



Trial Master File Reference Model

General Meeting

22 January 2018

Agenda

- ▶ Welcome
- ▶ Steering Committee Update – Karen, Paul, Wendy
- ▶ Change Control Board – Kelley
- ▶ TMF Plan Launch – Jamie
- ▶ HSRAA (SAG!) – Jamie
- ▶ Other Subgroup activity update – Karen and Leads
- ▶ TMF Summit in Orlando Summary – Lisa
- ▶ Upcoming industry mtgs:
 - DIA RSIDM: Betsy
 - Marcus Evans Conference: Eldin
 - eRegulatory Summit: Jane

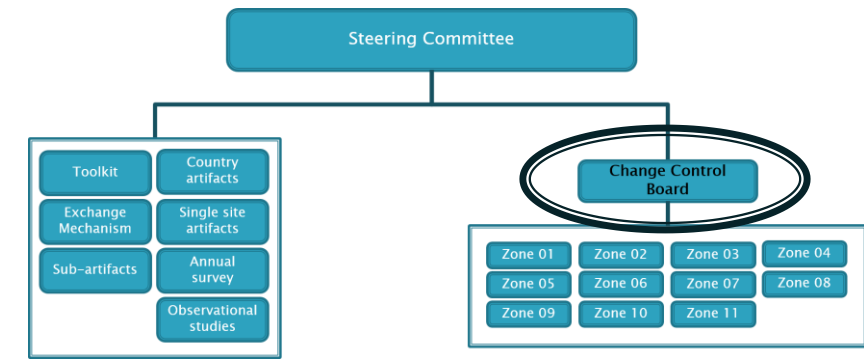
Steering Committee Update

- ▶ Two new Committee Members
 - Wendy Trimboli, Eisai
 - Paul Fenton, Montrium

Admin

- ▶ 53 new active project team members since last meeting
- ▶ 25 new subscribers to mailing list since last meeting

Change Control Board



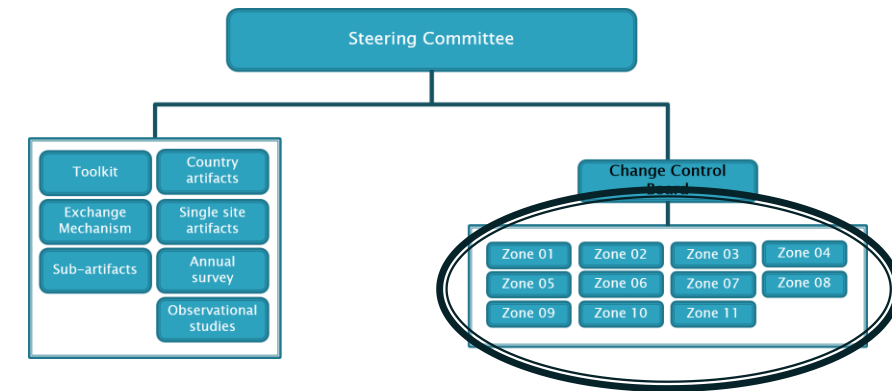
► Change Control Board Structure

- 15 members – no additional members needed
- Kelley Robinson, Pfizer: Chair
- Joanne Malia, Regeneron: Deputy Chair
- Gift Chareka, UCSF: Exchange Team Liaison
- Eldin Rammell: Steering Committee Liaison

► Deliverables to Date

- Meeting twice a month since October 2017
- Created and finalized: Change Control Procedure, RACI and CR Tracker
- Reviewed and categorized all current change requests
- Will be triaging change requests (61 received so far!) to Zone Teams shortly
- Submit requests here: <https://tmfrefmodel.com/feedback>

Change Control – Zones



▶ Role

- Groups of subject matter experts who are constituted to review proposed changes to the TMF Reference Model and make recommendations to the Change Control Board on their acceptance or rejection

