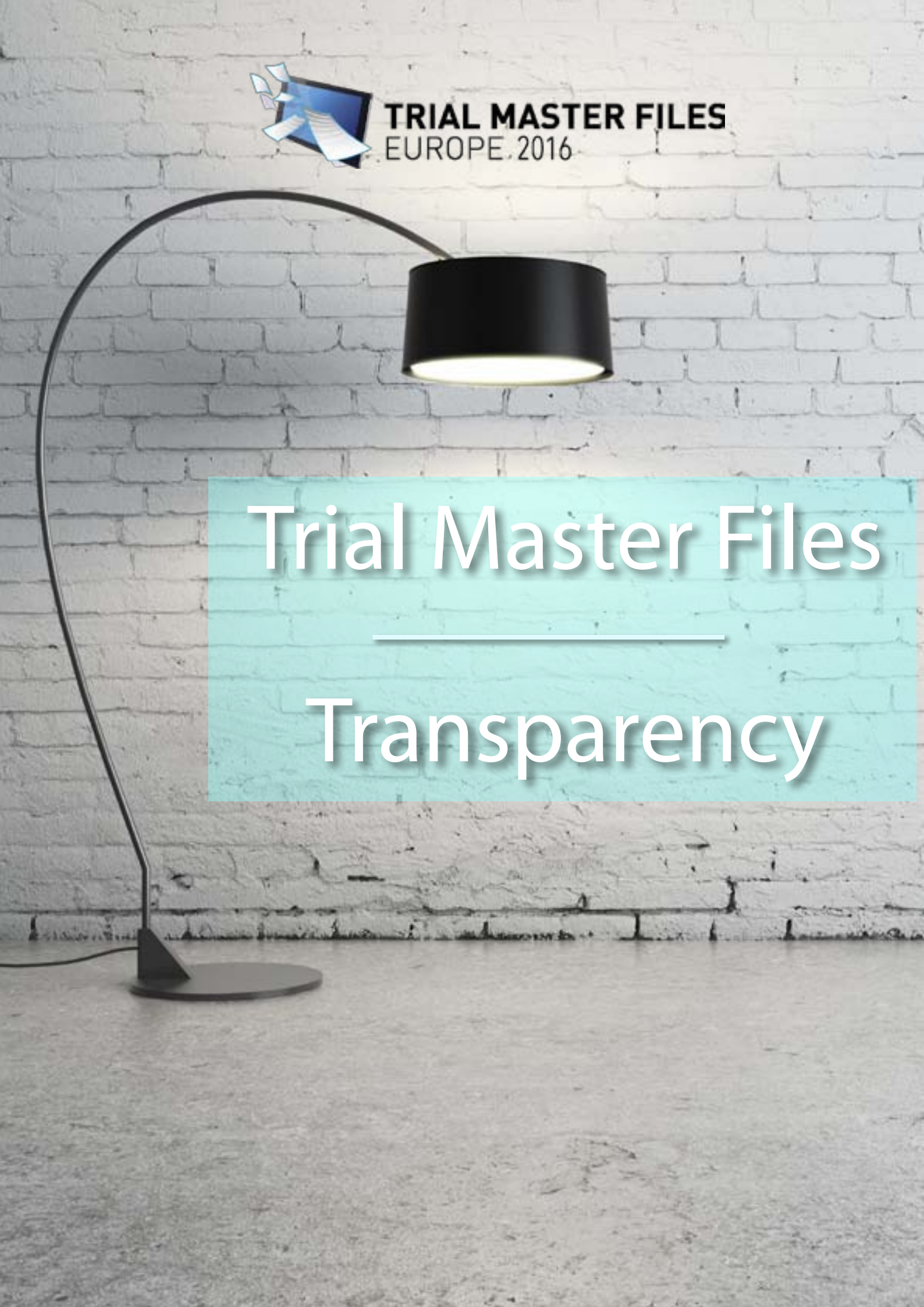
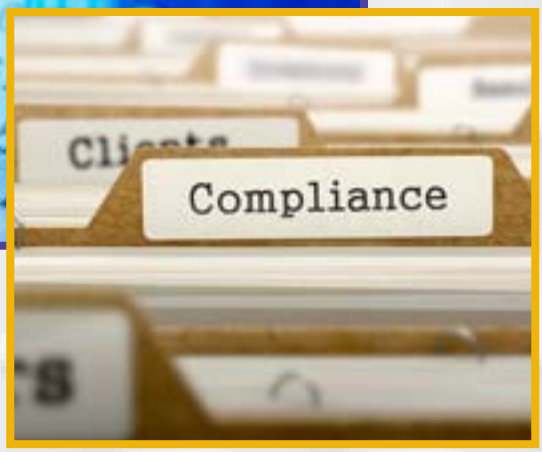

TRIAL MASTER FILES
EUROPE 2016
Trial Master Files
Transparency

Trial Master Files - Transparency



In striving towards having an inspection ready TMF, which comprises of thousands of documents and in most cases the work of multiple parties, it is the legal responsibility of a pharma or biotech firm to have a solid grasp on the actual status of the file. By having complete visibility on how far away the reality of an airtight Trial Master File is, this provides the pharma firm with an opportunity to alter the project's trajectory if needed. This transparency can be preserved via a range of avenues which include having: solid metrics, clear oversight, frequent exchanges with the CRO and accurate understanding of the required documents.

