M-Files QMS Benefits for Clinical Trial use

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M-Files QMS, the metadata-driven, regulatory compliant Enterprise Content Management (ECM) system, provides a refreshingly different approach for conducting clinical trials and managing their massive Trial Master Files and other documentation. The key idea is that M-Files is not just a trial-related document repository, but covers several trial-related processes, systems and databases with a single easy-to-use system, with everything linked together in a meaningful way. And when requirements evolve, M-Files evolves too without the need to embark on a risky, high-cost software customization project. Here are some details:

- M-Files QMS provides a powerful and easily configurable ***database for clinical sites and site personnel*** across all your investigational products, trials and phases, including all site documentation (e.g. site qualification reports, equipment etc.) and their personnel (e.g. FDA 1572 forms, CV's and other such content) with full version history and audit trail. The site database is useable for sponsor, CRO or SMO areas, and greatly helps site qualification, feasibility studies and quick initiation of new trials that utilize existing sites.

- M-Files QMS with clinical trial vault structure provides a set of ***CTMS features*** for tracking all clinical project tasks and activities on a trial-, country- and site-level. ***M-Files Dynamic Views*** and ***M-Files Reporting*** capabilities provide the necessary trial overview, while built-in ***M-Files Calendar*** maybe used to schedule trial monitoring visits, meetings, submissions deadlines, and provides a familiar overview of trial activities. Unlike typical CTMS systems, M-Files can be tailored without any programming, and without risk of breaking the 21 CFR Part 11 compliance features of the underlying M-Files core platform. Tailoring allows meeting trial-specific or IMP specific CTMS needs e.g. special investigator payment reporting etc. Finally, in M-Files all the trial activities and tasks are directly associated with all the documents produced. For example, drill down from a site monitoring visit to find all its documents like monitoring reports, confirmation letters etc.

- M-Files provides a powerful, ***metadata driven document repository*** for both essential trial documents and all working documents in a single system. M-Files metadata architecture all document are classified correctly upon save, and found later in all to correct places without locking them down to a single folder. It is possible to apply any TMF Indexing i.e. document classification structure, including but not limited to, DIA TMF reference model. Consider the following:

- A protocol amendment which is only applied in e.g. Germany will appear simultaneously in views:
  - Documents by Country/Germany
  - Documents by type/Protocol documents

- If a certain SOP is only followed on three sites, it is associated with them via metadata, after which it automatically appears under all three sites' documentation. There's no need to copy it into three folders, and if the SOP is updated, the same version is instantly and automatically present in all necessary locations.

- Unlike with many other trial related document systems, all relevant authoring and review work can, ***and should*** be done within the M-Files system from first early draft. This is a better process than just using the system as the 'final resting place' of trial documents, which then excludes the full audit trail of document related work. And using M-Files' M: drive for daily document work is as easy, if not easier, than using My Documents folder or similar familiar location.

- M-Files QMS provides means to finalize all trial documents with ***electronic and digital signatures***. No 3rd party software is necessarily needed as eSigning is available in M-Files configurable workflows out-of-the-box. Signing workflows can easily be tailored depending the document in question, and M-Files can provide the finalized, signed PDF documents the appearance of the signed documents with necessary signature manifestations, watermarks, special header/footer, stamps, and more. Finally, it is possible via a minor-to-moderate customization effort to integrate with well-known 3rd party signing providers from M-Files user interface, including but not limited to, ARX Cosign™, DocuSign™, Signom™ and ComSign™. Please contact us for details.

- M-Files metadata architecture allows you to show existing content in more than one virtual folder structure as needed, and also export the content in any desired folder structure. This allows many surprisingly simple and make-sense features, like:

  - Show all working documents in the familiar folder structure that makes sense to your team, (e.g. looks like the network drive or SharePoint folder trees you used before), or is according to your in-house TMF index as described in your SOPs. Then, show the very same content simultaneously in DIA TMF reference model structure for exporting purposes to your eSubs system for eCTD or RPS packaging.

  - Show all documents per site, including all unofficial documents and drafts, in one folder structure, but only show the finalized site TMF in another view.

- M-Files QMS makes a great ***Adverse Events*** follow-up system (AE, SAE, SUSAR) both for drug safety work during trial conduction as well as post-trial continuous pharmacovigilance. Everything about an

individual case, including all its classification data (indication, severity, concomitant medication etc.), potential follow-up cases, associated documents, faxes and email messages, and all the work done with the case can be instantly found. M-Files' MS Office integration can even fill most of your CIOMS report forms for you based on a normal MS Word template. Following with the metadata theme above, a serious adverse event (SAE) on e.g. site 123 will be found both in drug safety listing as well as site 123's documents.