▶ Zone Team Structure

- 7 of the 11 Zones have identified leads
 - SMEs still needed for all zones
- Leads still needed for the following zones
 - Zone 2: Central Trial Documents
 - Zone 9: Third Parties
 - Zone 10: Data Management
 - Zone 11: Statistics

- ▶ Please consider joining or leading a zone – time commitment is on average 1 hour a month

TMF Plan Template Working Group Update

TMF Plan Template Initiative

– Objective/Scope/Team

- ▶ **Objective:** Develop a cross-industry usable, simplistic TMF Management Plan template.. Guidance provided on how to deal with variations depending on study size, phase, type.
- ▶ **Scope:** Template to be used for studies that are Early Phase I - Phase IV, Investigational Drug and Medical Device, Biologics.
- ▶ Team has been meeting since March 2017.

Name	Company
Deborah Castellana	Celgene
Elaine Berry	The Emmes Corporation
Etienne Hinton	Duke Clinical Research Institute
Jamie Toth - Lead	Daiichi Sankyo, Inc.
Jennifer Eberhardt	Shire
Brenda Brown	Pfizer
Lisa Mulcahy	Mulcahy Consulting
Marion Mays	PhlexGlobal
Menzi Reed	Pharma Consulting Group
Mike Czaplicki	GSK
Dina Antonacci	Mallinckrodt Pharmaceuticals
Marie Christine Poisson-carvajal	Pfizer
Anne-Mette Varney	Novo Nordisk
Sarah Curno	Hedian Records Management
Linda Hoppe	Veeva
Lorna Patrick – Co-Lead	Quotient Clinical
Meghan Page	Shire
Luisa Monica	LMK Clinical Research Consulting
Wendy Trimboli	Esai

TMF Plan Template Initiative

– Status

- ▶ 13 sections, ~21 pages
- ▶ Includes green guidance text and blue insertion prompt text
- ▶ Comprehensive
- ▶ Final draft sent to TMF Ref Model SC for review; due by 26-Jan
- ▶ Looking to finalize and post on tmfrefmodel.com by mid-February

[This TMF Plan Template Version 1.0 January 2018 was authored by the TMF Plan Template SubGroup of the TMF Reference Model Working Group. Replace with company header information.]

1	Approvals.....	3
2	Document Version History.....	4
3	Definitions and Abbreviations.....	5
4	Introduction.....	6
5	TMF Oversight & Access Arrangements.....	8
	5.1.1 RACI Matrix.....	8
	5.1.2 Access arrangements.....	9
	5.1.3 TMF Maintenance delegated to a CRO.....	9
	5.1.4 For Inspections/Audits.....	10
6	TMF Content.....	11
	6.1 TMF format.....	11
	6.1.1 TMF file structure/index/content map/specifications.....	11
	6.2 Authoritative Sources.....	11
	6.2.1 Originals.....	12
	6.2.1.1 Wet ink and raised seals.....	12
	6.2.2 Relevant Correspondence.....	12
	6.2.3 Unblinded Documents.....	13
	6.2.4 Translations.....	13
7	Document Disposition.....	14
	7.1.1 Retention.....	14
	7.1.2 Destruction.....	14
	7.1.3 Legal Hold.....	14
8	Applicable SOPs.....	15
9	TMF Training.....	16
10	Conducting TMF Reviews.....	17
	10.1 TMF Review Plan.....	
	10.2 TMF Review Documentation.....	
11	Transfers of TMF.....	
12	Archiving the TMF.....	
	12.1 Sponsor Portion of the TMF.....	
	12.2 Investigator Portion of the TMF.....	
13	Appendix.....	

