A Leaner and More Proportionate Approach to Reporting Risks in Clinical Trials

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INTRODUCTION / BACKGROUND

The European Medicines Agency, in their recent reflection paper[1], suggests that the current approach to clinical quality management is in need of review and reorientation. The paper aims to encourage and facilitate the development of a more systematic, prioritised, and risk based approach to quality management of clinical trials, in which GCP complements existing quality practices.

During the conduct of a trial, management overview of the risks encountered relies on if (and how) risks are flagged, and next reported; a prerequisite for risk mitigation/risk acceptance to take place next. At the same time, the process of risk management and the decision-making steps involved also need to be documented, in line with GCP requirements. Risk based quality management is needed, preferably designed as a lean and proportionate 'consumable' or product.

Can the key to leaner and more proportionate risk based trial management be in making better use of IT?

METHODS

On display is a trial with emphasis on central monitoring, but site visits do occur (based on expected potential or actual flagged risks). In the planning phase, risks 'that really matter[1]' are identified, categorised to either 'minor', 'major', or 'critical', with matching follow-up for mitigation / acceptance. All is documented in the (trial specific) Monitoring Plan. Guidance is also provided on how to deal with unexpected risks, that may be flagged along the way of the trial's life cycle. Concretely, each risk category is tied to a different turn-around-time for management review.

OpenClinica (OC)[2] is an open source, low cost, web-based eCRF application. OC can easily be programmed to send e-mail alerts to the monitor/trial coordinator, once a pre-defined risk is met (in Figure 1; when a serious AE is entered, or when an AE is entered with a probable or definitive relationship to the intervention tested). The monitor/trial coordinator takes notice of the risk, reviews (remotely, Figure 2), and assigns the risk category.

JIRA[3] is a low-cost web-based team tracking tool, providing issue tracking and prioritisation of team actions. In a JIRA project, risks flagged via OC / site visits / central monitoring will be manually entered, automatically assigned a unique number, categorised and assigned to a certain user (Figure 3). JIRA entries are logged (audit trail).

The (authorised) JIRA project users can comment on, forward, escalate, or link, etc. the risk. Eventually the risk gets 'closed'. A user-specific dashboard displays real-time metrics such as issues 'open', 'in progress' (Figure 3). Moreover, Trend Analyses, Key Performance Indicators[4], etc. are visible to all *ad hoc.*

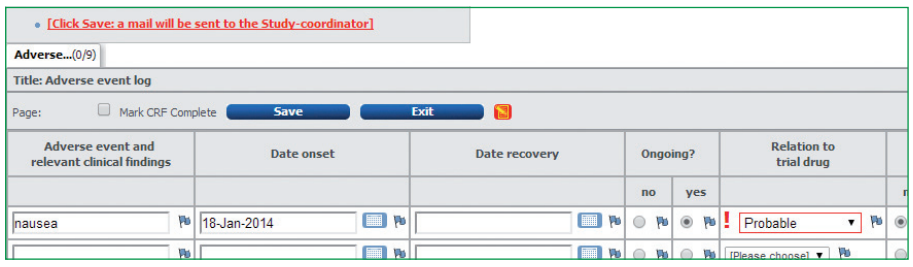

Figure 1: Data entry action, alert pops up, if pre-defined 'probable' field selected. If saved like this, e-mail is sent.

	Study Subject	AE_AdverseEve	AE_StartDate_E1_C1_	AE_Serious_	AE_Relation	AE_AdverseE	AE_StartDate	AE_Relation_	A
3	F01001	headache	7-1-2014	no	no			0	
4	F01002	rash	7-1-2014	no	possibly			0	
5	F01003	appendicitis	9-1-2014	yes	no	sore foot left	9-1-2014	possibly	
6	F01004	headache	18-1-2014	no	probably			0	
7	F01005	nausea	18-1-2014	no	probably			0	

Figure 2: Central monitoring action/review. 'dataset' export to MS-Excel, contains all AEs reported thusfar.

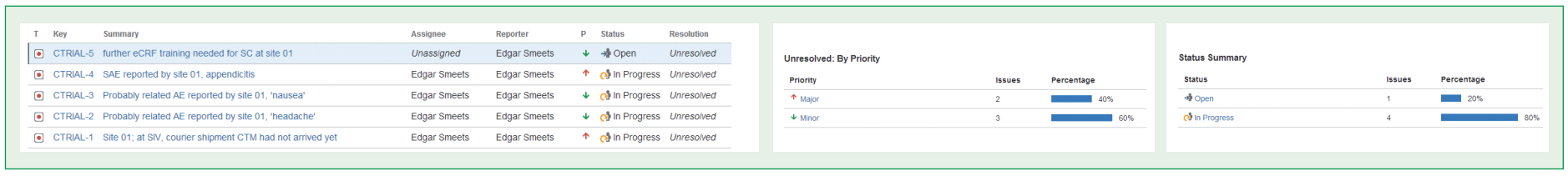

Figure 3: A few overviews from JIRA

CONCLUSION / DISCUSSION

(Central) Monitoring (Visit) Report Improvements -> Added Value to Management Review[4]

Based on the above, the study monitor's role is efficient, with leaner reporting to study management. The monitor's report consists of pre-defined topics. With each, the first question is 'was a risk flagged?' If so, the unique JIRA number(s) is/are entered. The report reviewer uses the unique number to find necessary details in the project's JIRA. Other monitoring findings (i.e. the ones that matter less) are briefly described. The chance of important risk related information going astray, is minimal. Reporting in this manner has potential towards quicker and better decision making.

Footnotes:

1. *Reflection paper on risk based quality management in clinical trials. European Medicines Agency. Nov. 2013*
2. *Please visit www.OpenClinica.com for details. Community Version 3.1.4.1 was used. Use of this version is without cost*
3. *JIRA by Atlassian. www.atlassian.com. v6.1.5 was used. 10 users can be assigned for 10 USD/month*
4. *e.g. in order to comply with ISO 9001: 2008 'Quality Management System'*

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