Drug Administration"
          }
        ]
      },
       "status": "approved",
       "date": "2023-09-01"
```

```
      },
    {
      "type": {
        "coding": [
          {
            "system": "http://terminology.hl7.org/CodeSystem/regulatory-approvals",
            "code": "EMA",
            "display": "European Medicines Agency"           }
        ]
      },
       "status": "approved",
       "date": "2023-10-15"
      }
    }
  ]
  "ethicsApproval": [
    {
      "country": {
        "coding": [
          {
            "system": "urn:iso:std:iso:3166",
            "code": "US",
            "display": "United States"
          }
        ]
      },
      "status": "approved",
      "date": "2023-09-05"
    },
    {
      "country": {
        "coding": [
          {
            "system": "urn:iso:std:iso:3166",
            "code": "FR",
            "display": "France"
          }
        ]
      },
      "status": "approved",
      "date": "2023-10-10"
    }
  ]
  "siteIRBApproval": [
    {
      "site": {
        "reference": "Location/site-001",
        "display": "Clinical Research Facility A"
      },
      "status": "approved",
      "date": "2023-09-20"
    }
  ]
  "relatedArtifact": [
    {
      "type": "documentation",
      "classifier": [
        {
          "text": "Protocol"
        }
      ],
      "label": "Study Protocol Document",
      "display": "Study Protocol for ResearchStudy ST-123456",
      "citation": "Protocol Version 1.0, dated 2022-01-01",
      "document": {
        "url": "http://example.org/documents/protocol-001.pdf",
```

```
        "title": "Study Protocol"
      },
      "publicationStatus": "active",
      "publicationDate": "2022-01-01"
    }
  ]
}
```


4.1.2 Site Object (Location and Organization)

Purpose: Models the physical and organizational details of study sites.

Key Data Points:

- resourceType: Location
- id / identifier: Unique identifier for the site. (can have multiple)
- name: Name of the study site.
- description: Detailed description of the site.
- address: Physical address of the site, including postal code, city, and country. (can have multiple)
- telecom: Contact information, including phone numbers and email addresses. (can have multiple)
- organization: Reference to the Organization resource that manages the site.
- type: Classification of the site (e.g., academic, hospital, private practice).
- createdAt - The date the site was created
- updatedAt - The date when the site was last updated
- parentSiteId - Parent site id
- subSiteIds - Ids of sites that fall under the site (can have multiple)
- researchStudies - See researchStudies (can have multiple)
- siteIRBApproval: Extension that tracks the IRB Ethics approval dates for the site.
- milestones: Tracks Milestones that occur at the site, including their name, status, date, and description.
- status: Operational status of the site (e.g., active, inactive).
    - Configuring

- Startup
- Active
- Maintenance
- Preclosed
- Closed
- Suspended
- Withdrawn

- managingOrganization: The organization responsible for the site's operations.
- Contacts: Contacts located at the Study-Site (can have multiple)

4.1.2.1 Study-Site Object (Location) JSON Example

```
{
  "resourceType": "Location",
  "id": "site-001",
  "identifier": [
    {
      "use": "official",
      "system": "http://example.org/sites",
      "value": "Site-001"
    }
  ],
  "name": "Clinical Research Facility A",
  "description": "A primary site for conducting Phase III trials.",
  "address": {
    "line": ["123 Main St"],
    "city": "Metropolis",
    "state": "NY",
    "postalCode": "10001",
    "country": "US"
  },
  "telecom": [
    {
      "system": "phone",
      "value": "+1-555-1234",
      "use": "work"
    },
    {
      "system": "email",
      "value": "contact@clinicalresearchfacilitya.com",
      "use": "work"
    }
  ],
  "managingOrganization": {
    "reference": "Organization/org-001",
    "display": "Managing Org ABC"
  },
  "status": "active",
  "type": [
    {
      "coding": [
        {
```

```
          "system": "http://terminology.hl7.org/CodeSystem/location-physical-type",
          "code": "site",
          "display": "Clinical Trial Site"
        }
      ]
    }
  ],
  "milestones": [
    {
      "id": "milestone-003",
      "name": "Site Activation",
      "status": "complete",
      "dateTime": "2023-07-01T00:00:00Z"
    }
  ],
  "siteIRBApproval": [
    {
      "status": "approved",
      "date": "2023-09-10"
    }
  ],
  "extension": [
    {
      "url": "http://example.org/fhir/StructureDefinition/location-created-at",
      "valueDateTime": "2023-01-01T08:00:00Z"
    },
    {
      "url": "http://example.org/fhir/StructureDefinition/location-updated-at",
      "valueDateTime": "2023-06-01T08:00:00Z"
    },
    {
      "url": "http://example.org/fhir/StructureDefinition/location-parent-site-id",
      "valueReference": {
        "reference": "Location/parent-site-001",
        "display": "Main Research Facility"
      }
    },
    {
      "url": "http://example.org/fhir/StructureDefinition/location-subsite-ids",
      "valueReference": [
        {
          "reference": "Location/site-002",
          "display": "Subsite 1"
        },
        {
          "reference": "Location/site-003",
          "display": "Subsite 2"
        }
      ]
    }
  ],
  "researchStudies": [
    {
      "reference": "ResearchStudy/study-001",
      "display": "Phase III Study on Drug Y"
    }
  ],
  "contacts": [
    {
      "name": {
        "family": "Smith",
        "given": ["John"],
        "prefix": ["Dr."]
      },
      "telecom": [
        {
```