DRAFT

From SAG to HSRAA



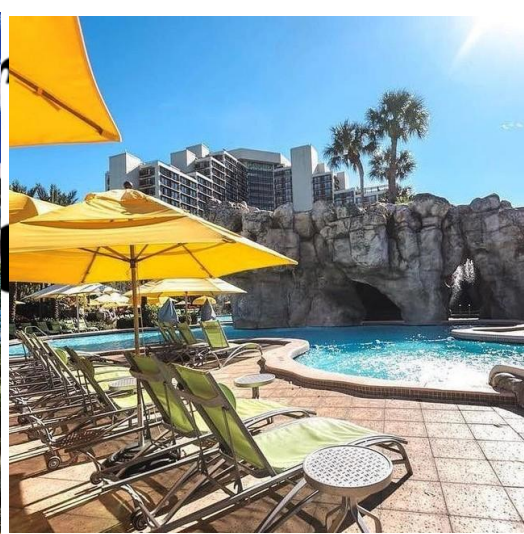
- ▶ With effect from 1st January 2018, the Scientific Archivists Group (SAG) has changed its name to the Health Sciences Records and Archives Association (HSRAA), reflecting more clearly the scope of the group's activities. In alignment with the adoption of a new name, the association has also launched a new website (<http://the-hsraa.org>) and new branding.
- ▶ As the Health Sciences Records and Archives Association, the group will continue to support a wide variety of roles with responsibility for records and archives, including archivists, records managers, document administrators and file specialists, as well as specialist roles within health sciences organisations, such as GLP Archivist, GCP Archivist, TMF Process Owners and QA Managers, to name but a few.
- ▶ The objectives of the Association are:
 - to raise the profile of records management and archiving as business-critical activities in health sciences;
 - to improve the professional competencies of records managers and archivists;
 - to encourage the consistent interpretation of pertinent laws, regulations and guidance; and
 - to influence the regulatory environment.
- ▶ Annual Conference
 - 25–27 April 2018, Brighton, UK
 - <http://bit.ly/hsraa2018>
 - Pre-conference workshop: TMF Essentials

Exchange mechanism update

- Exchange Mechanism
 - XML standard to support data transfer between eTMF systems
- Reviewing feedback on draft Specification
 - Technology review – eTMF Vendors
 - Business review – Sponsors / CROs
 - Anticipate March/April completion
- Next major hurdle – Exchange Roadtest
 - Requires willing vendor and business volunteers
 - Focused, but time-bound effort
 - Interested? Notify your vendor and email exchange@tmfrefmodel.groups.io

Activity Other Subgroups

Group	Lead
Metadata	Todd Tullis
Implementation toolkit / Upgrade User Guide <ul style="list-style-type: none">• Drafts were submitted to the SC for feedback late last year (feedback received)• Feedback from SC to be addressed (Jan/Feb)• Updated version submitted for SC approval (Feb/Mar)• SC Approvals and release (March – if approved)	Mike Czaplicki / Lisa Mulcahy
Sub-artifacts	Karin Schneider
Country specific artifacts	Eleanor Hewes
TMF Plan Template	Jamie Toth
Exchange Mechanism	Paul Fenton / Elvin Thalund
Change Control Board	Kelley Robinson / Joanne Malia



Welcome to the 7th US TMF Summit
January 16-18 2018, Orlando

It's All About Inspections!



7TH

TMF
TRIAL MASTER FILE SUMMIT

*Refine QC and Operations for an Inspection-Ready TMF and
Strategic Oversight of Trials and Vendor Performance*

Chair Introductions

Jamie Toth

- ▶ Based in Basking Ridge, NJ...and Jersey born and raised!
- ▶ Head of TMF Operations at Daiichi Sankyo, Inc.
- ▶ Previously worked at Covance for 8 years
- ▶ Over 20 years in Pharma Industry in both Informatics/IT and Clinical Operations



Marie-Christine Poisson-Carvajal

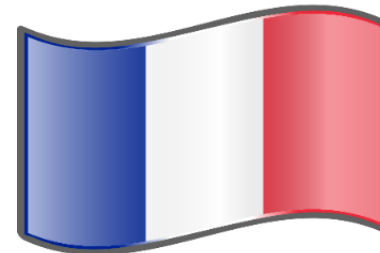
- Based in Cambridge, MA... and born and raised in Paris... France!
- Head of TMF Operations at Pfizer
- Over 30 years in Clinical Research and Operations both in Pharma Industry and CROs

