An Update on the CDISC Investigator Site File (ISF) Initiative

Jamie Marie Toth, Sr. Director Global TMF Management & Records – BeOne Medicines USA Inc (formerly BeiGene USA Inc.) and CDISC TMF Reference Model Steering Committee Member

Dr. Torsten Stemmler, Head of GCP-Inspection Unit, BfArM

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Meet the Speaker

Jamie Marie Toth

Title: Sr. Director, Global TMF Management & Records and CDISC TMF Reference Model Steering Committee Member

Organization: BeOne Medicines USA Inc. (formerly BeiGene USA Inc.)

Jamie is Global Head, Trial Master File Management & Records at BeOne Medicines USA Inc (formerly BeiGene USA Inc.), home based in New Jersey, USA.

She is a Steering Committee member for the CDISC TMF Reference Model Working Group and the Incoming Chair Elect. She is on the Board of Directors for the Health Sciences Records and Archives Association (HSRAA) and on the Board of Directors for the Association for GxP Excellence (AGxPE).

Jamie has led many industry workstreams for TMF/eTMF including the clinical trials email guidance and the TMF Plan Template with industry colleagues and is currently a co-liaison to the CDISC ISF Reference Model initiative.

Meet the Speaker

Dr. Torsten Stemmler

Title: Head of GCP Inspection Unit

Organization: Federal Institute for Drugs and Medical Devices

Dr. Torsten Stemmler earned his PhD in Biology (Neurobiology and Psychophysics) from the University of Bremen, Germany, in 2011. Following his doctoral studies, he pursued postdoctoral research at RWTH Aachen, focusing on visual perception. His career took a dynamic turn when he retrained as a Data Manager, developing database solutions at the University Hospital Aachen. In 2017, he brought his expertise to the Federal Institute for Drugs and Medical Devices, where he serves as a GCP Inspector, ensuring compliance with Good Clinical Practice standards.

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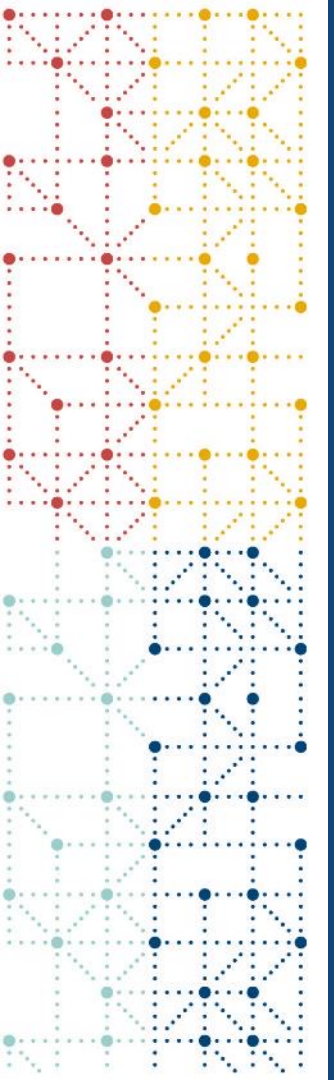
Agenda

1. What is the ISF Initiative
2. ISF Initiative Timelines & Next Steps
3. Feedback from the Regulator



What is the ISF Initiative?

ISF Initiative Co-Leads

Matt Lowery

CEO / Principal Consultant
The Pathways Group

Aryn Knight, BS, CCRP

Associate Vice President
Clinical Innovation and Research Institute
Memorial Hermann Health System
Society of Clinical Research Associates (SoCRA), Houston Chapter Chair

Overview

TMF RM SC Liaisons:
Jamie Toth and Dawn Niccum

Co-leads:
Aryn Knight, Clinical Innovation and Research Institute, Memorial Hermann Health System
Matt Lowery, The Pathways Grp, LLC

Goal:
To develop an Investigator Site File (ISF) reference model for sites to use that supplements the TMF Reference Model with the intention of standardizing ISF structure, file naming conventions, and how/where site-level essential records are filed.

Committee: ~46 members across all aspects of the industry who have an interest ***in*** and experience ***with*** ISF/TMF/regulatory including sites, sponsors, CROs, service providers/vendors, consultants.

Sub teams:

- **Evaluation**: Review of existing ISF structures
- **Standards**: Setting standards
- **Proofing**: Review of deliverables
- **Outreach**: Presentations, publications, and white papers
- **Training**: Training the industry on ISF RM

Expected Benefits

Increased Efficiency

Facilitate consistent document filing practices which reduces time spent preparing for monitoring visits, audits, or inspections.

Simplify the training process for new site staff and reduces errors in filing.

Improved Collaboration

Streamline document exchange and improved communication between sites and sponsors.

Make it easier for auditors and inspectors to locate and review documents without having to understand a unique filing system for each site.

Enhanced Compliance

Ensure adherence to GCP and ICH guidelines which enables better ISF and TMF quality.

Facilitate inspection readiness and enable proactive risk identification.