```
          "system": "phone",
          "value": "+1-555-5678",
          "use": "work"
        },
        {
          "system": "email",
          "value": "drsmith@researchfacility.com",
          "use": "work"
        }
      ]
    }
  ]
}
```


4.1.3 Contact Object (Practitioner and PractitionerRole)

Purpose: Represents the professionals involved in the study, capturing their roles and contact information.

Key Data Points:

- Practitioner.identifier: Unique identifier for the individual.
- Practitioner.name: Full name of the professional.
- Practitioner.qualification: Professional qualifications, certifications, and credentials.
- Practitioner.telecom: Contact information including phone numbers and email addresses.
- PractitionerRole.role: The specific role of the professional within the study (e.g., principal investigator, study coordinator).
- PractitionerRole.specialty: Area of specialty or expertise (e.g., oncology, cardiology).
- PractitionerRole.location: Reference to the Location resource, indicating where the practitioner is active.
- PractitionerRole.period: The time period during which the professional is involved in the study.

4.1.3.1 Contact Object (Practitioner and PractitionerRole) JSON Example


```
{
  "resourceType": "Practitioner",
  "id": "practitioner-001",
  "identifier": [
    {
      "use": "official",
      "system": "http://example.org/practitioners",
      "value": "DrSmith-001"
    }
  ],
  "name": [
    {
      "use": "official",
      "family": "Smith",
      "given": ["John"],
```

```
      "prefix": ["Dr."]
    }
  ],
  "telecom": [
    {
      "system": "phone",
      "value": "+1-555-5678",
      "use": "work"
    },
    {
      "system": "email",
      "value": "drsmith@hospital.org",
      "use": "work"
    }
  ],
  "qualification": [
    {
      "code": {
        "coding": [
          {
            "system": "http://terminology.hl7.org/CodeSystem/v2-0360/2.7",
            "code": "MD",
            "display": "Doctor of Medicine"
          }
        ]
      }
    }
  ],
  "practitionerRole": [
    {
      "role": {
        "coding": [
          {
            "system": "http://terminology.hl7.org/CodeSystem/practitioner-role",
            "code": "principal-investigator",
            "display": "Principal Investigator"
          }
        ]
      },
      "specialty": [
        {
          "coding": [
            {
              "system": "http://terminology.hl7.org/CodeSystem/practitioner-specialty",
              "code": "cardiology",
              "display": "Cardiology"
            }
          ]
        }
      ],
      "location": [
        {
          "reference": "Location/site-001"
        }
      ],
      "period": {
        "start": "2023-01-01",
        "end": "2024-12-31"
      }
    }
  ]
}
```

4.1.4 Participant Object (ResearchSubject)

Purpose: Manages data related to participants in the study, tracking their involvement and status.

Key Data Points:

- identifier: Unique identifier for the participant within the study.
- individual: Reference to the Patient resource if the participant is also a patient.
- status: Enrollment status of the participant (e.g., candidate, enrolled, off-study).
- study: Reference to the ResearchStudy the participant is involved in.
- period: The duration of the participant's involvement in the study.
- consent: Documentation of consent status, including links to signed consent forms.
- assignedArm: The study arm to which the participant is assigned.
- actualArm: The study arm the participant actually follows, if different from the assigned arm.
- adverseEvents: Records of any adverse events experienced by the participant during the study.
- site: Reference to the Location the participant is enrolled at.

4.1.4.1 Participant Object (ResearchSubject) JSON Example


```
{
  "resourceType": "ResearchSubject",
  "id": "participant-001",
  "identifier": [
    {
      "use": "official",
      "system": "http://example.org/participants",
      "value": "P-123456",
      "type": {
        "coding": [
          {
            "system": "http://terminology.hl7.org/CodeSystem/v2-0203",
            "code": "MR",
            "display": "Medical Record Number"
          }
        ]
      },
      "assigner": {
        "display": "Hospital A"
      }
    }
  ],
  "status": "active",
  "study": {
    "reference": "ResearchStudy/study-001",
    "display": "Phase III Study on Drug Y"
  },
  "assignedComparisonGroup": {
    "reference": "Group/group-001",
    "display": "Control Group"
```