Karen Roy

- Based in Amersham, United Kingdom (from Johannesburg, South Africa)
- Senior Vice President at Phlexglobal Ltd
- 25 years Life Sciences experience (CRO and eTMF Vendor)
- Started the TMF Reference Model in 2009 – Chairman of the Steering Committee

TRIAL MASTER FILE
TMF
REFERENCE MODEL

Welcome to 262 Attendees!



THE MASTER FILE
TMF
REFERENCE MODEL

AbbVie
Advanced Clinical
Agensys
Agilent Technologies, Inc.
Agios Pharmaceutical
Akros Pharma Inc.
Alkermes
Allergan
Alnylam Pharmaceuticals
Altria Client Services LLC
Amgen
Aris Global
Array BioPharma, Inc.
Astellas
AstraZeneca
AveXis, Inc.
Bayer Pharmaceutials
Bellicum Pharmaceuticals
Biogen
BioMarin Pharmaceutical Inc.
Biotech
Bioverativ
Boehringer Ingelheim
Bristol-Myers Squibb
C. R. Bard, Inc.
Calithera Biosciences
Ce3, Inc.
Celerion
Celgene
Chiesi USA, Inc.
Chugai Pharma USA
Cidara
ClinDisc s.r.o.
Clovis Oncology
Colorado Clinical Consulting
Cook Medical
Corementum
CPC Clinical Research
CR Bard
CSL Behring
Daiichi Sankyo
Dart NeuroScience
DRS Corp.
DrugDev, Inc.
Duke University Medical Center
Edwards Lifesciences
Eisai
Eli Lilly and Company
Emergent Biosolutions
Enterin, Inc.
FibroGen
Florence
George Washington University School of Medicine
Global Blood Therapeutics
Global Clinical Connections

148 Sponsor Attendees
94 Companies

27 CRO Attendees
18 Companies

80 Vendor / Consultant Attendees
38 Companies

7 Site Attendees
7 Sites

Greenwich Biosciences
GSK
Halozyme Therapeutics
Health Decisions
Immunocore Ltd.
ImmunoGen
INC Research
Indivior Inc
Inovio
inSeption Group
Insmid
Ionis Pharmaceuticals, Inc.
IQVIA
Juno Therapeutics, Inc
Just in Time GCP
Karyopharm
LMK Clinical Research Consulting
Ludwig Institute for Cancer Research
MacroGenics, Inc.
Mallinckrodt Pharmaceuticals
MasterControl
Medidata Solutions
Medimmune
Medpace
Menlo Therapeutics
Merck
Minnesota Gastroenterology P.A.
Mitsubishi Tanabe Pharma Development America
Montrium
Mulcahy Consulting
Mylan
Nant BioScience, Inc.
NCGS
Nektar Therapeutics
Novo Nordisk
Paragon
Parion Sciences, Inc
PATH
Pfizer
Pharmacyclics
Philips
Phlexglobal
PPD
PRA Health Sciences
Proteon Therapeutics, Inc.
PSI Pharma Support America
Puma Biotechnology
R.J. Reynolds Tobacco Company
RAI Services Company
Regeneron
Retrophin, Inc
Rho
Roche
Safe Biopharma Association
Sage Therapeutics
Samsung Bioepis
Samumed, LLC
Sarepta Therapeutics, Inc
Seattle Genetics
Shire
Siemens Healthineers
Stryker
Sucampo Pharmaceuticals, Inc.
Sunovion
Supernus Pharmaceuticals, Inc.
Syntel
Syros Pharmaceuticals Inc.
Takeda
Technical Resources International
Texas Health Institute
The Avoca Group
Theravance Biopharma
TransPerfect
Ultragenyx
United Therapeutics
University of Florida
Vaccin Systems
VaccinTech
Vetrek
Vince & Associates Clinical Research
Vital Therapies
WAVE Life Sciences
Westat
Wintona
Wintona Clinical Research
Wintona Clinical Research
Xencor Inc.
Zoll Medical Corporation