CRO Oversight

In commissioning a CRO to manage a clinical trial, according to EU regulations the pharma or biotech firm is still responsible for the trial and so they need to retain complete oversight. Inevitably, a sponsor's access to the TMF will be required, which is simplified by the electronic format. The sponsor will also have to decide what proofing needs to be sent by the CRO, so they can ensure the required level of documentation is obtained. Sponsor representatives need to at any given point have an awareness of the project's progress and its level of quality. UK regulatory body MHRA clarifies that this should stretch to the presence of guidance in the organization to assist the Chief Investigator in maintaining the files via audits. The body added that outsourced workers can be held accountable with oversight documents and plans held by the sponsor's governance department.

In Pharma IQ's 2015 industry research, the effective management of CRO interactions – was voted as the predominant focus for the following 12 months.

When outlining an oversight strategy it is wise to establish the CRO's awareness of their responsibilities at the start of the project. This also provides a good opportunity to finalise aspects like how often documents should be uploaded, QC checks and oversight guidelines for the sponsor.

An e-tmf system, coupled with quality metrics that enable the collation of special overview reports, can provide a dashboard view to a sponsor so they can

fully grasp the status of the TMF. This can reveal for example how many of the file's 10,000 documents received spot checks from the CRO and what findings have been uncovered.

Standardising quality metrics

Despite the power of quality metrics, in a recent research survey, only 10% of participants noted implementing and improving a metrics programme as a top priority for the next 12 months. In response to those who may not be fully utilizing the scope of quality metrics, Linda Hoppe of UCB noted that in the creation of these metrics it's important to respect an e-tmf system's capabilities.

She noted that the creation of TMF metrics are important to monitor and keep oversight of the TMF quality & completeness, it's important to choose those which are quantitative and measurable.

Linda Hoppe adds that the DIA reference model should be considered as an agreed industry standard as this would eradicate the need for mapping between different TMF structures. The use of a global industry standard would also enable the exchange and integration of information.

Integration and frequent exchange of information

Outsourcing provides the advantage to preserve resources and potential costs with operational business being conducted by an external party. In some cases, the presence of high quality and knowledgeable partners can result in less knowledge being retained in-house, which some chart as an advantage. However, some have noted that could cause complications in regards to visibility. One solution for this is the facilitation of reliable integration and the exchange of information.

With maintaining an up-to-date information exchange between sponsor and CRO, Linda Hoppe noted that the most common mistake seen is that expectations are not transparent enough or clearly addressed. In achieving this, a project plan should be created, which clearly addresses timelines, accountabilities, communications and risk management tactics so that all involved parties understand the expectations and responsibilities. After this point, she clarified: "I think it's essential to have regular meetings [and] calls, to align on what the expectations

[and hurdles are] and where improvement is needed."
Automated data transfers which operate in the background of daily business can be applied to simplify this process in places. Also, it's crucial that the systems of the sponsor and CRO are interoperable. Data points can cause issues in this regard.

The use of eTmF applications are seen as the most popular exchange method for TMF documents from pharma to CRO, with post or portal being the least popular. Within last year's 2015 Pharma IQ TMF research, simplified collaboration with external parties, enhanced visibility, higher TMF quality and increased operational efficiency were all labeled as dominant benefits to an electronic TMF system. Full e-TMF integration can take upwards of 12 months, a airtight compliant e-tmf system could require two to three years.

Grasp of essential documents

With the trend of R&D outsourcing is retaining its surge and the substantial level of CRO players in the market, alongside to maintaining continuous up-to-date information exchange with sponsors, good quality TMFs are seen as a key differentiator.

In producing an inspection ready TMF for a sponsor, a CRO must hold an accurate understanding of what essentials documents are required. The potential consequences of lacking this awareness would surface in inspection findings declaring that the TMF is not current. In more serious cases, depending on which documents are missing in the file, major or critical findings could be issued, which could snowball into a refusal of the submission or even a loss of marketing authorization.

Education again is the key to preventing these outcomes, by ensuring all staff are aware of what needs to be filed, when and where. Periodic file reviews will assist in the management of this. An apt tactic to apply is to build this knowledge in as a standard operating procedure (SOP) requirement.

The achievement of transparency within the range of aspects discussed can be significantly instrumental in obtaining an inspection ready TMF.

Resources:

1 http://www.pharma-iq.com/clinical/white-papers/the-state-of-trial-master-files-2015-survey
2http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2013/02/WC500138893.pdf
3 http://forums.mhra.gov.uk/showthread.php?1665-MHRA-produced-FAQs-for-Trial-Master-Files-(TMF)-and-Archiving

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In September 2016, join 70+ industry experts in Barcelona to address the biggest challenges hindering the successful development and management of TMFs.

Reasons to Attend

- **CASE STUDY:** UCB Share Their TMF Insights
  Linda Hoppe, Trial Master File Manager, UCB
- CRO Interactions – Best Practice Management session
- Optimizing Performance and Quality Metrics to Improve TMF Processes

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