```
  },
  "actualComparisonGroup": {
    "reference": "Group/group-002",
    "display": "Treatment Group"
  },
  "site": {
    "reference": "Location/site-001",
    "display": "Clinical Research Facility A"
  },
  "progress": [
    {
      "type": {
        "coding": [
          {
            "system": "http://terminology.hl7.org/CodeSystem/research-subject-progress",
            "code": "screening",
            "display": "Screening"
          }
        ]
      },
      "subjectState": "eligible",
      "milestone": "Informed Consent Signed",
      "reason": "Subject agreed to participate",
      "startDate": "2023-06-01",
      "endDate": "2023-06-05"
    }
  ],
  "subject": {
    "reference": "Patient/patient-001",
    "name": [
      {
        "family": "Doe",
        "given": ["John"]
      }
    ],
    "address": [
      {
        "line": ["123 Main St"],
        "city": "Metropolis",
        "state": "NY",
        "postalCode": "10001",
        "country": "US"
      }
    ],
    "contact": [
      {
        "relationship": [
          {
            "coding": [
              {
                "system": "http://terminology.hl7.org/CodeSystem/v2-0131",
                "code": "E",
                "display": "Emergency Contact"
              }
            ]
          }
        ],
        "name": {
          "family": "Smith",
          "given": ["Jane"]
        },
        "telecom": [
          {
            "system": "phone",
            "value": "+1-555-5678",
            "use": "home"
```

```
            }
          ]
        }
      ],
      "telecom": [
        {
          "system": "phone",
          "value": "+1-555-1234",
          "use": "mobile"
        },
        {
          "system": "email",
          "value": "johndoe@example.com",
          "use": "home"
        }
      ],
      "gender": "male",
      "birthDate": "1980-01-01",
      "communication": [
        {
          "language": {
            "coding": [
              {
                "system": "urn:ietf:bcp:47",
                "code": "en",
                "display": "English"
              }
            ]
          },
          "preferred": true
        }
      ]
    }
}
```


4.1.5 (FUTURE) Trial Document Object (DocumentReference)

Purpose: Standardizes the management and exchange of clinical trial documents, ensuring proper classification, metadata management, and version control.

Key Data Points:

- identifier: Unique identifier for the document.
- status: Status of the document (e.g., current, superseded).
    - Current
    - Draft
    - Superseded
    - Effective
    - Approved
    - Obsolete

- name: Name of the document
- topic: Topic of the document
- type: Type of document (e.g., protocol, informed consent, IRB approval).
- TMF level: For TMF documents, the TMF level
- TMF zone: For TMF documents, the TMF zone
- TMF section: For TMF documents, the TMF section
- TMF Artifact: For TMF documents, the TMF artifact
- TMF sub-artifact: For TMF documents, the TMF subartifact
- TMF Index Number: For TMF documents, the TMF Index Number
- researchStudies: For TMF documents, the associated Studies
- site: For TMF documents, the associated Site
- country: For TMF documents, the TMF country
- language: For TMF documents, the TMF language
- associatedContact: For TMF documents, the associated contact
- associatedOrganization: For TMF documents, the associated organization(s)
- subject: Reference to the related study or participant.
- author: The individual or organization that authored the document.
- custodian: The entity responsible for maintaining the document.
- description: A summary of the document's content.
- date: Different types of dates
    - expiry date
    - visit date
    - signature date
    - effective date
    - created date

- version: Version number of the document, with metadata tracking changes and revisions.
- content: Reference to the actual content of the document, including format (e.g., PDF, XML) and location.

4.2 Use Cases

- Study Start-Up: Facilitating quick and secure exchange of study protocols, site information, and investigator data between sponsors and sites.
- Site Management: Allowing study sites to share operational data securely with multiple stakeholders using a standardized format.
- Trial Management: Allowing trial managers to share milestones, events
- eTMF Collection and Document Management: Standardizing the upload and retrieval of essential documents like informed consent forms, ensuring they are correctly associated and classified to relevant studies and sites.

4.2.1.1 Trial Document Object (DocumentReference) JSON Example


```
{
  "resourceType": "DocumentReference",
  "id": "doc-001",
  "identifier": [
    {
      "use": "official",
      "system": "http://example.org/documents",
      "value": "ICF-123456"
    }
  ],
  "name": "Informed Consent Form",
  "status": "current",
  "type": {
    "coding": [
      {
        "system": "http://loinc.org",
        "code": "34108-1",
        "display": "Informed Consent Form"
      }
    ]
  },
  "topic": {
    "text": "Informed Consent Form for Clinical Trial"
  },
  "extension": [
    {
      "url": "http://example.org/fhir/StructureDefinition/tmf-level",
      "valueString": "Site"
    },
    {
      "url": "http://example.org/fhir/StructureDefinition/tmf-zone",
      "valueString": "Central Trial Documents"
    },
    {
      "url": "http://example.org/fhir/StructureDefinition/tmf-section",
      "valueString": "Subject Documentation"
    },
    {
      "url": "http://example.org/fhir/StructureDefinition/tmf-artifact",
```