TRIA MASTER FILE
T MF
REFERENCE MODEL

Pre-Conference TMF Training Day

16 January 2018

▶ 3 workshops

◦ Breakfast – Building the Foundation

- What is the TMF? What does content in the TMF look like? Who creates the content in the TMF? Where is TMF content located? How is TMF content managed?

◦ Afternoon – Keys for Success – Operationalizing Your TMF

- 4 challenging TMF management topics discusses: Sponsor and CRO periodic quality checks, Multiple repositories that hold TMF content, Change management for the TMF management process, and Management of eTMF system periodic releases

◦ Dinner – Outline Your Management of the TMF – the TMF Plan

- Primer of the requirements of a TMF Plan, announcement that the TMF RM TMF Plan is almost ready for public posting, 3 challenging situations to consider at the creation of the creation of the TMF Plan: Quality review of the TMF, Locations of content, and Considerations for inspections

Day 1

17 January 2108

► Topics of the Presentations:

- Recent regulatory updates impacting the management of the TMF
- Quality of the TMF
- Accurate resourcing for TMF management
- *In house* TMFs at Sponsor
- Collaboration culture (within sponsor and with CRO/Vendors) using metrics and reporting
- Bringing the TMF 'in-house'
- Rapid implementation of the eTMF system
- Using the eTMF configuration to meet business imperatives
- 3 Panels of experts sharing their perspectives for challenges and solution

• Theme of questions:

- Risk-based approach to quality activities
- Getting support for creating a TMF Operations group
- Manual and electronic migration process, plan, and documentation of transfers of TMF from vendor to the sponsor. Integrations and the upcoming TMF RM exchange mechanism.
- What paper documents can be destroyed? Has the MHRA provided their "official" notes from the "TMF Day" last September (no they have not)
- Voice of the people managing the TMF is important to consider in helping them change their habits... finds the few comments that will make the most impact to the process adoption.
- Specific eTMF implementation case studies and associated metrics
- Questions varied from those that are experienced in TMF management to those new to it. Smaller companies are trying to find their way to compliant TMF management with small (shared) numbers of resources
- Metrics, KPIs – How to use them for what they are?
- Challenges ensuring completeness and accuracy of the TMF content (i.e., expected/required documents collectively)

Day 2

18 January 2108

► Topics of the Presentations:

- Quality of the TMF; starts at beginning of the trial and is grounded in training of staff; risk based oversight; rolling audit strategy; monitored, measured, and reported
- Mergers & Acquisitions
- Digital signatures and the TMF
- Staffing for compliant TMF management
- Collaboration with CROs *and sites*
- Preparing for an upcoming inspection of the TMF
- 2 Panels of experts sharing their perspectives for challenges and solution

• Theme of questions/comments:

- Are quality requirements defined by the regulators?
- Risk-based Quality Checks... where can risk be taken? Does every TMF record have to undergo QC? Who monitors and who is responsible?
- How can TMF management be improved at the site... ISF... level? What are opportunities ahead?
- Collaboration across and with the triangle of sponsor – CRO – Site ISF for complete inspection readiness. How is this accomplished?
- Questions about ways used for enhanced CRO– Sponsor collaboration?

