Responses to Questions Raised During the TMF Reference Model e-Mail Communications Webinar on 15-Jan-2021

Q1 If you file contemporaneously, how do you avoid filing duplicates? How do you define when the e-mail correspondence is final?

> **A1** Please see the "File as you go" section and the "Determining the final e-mail" section on page 6 of the Guidance.

Q2 What is your recommendation regarding the use of zip files to upload multiple e-mails relevant to same subject or related correspondence?

> **A2** This is not considered a best practice.

Q3 How do you ensure that CROs file only *relevant* communication with sites and not *all* communications with sites? The latter is easiest for them because they don´t need to make a decision on relevance?

> **A3** Establish a clear definition of what constitutes a relevant communication and embed compliant practice within your organisation. Document relevant communications "business rules" early during the creation of the TMF Plan and document the filing in the TMF Plan to avoid issues later.

Q4 Should you save each individual e-mail within an e-mail thread? Or should you save the entire thread as a single entity once the subject matter is closed?

> **A4** You may save the entire thread as a single entity once you have determined the subject matter is closed. However,
> - knowing which is the "final" e-mail can be difficult and
> - dependant on e-mail branching or changes to the subject matter, it can also be difficult to ensure that ALL the messages in the thread are included in the "final" e-mail.
>
> Please see the section "Changes to the Subject Matter of an e-Mail" on page 10 of the Guidance and the accompanying illustration "Fig 1: Diversifying e-mail threads".

Q5 If e-mails are copied at time of origin to a central e-mail address (repository) and a "pointer" in the TMF states that is the location of e-mails, is this considered "filing in the TMF"?

> **A5** This depends entirely on each organisation's rules.
>
> There is no requirement to have all TMF content co-located and so an organisation may choose to keep e-mails within its e-mail client. Where e-mail communications are retained elsewhere, this should be signposted in the TMF Index provided to the inspector during regulatory inspections.
>
> However, potential problems associated with this approach are
> - MHRA regulatory expectations are that inspectors will have direct (not supported or guided) access to the TMF: this will be difficult (if possible at all) to achieve if e-mails are retained in the e-mail client unless the inspector has an "…@organisation.com" e-mail address;
> - communications are not necessarily readily available;

- communications are not necessarily effectively organised or maintained in context e.g. by section or alongside the artefact to which they relate; and
- it may be difficult to argue that the TMF is contemporaneous if e-mails are not filed within the TMF.

It is good practice to keep communications within the relevant section of the TMF, because:

- e-mail communications are an important component for inspectors that enable them to reconstruct key study activities and understand decisions taken; and
- absent, sparse, and incomplete e-mail trails are a common area for regulatory inspection findings.

Q6   One of the primary reasons for e-mail being such a pain point is that we tend to just dump all e-mails into the TMF without any evaluation of their relevance. How do we get teams to feel more confident with understanding what is relevant and what is not?

A6   Each organisation should clearly define "relevant correspondence" or "relevant communications" then share, educate, and train staff (including CROs and other partners) on the definition and requirements. Make sure that expectations are clarified and clearly communicated in instructional information e.g. SOPs, work instruction, TMF conventions and "business rules" etc.

Q7   If the e-mail is filed in .msg format with attachments, but it is a rule to share only viewable renditions with Inspectors and the rendition does not contain the attachment, is this an issue?

A7   It depends on how the system renders .msg messages. Some systems allow the attachment to be downloaded from the rendered version in the eTMF. If that is not the case, you will need to know where the attachment is filed if filed separately e.g. filed with the specific artifact.

Q8   Would it be fair to apply this "e-mail" guidance to instant messaging solutions as well?

A8   The Guidance does not provide recommendations regarding Instant Messaging. Discuss the options available with your IT and Legal departments.

Q9   Should you rename the e-mail when saving it in the eTMF or should it be saved with the name auto-generated by the e-mail client? The first would be useful to explain the topic (especially if the subject line is not exhaustive)?

A9   It depends on how the system saves messages: eTMFs will vary on how the file names are handled, you may also use metadata to describe the message if necessary.

If saving directly from Outlook to .msg format, you will have opportunity to re-name the message with a name that is self- explanatory and meaningful.

Q10 Should you use .pst format for archiving? You can export all your e-mails (thousands) from your Outlook in one .pst file and then (before filing) unzip and file. They will be all in its native format with attachments.

A10 No, the main problems with .pst files are:
- it is not an archiving /long-term format;
- it is a proprietary Microsoft format so unsuited to those using alternative e-mail clients e.g. Lotus Notes, G-mail etc.
- it is often restricted to 2 GB file size;
- it is notoriously unreliable, never intended to store large amounts of data long-term;
- it is prone to corruption especially if the file grows beyond the limit or is accessed by more than one user at a time;
- risk of data loss (most .pst files are locally with no routine backup); and
- it complicates the e-discovery process because .pst files are effectively "off the grid".

Q11 Is it acceptable to keep e-mails in a central study inbox and have a pointer or NTF pointing to the storage location (i.e. can the central study inbox be considered a part of the TMF)?

A11 See A5 above.

On a more general point, NTFs should not be used to record routine filing practices, but used in extraordinary circumstances to explain exceptional situations and the remedial action(s) taken to prevent recurrence.

Q12 Is it a good idea to store relevant e-mails in the dedicated location in the eTMF according to the topic e.g. and e-mail of sending a protocol stored in the eTMF protocol section?

A12 It is for each organization to provide guidance on the filing of relevant communication. In addition, the TMF Reference Model does have a relevant communications section within each zone for filing.
For options, please see the section "Filing Locations / Classification" on p7 of the Guidance.

Q13 Is it acceptable to file all e-mails in one location in TMF instead of in various sections, especially if subject lines are clear?

A13 See A5 above.

For options, please see the section "Filing Locations / Classification" on p7 of the Guidance.

Q14 As embedded links are typically used to enhance communications and provide information with ease and expediency to the readers, does limiting its use for archiving ease then reduce the effectiveness of communication?

A14 Avoid the use of embedded links in e-mails because of the difficulties of maintaining traceability between the e-mail and contents in the embedded link. Please see the section "Embedded links" on pp9-10 of the Guidance.