```
      "valueString": "Informed Consent Form"
    },
    {
      "url": "http://example.org/fhir/StructureDefinition/tmf-sub-artifact",
      "valueString": "Subject Consent Form"
    },
    {
      "url": "http://example.org/fhir/StructureDefinition/tmf-index-number",
      "valueString": "02.02.03"
    }
  ],
  "researchStudies": [
    {
      "reference": "ResearchStudy/study-001",
      "display": "Phase III Study on Drug Y"
    }
  ],
  "country": [
    {
      "coding": [
        {
          "system": "urn:iso:std:iso:3166",
          "code": "US",
          "display": "United States"
        }
      ]
    }
  ],
  "language": {
    "coding": [
      {
        "system": "urn:ietf:bcp:47",
        "code": "en",
        "display": "English"
      }
    ]
  },
  "site": [
    {
      "reference": "Location/site-001",
      "display": "Clinical Research Facility A"
    }
  ],
  "author": [
    {
      "reference": "Practitioner/practitioner-001",
      "display": "Dr. John Smith"
    }
  ],
  "custodian": {
    "reference": "Organization/org-001",
    "display": "Managing Organization"
  },
  "date": [
    {
      "value": "2023-06-15",
      "type": "expiry",
      "display": "Expiry Date"
    },
    {
      "value": "2023-05-01",
      "type": "visit",
      "display": "Visit Date"
    },
    {
      "value": "2023-05-05",
```

```
      "type": "signature",
      "display": "Signature Date"
    },
    {
      "value": "2023-06-01",
      "type": "effective",
      "display": "Effective Date"
    },
    {
      "value": "2023-05-01",
      "type": "created",
      "display": "Created Date"
    }
  ],
  "associatedContact": [
    {
      "reference": "Practitioner/practitioner-002",
      "display": "Dr. Jane Doe"
    }
  ],
  "associatedOrganization": [
    {
      "reference": "Organization/org-002",
      "display": "Regulatory Organization"
    }
  ],
  "version": "1.0",
  "description": "Informed Consent Form for the Phase III Study of Drug Y",
  "content": [
    {
      "attachment": {
        "contentType": "application/pdf",
        "url": "http://example.org/documents/consent-form-001.pdf",
        "title": "Informed Consent Form",
        "creation": "2023-05-01T08:00:00Z"
      }
    }
  ]
}
```

5 Impact Assessment

5.1 Compatibility

The CRISI standard is designed to not conflict with existing CDISC standards, such as ODM, and will complement other standards like eTMF EMS for eTMF archive exchange. By leveraging FHIR, CRISI ensures compatibility with broader healthcare systems, enhancing the interoperability of clinical trial data with EHRs and other healthcare data sources.

5.2 Impact on Stakeholders

Regulatory Bodies: Enhanced data consistency and easier access to study data for regulatory review.

Clinical Research Organizations (CROs): Streamlined operations and reduced overhead in managing study data across multiple systems, especially Clinical Sites.

Software Vendors: Opportunities to develop compatible tools that align with the new standard, expanding their market reach.

6 Implementation Plan

6.1 Development Process

Phase 1 (Q4 2024): Finalize the CRISI standard draft and submit for CDISC review.

Phase 2 (Q1 2025): Conduct pilot implementations with selected sponsors, CROs, and sites.

Phase 3 (Q3 2025): Collect feedback, refine the standard, and prepare for broader adoption.

6.2 Resources Required

Technical Experts: FHIR specialists, clinical research informatics professionals.

Financial Support: Funding for pilot projects and development resources.

Stakeholder Engagement: Collaboration with sponsors, CROs, regulatory bodies, and software vendors.

6.3 Review and Approval Process

6.3.1 Proposed Review Steps

Internal Review (Q4 2024): CDISC internal team review.

Pilot Testing (Q1 2025): Real-world testing of the standard in selected studies.

Public Review (Q2 2025): Open the standard for public comment and feedback.

Final Approval (Q3 2025): CDISC board approval and publication.

6.3.2 Feedback Mechanism

A dedicated platform will be established for stakeholders to submit feedback during the public review phase, including online surveys, focus groups, and public forums.

7 Conclusion

The CRISI standard represents a significant advancement in clinical trial operations, addressing the critical need for standardized data exchange across research systems. By adopting CRISI, the clinical research community will benefit from reduced study initiation times, enhanced operational efficiency, and greater flexibility in software application use, all while ensuring robust interoperability with existing and future healthcare systems.

8 Appendices

CRISI Data Elements Definitions

Pilot Project Case Studies

References and Further Reading