Upcoming Event – eRegulatory Summit Lisbon – 24–26 April

TMF / eTMF Workstream (parallel to RIM/IDMP Compliance)

<https://lifesciences.knect365.com/eregulatory-summit/agenda/1>

DAY 1:

- ✓ Requirements & Mock Inspection with Danish Medicines Agency
- ✓ Industry feedback: Inspection Readiness strategies (Roche)
- ✓ Montrium & MasterControl technology spotlights
- ✓ Active management & leveraging data (Regeneron)
- ✓ Round table session on TMF Management (GSK)
- ✓ Impact of **BREXIT** on EMEA and Industry Regulations

DAY 2

- ✓ Pros & Cons of Fully validated eTMF vs Hybrid (GSK vaccines)
- ✓ Moving to an eTMF – challenges and opportunities (Biogen)
- ✓ Implementing an eTMF & adopting the **Reference Model** (Cancer Research UK)
- ✓ Accountable **Oversight** / Regulatory expectations (Mylan)
- ✓ Outsourcing environment impact on eTMF (Boehringer Ingelheim)
- ✓ Sponsor & CRO dual dialogue & communication throughout the **TMF Management Plan**
- ✓ Global Inspection Support through effective management & maintenance of TMF
- ✓ eTMF & **interoperability**: strategies for success

DAY 3 – no TMF workstream

TRIAL MASTER FILE
TMF
REFERENCE MODEL

Upcoming event

- ▶ **TMF & Clinical Operations Quality Excellence**
 - New conference organized by Marcus Evans events
 - Wide ClinOps scope to encourage attendance from broad range of stakeholders
 - Topics include: Quality processes; Data integrity; Vendor oversight; Inspection readiness
 - 19–21 March 2018, Berlin, Germany
 - <http://bit.ly/me-tmf>
 - Includes a specific TMF Reference Model session: ‘RM Deliverables & their Impact on TMF Quality’.... focus on outputs from all of the sub-teams

Regulatory Submissions, Information, and Document Management Forum

 Feb 05, 2018 7:00 AM -
Feb 07, 2018 3:00 PM

 Bethesda North Marriott Hotel
and Conference Center
5701 Marinelli Road,
North Bethesda, MD 20852
USA

REGISTER

<http://www.diaglobal.org/en/conference-listing/meetings/2018/02/regulatory-submissions-information-and-document-management-forum>

TRIAL MASTER FILE
TMF
REFERENCE MODEL

DIA RSIDM

▶ Tracks

- **RIM Business** track addresses processes for obtaining and managing regulatory information, organizational impact, and key issues shaping the global regulatory and business environments.
- **RIM Technology** track focuses on standards related to submission of regulatory information, tools to effectively manage the information, implementation experiences and results, and implications for refinement.
- **Electronic Regulatory Submissions (ERS)** track explores the submission process, regulatory requirements and new developments, best practices in regulatory submissions and industry adoption techniques.
- **Electronic Document Management (EDM)** track examines the processes, systems, and best practices for content management across the product lifecycle, including alignment with the RIM system for optimal use of regulatory information.

▶ Link to agenda

- http://www.diaglobal.org/Tools/Content.aspx?type=eopdf&file=%2fproductfiles%2f6641340%2f18003_program%2Epdf