- During early trial conduction there's need for several ***submissions for regulatory and ethical approvals***. What this means is shipping document collections with necessary cover letters for authorities and committees, tracking all communication and clarification requests going to either direction, capturing essential documents and letter coming back, and following up the deadlines associated with this critical phase. M-Files provides great tools for tracking these type of submissions. A single document (i.e. final protocol or Informed Consent form) may be included in several submissions simply by including it via metadata to necessary outgoing submission collections. Once sent out for approval, M-Files built-in Document Collection feature allows 'freezing' a certain set of documents shipped out in their current versions. Later the documents may evolve to new updated versions, but the document collection will still show the exact versions that were sent out.

- M-Files system is ***configurable to an unprecedented level***. Instead of thinking all possible use scenarios in advance, and building those into a huge and complex user interface, we will more likely ask you: here's the default M-Files Clinical Trial vault. Tell us what's missing, and a few hours later it will be there. Need to follow special toxicology reporting? Need to classify sites by who has certain dental imaging in place? Need to notify instantly your drug safety committee members when a new SAE case was recorded? No problem! *We are well aware that this may sound like a bold statement. We hope to show some of these feature live, as this is just a more convincing approach than providing any marketing literature on this topic.*

- ***Emails*** are surprisingly vital key document type for clinical trials today. Emails form 90 - 100% of essential trial correspondence. Emails remain the de facto standard for communication and even limited document exchange between companies, subcontractors and clinical sites. M-Files provides unprecedented ease for tracking essential emails simply by drag & drop within your email program, followed by instant classification e.g. what site these emails are about, what TMF area or areas is covered (contracts, personnel, facilities, an ongoing adverse event, IMP shipments etc.).

- In clinical trials a lot of ***paper documents need to be scanned***, often due to the need to provide a handwritten signature. Using M-Files client software user is presented with a local virtual M: drive, where any documents can be saved or scanned directly, just like saving them to My Document folder or your C: drive. Documents are instantly saved to the common repository or to a common Cloud Vault via a ***local*** M: drive. This provides efficiency and ease of use which is simply not achievable with any web-based systems. M-Files excellent scanner support covers both personal, pc-connect desktop

scanners and central network scanners and multi-function devices. Documents can be classified as you scan, or do a mass scan operation first, followed by metadata classification which then makes the scanned document appear in correct locations of the TMF.

- Many clinical trial activities take place on clinical sites i.e. 'on the road'. In many cases CRAs and other trial personnel need to work in absence of any network connection. ***M-Files Offline use*** allows keeping essential documents and data (e.g. contact information and site visits) locally on your Windows laptop, and work on any documents on site or during travel. Once connected to your M-Files server, everything gets synchronized with the server, without the need to manually move files around.

- Clinical trials are often long and complex projects. ***Unforeseen mid-trial personnel changes*** are one of the biggest risks for quality, compliance and timelines. M-Files folder-less metadata architecture helps recovering from personnel changes by providing a single view containing everything about any given person: everything that this person created, modified, signed, was currently working on, or that was assigned to this person can easily be found, and assigned to someone else. Any person can take the Substitute user role in M-Files (built-in feature) which automatically gives the new person all the credentials but also all the responsibilities of the person who just left.

- Clinical trials are very seldom conducted by one sponsor company directly involving one or more sites. Instead there are several companies involved e.g. CROs, SMOs, IT system providers, investigational product provider, delivery and shipping companies, individual freelancer CRA's, and so on. Sharing content live is still not trivial, and the fact that so much can only be shared by sending email is a clear testimony of that. Even going to Cloud does not alone solve the trusted sharing puzzle; an isolated silo in the Cloud is still a silo. M-Files unique metadata driven permissions allows ***safe and easy sharing of content with external parties***, and frees organizations' IT departments from setting up and constantly maintaining access control rules and security group memberships. As the sponsor company, let your CRO access your clinical trial system, and follow up both their performance and document filing in almost real time. As a CRO capture all trial activities, and securely share finalized trial content you're your customer on a project-by-project basis. Here's how:

    - If the trusted external user e.g. a freelancer CRA is a new collaborator, ask your IT team to sign necessary paperwork, provide this person login credential, and walk through the initial login.
    - As a trial administrator, set up a new project in M-Files
    - Add necessary personnel to the project as its metadata
    - Now the external person can only see the project or projects he/she has been involved with, but nothing else. The same applied to all content about the project e.g. sites, visits, personnel and all documents.
    - For any mid project changes trial administrator only needs to keep the trial team list up to date in M-Files, no IT involvement needed unless user needs helpdesk support

- At any time get a full picture of actual current permissions: see who has access to which projects, or the other way around, a full list of all content a given person has access to
- As M-Files keeps a full version history also about the project itself (not just its documents) it is possible to see not only who has access to the project now, but also who has had access in the past, and who authorized the change that let this person in or out of the project

- As a system with full audit trail, compulsory version history and soft delete, M-Files allows ***recovering from user mishaps*** without resorting to backups. For any given document collection, or any work done by e.g. given person, it is possible to 'wind back the clock' or un-delete any content using only M-Files itself.