A word from co-lead, Matt Lowery

ISF Initiative Timeline & Next Steps

Timeline

STAGE 1

Launch - February 2024

Call for volunteers from sites, sponsors, CROs & vendors

Kickoff – April 2024

Initiative kicked off with ~46 volunteers; subteams (5) formed

STAGE 2

Subteam activity – April–August 2024

Evaluation of existing ISF structures completed; first draft of ISF RM developed

September – November 2024

Standards team reviewed draft and existing standards to ensure alignment; second draft of ISF RM

STAGE 3

Proofing – November–December 2024

Proofing team reviewed second draft of ISF RM; finalized draft is ready for review

STAGE 4

CDISC Review – January-June 2025

ISF RM provided feedback to TMF RM V4

ISF RM is ready for 1st stage of CDISC review with TMF RM SC

Review ~97 comments from CDISC TMF RM SC/ Follow ups related to comments.

Targeted Review with Site Stakeholders

Resubmit for 2nd stage of CDISC review with TMF RM SC

Meet with CCB and allow review.

We are here!

STAGE 5

Public launch – Target: July 2025

Training to begin after public launch/comments

Outreach is ongoing with presentations & updates at various conferences, webinars, etc.

ISF RM Release 1.0

Zone	Section	Sub-Section	Artifact/Record
01_Planning	01_01_Feasibility	n/a	Feasibility Documentation
01_Planning	01_01_Feasibility	n/a	Technical Capabilities Questionnaire
01_Planning	01_02_Recruitment Plan and Progress	n/a	Recruitment Plan
01_Planning	01_02_Recruitment Plan and Progress	n/a	Recruitment Progress
01_Planning	01_03_ISF and Source Data Plans	n/a	Document Transfer Documentation
01_Planning	01_03_ISF and Source Data Plans	n/a	Evidence of Quality Review
01_Planning	01_03_ISF and Source Data Plans	n/a	Source Document Agreement
01_Planning	01_03_ISF and Source Data Plans	n/a	Source Documentation List
01_Planning	01_03_ISF and Source Data Plans	n/a	ISF Material Master File Index
01_Planning	01_03_ISF and Source Data Plans	n/a	ISF Plan
01_Planning	01_03_ISF and Source Data Plans	n/a	ISF Report
01_Planning	01_04_Relevant Communications	n/a	Relevant Communications
01_Planning	01_05_Tracking Documentation	n/a	Tracking Information
01_Planning	01_06_Meeting Materials	n/a	Other Meeting Agenda
01_Planning	01_06_Meeting Materials	n/a	Other Meeting Attendance Sheet
01_Planning	01_06_Meeting Materials	n/a	Other Meeting Minutes
01_Planning	01_06_Meeting Materials	n/a	Other Meeting Presentation Materials
01_Planning	01_07_Filenotes	n/a	Filenote
02_Study Information	02_01_Recruitment Materials	n/a	Advertisements for Subject Recruitment
02_Study Information	02_02_Study Contact Details	n/a	Sponsor/CRO Contact Details
02_Study Information	02_03_Product or Device Materials	n/a	Investigational Medicinal Product Documentation
02_Study Information	02_03_Product or Device Materials	n/a	Investigator's Brochure
02_Study Information	02_03_Product or Device Materials	n/a	Investigator's Brochure Addendum
02_Study Information	02_03_Product or Device Materials	n/a	Investigator's Brochure Extension
02_Study Information	02_03_Product or Device Materials	n/a	Investigator's Brochure Safety Relevant Changes
02_Study Information	02_03_Product or Device Materials	n/a	Package Insert
02_Study Information	02_03_Product or Device Materials	n/a	Summary of Product Characteristics
02_Study Information	02_04_Insurance	n/a	Insurance Certificate
02_Study Information	02_04_Insurance	n/a	Insurance Policy
02_Study Information	02_05_Study Materials	02_05_01_Protocol and Amendments	Clinical Investigation Plan (Devices)

- 01_Planning
- 02_Study Information
- 03_Regulatory or Ethics Review
- 04_Site Documentation
- 05_Contracting and Indemnity
- 06_IP and Trial Supplies
- 07_Testing Facility
- 08_Monitoring
- 09_Safety
- 10_Data Management

These Zones/Sections are aligned into time based/phases based on how an Inv. Site handles their Operations

ISF Release 2.0 will be part of Version 4.0 TMF RM

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Ongoing & Future Activities

- After formal CDISC internal review, **public comment** will commence – likely in June/July.
- ***ISF Release 1.0 to launch in 2025***.
  - This version will be in alignment with TMF RM 3.3.1.
- ***Alignment with TMF RM v4.0*** activities will take place; feedback already given.
  - These will go into ISF Release 2.0 and be part of V4.
- **Outreach** is ongoing and will continue throughout the initiative.
- **Training** will be provided upon publication of the final Release1.0 ISF reference model.

Feedback from the Regulator

Torsten Stemmler

Feedback from the Regulator

1. Is there anything about the ISF initiative that you would caution us on from a regulatory authority point of view?

2. What should we take into consideration when developing the ISF RM that would assist inspectors and/or make inspections easier/more streamlined?

3. How will standardization of ISFs - both paper and electronic - to reconstruct the trial events?

4. What suggestions do you have that you think will support the development of a standardized ISF reference model aligned with ICH E6(R3) principles, to promote inspection readiness, data integrity, and risk-based monitoring?

5. What are the key risk areas that ISF standardization will help to address in the inspector's opinion?

6. From the inspector's perspective, how could sites transition smoothly to a standardized ISF structure?

7. How does the ISF standard facilitate inspection readiness and enable proactive risk identification?

8. What past findings can you share from site audits/inspections related to ISF or essential records?

Thank You!