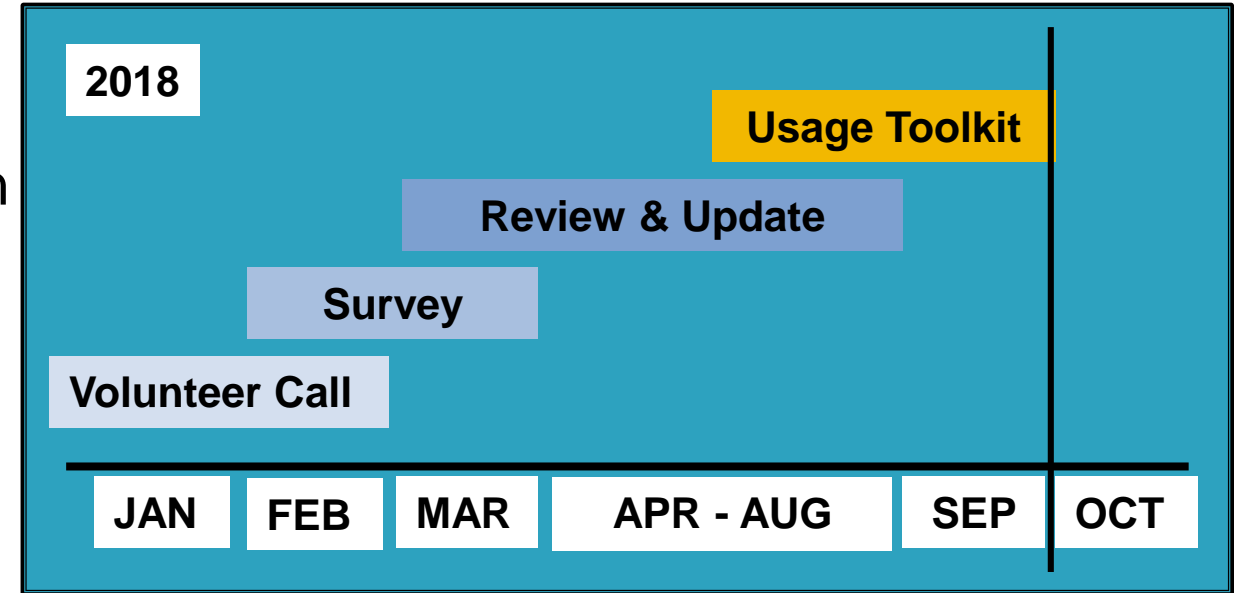
DIA RSIDM:

Exhibiting Companies

- Ideagen Plc
- IRISS Forum
- Cunesoft Inc.
- Cardinal Health
- RegDocs365
- ENNOV
- Planet Pharma Solutions
- PAREXEL
- Generis
- Pharmaceutical eConsulting Inc.
- Veeva Systems
- i4i Inc.
- ACUTA LLC
- Extedo, Inc.
- Schlafender Hase Inc.
- IQVIA
- Litera Microsystems
- Omnicia Inc.
- NNIT Inc.
- Wingspan Technology Inc.
- Sylogent
- LORENZ Life Sciences Group
- Cabeus, Inc.
- Author-it Software Corporation
- DitaExchange
- RegCheck
- IDENTIFICA
- Intagras, Inc.
- HighPoint
- Biologics Consulting
- AMPLEXOR Life Sciences
- ArisGlobal
- Instem
- DXC Technology
- OpenText
- Synchrogenix
- ShareVault
- Montrium
- Paragon, now part of CGI
- PRA Healthsciences
- Dossplorer
- MasterControl
- Accenture
- FDA CDER Office of Business Informatics
- DDi LLC
- Corementum Enterprises Inc.

Frame for the Destruction of Paper Refresh Activities – Call for Volunteers

- ▶ Framework was published in 2012.
- ▶ Used widely by many companies to define policies and SOPs for the creation of certified copies and destruction of paper documents.
- ▶ It is time to Review and Update the current recommendations in the framework based on industry technology & process changes and regulatory agency publications/advice.



- Call for volunteers in the following areas:
 - Survey Team
 - Requirements from Quality, Records Management, Regulatory, Technical and Legal perspectives,
 - Creation of Toolkit for implementation

Contact Lisa Mulcahy for more information and to be added to team.

Send Lisa an email:
mulcahyconsulting@comcast.net

TMF RM General Meetings

- ▶ 19-Mar
- ▶ Add to your calendar NOW or download the calendar file (.ics file) when you receive the meeting notification from MailChimp
- ▶ Outlook Meeting Request no longer distributed



QUESTIONS?

Join the TMF Reference Model Yahoo! Discussion Group

<https://groups.yahoo.com/neo/groups/tmfrefmodel/info>

- Knowledge sharing
- Networking
- Too Much Fun!

Join the TMF Reference Model Project Team
(but be prepared to work!)

<http://tmfrefmodel.com/join>