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Protocol Feasibility Workflow Using an Automated Multi-country Patient Cohort System

Iñaki SOTO-REY[a,1], Benjamin TRINCZEK[a], Töresin KARAKOYUN [b], Martin DUGAS[a] and Fleur FRITZ[a]
[a] *Institute of Medical Informatics, University of Münster, Germany*
[b] *Coordination Centre for Clinical Trials, Medical Faculty at the Heinrich-Heine-University Hospital Düsseldorf, Germany*

Abstract. The Electronic Health Record for Clinical Research (EHR4CR) project aims to improve the current process of clinical trials, providing a technological platform that supports the design and execution of trials. For the protocol feasibility scenario, the system currently allows the user to create a set of in-/exclusion criteria to find patients matching these criteria across sites located in several countries. The automated multi-country patient cohort system developed in EHR4CR implies substantial changes on the current protocol feasibility process, which will be reflected in this study.

Keywords. Clinical Trials as Topic, Feasibility Study, Electronic Health Record, Workflow

Introduction

Clinical Trials (CTs) hold a key position in the development, improvement and production of new medication and therapeutic procedures. The cost of the design and execution of CTs has been increasing during the last years [1]. Furthermore, CTs are very often delayed or the initial budget substantially increased due to various reasons such as poor or defective study designs, lack of information or communication problems in the phase of protocol feasibility (PF) [2].

Every CT starts with a feasibility study, also called PF. In this phase, it is evaluated whether it is feasible to run the CT in a particular geographical region. This evaluation includes timelines, targets and cost [3]. Over the last few years, research has been intensified on patient recruitment and trial execution, whereas the PF phase has been placed in a secondary position. However, according to the experts, the PF phase holds a great need and potential for improvement [4].

The EHR4CR project [5] aims to improve the current process of CTs providing a technological platform that allows both research and medical institutions to efficiently perform all the steps involved in the design and execution of CTs. This is achieved

[1] Iñaki Soto-Rey, Inaki.SotoRey@uni-muenster.de.

through a better leveraging of routinely collected clinical data in the trial design and execution life-cycle [6].

For the PF scenario of the EHR4CR project, the system currently allows the user to build queries based upon in-/exclusion criteria and find patients matching these criteria across several countries and sites [7]. The purpose of this study is to demonstrate how an automated multi-country patient cohort system, such as the EHR4CR system, changes the current PF process by automatizing many of the steps implied.

1. Methods

Our first activity was to define the current (as-is) process in order to estimate how the EHR4CR system can improve it. There is no established general PF workflow and almost every one of the nine companies of the European Federation of Pharmaceutical Industries and Associations (EFPIA) companies participating in the project (see Acknowledgements) follows a slightly different process. With the purpose of defining a common new (to-be) process we have followed the DELPHI method [8] executing it in two phases (first Nov-Dec 2013, second Dec 2013-Jan 2014). Representatives of the nine EFPIA companies involved in the EHR4CR project participated in the study and answered the two questionnaires correspondent to the DELPHI phases. The first questionnaire contained one task and the second two tasks and four questions, all free text written, described below:

- First phase/questionnaire: Task to describe the current process of PF identifying all the steps and actors involved.
- Second phase/questionnaire: It contained the as-is common process resulted from the first questionnaire and the proposed to-be process supported by the EHR4CR system. The language used for modelling these processes was the Business Process Model and Notation (BPMN) v2.0 [9]. The clinical trial experts had to review the two processes and decide whether it fulfilled all the steps involved in PF. Additionally, they were asked about how the EHR4CR system could be improved and which modifications would be necessary so that the EHR4CR system in the future can cover all of the steps involved in PF.

2. Results

As a result of the two DELPHI phases, we obtained the concerted as-is and to-be protocol feasibility processes, as well as some interesting new possible features for the EHR4CR system that will be analysed in the discussion. The actors and process steps involved in the as-is and to-be processes are described as follows:

2.1. Actors

- Feasibility project team (FPT): a team consisting of a feasibility leader, statisticians, business intelligence consultants and other feasibility experts.
- Country feasibility manager(s) (CFM(s)): one to several country feasibility expert(s). If there is only one, he/she is also called “Global feasibility manager”, having the overview about all potential countries. If there are

several CFMs, each of them usually is responsible for one to some countries. Depending on this role's interpretation, some tasks of the CFM(s) might be taken over by the FPT.

- Site feasibility manager (SFM): a site feasibility expert.
- Principal investigator (PI): responsible person for investigation and research at the site.

2.2. As-is PF process

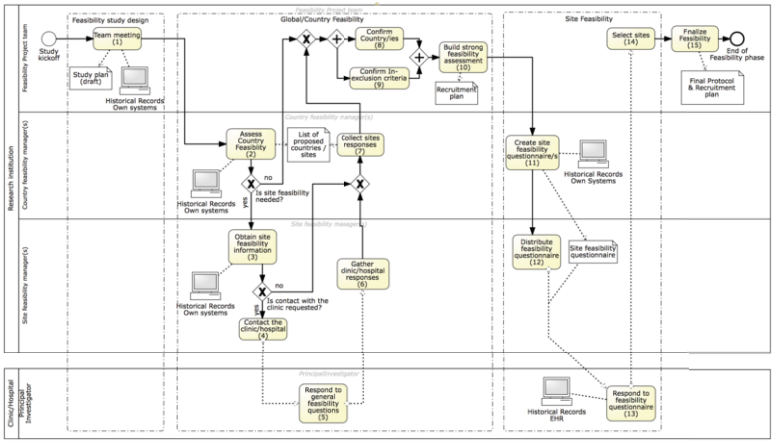

Figure 1. As-is PF process.

The process takes place at two companies or sites: the sponsor (research institution) and site (clinic/hospital). It depicts information gathering and refinement of the PF from the early plan, drafted by the FPT, down to the expert's knowledge and opinion (SFM, PI) and back to the FPT.

The PF phase starts with (a) preliminary meeting(s) (1) where the outline of the study is drafted by the FPT. Secondly, the CFM(s) perform(s) the assessment of countries that should participate in the study (2). This task may, in some companies and cases, need the assistance of a SFM. If so, the SFM checks historical records and company-owned systems (3). Eventually, PIs at the clinics are asked about predisposition for the trial and general feasibility questions (4, 5, and 6). Subsequently, the CFM(s) collect(s) the information from the sites and elaborate(s) an assessment of countries (7).

At this stage, the FPT has collected enough information to determine the in-/exclusion criteria for candidate sites and patients (8) and confirms the list of participating countries (9). With this a detailed (also called "strong") feasibility assessment is built, which is reflected in a document called recruitment plan or "extended synopsis" (10).

The CFM(s) receive(s) the recruitment plan and use(s) it as a basis to create a feasibility questionnaire with the support of historical records and company-owned systems (11). This questionnaire contains structural and organizational questions as well as a commitment of number of patients that will be enrolled at the site for this specific study and it is distributed by the SFM (12) via email, fax or company-owned

systems. In some cases, telephone calls or personal meetings are arranged between the SFM and the PI in which these questionnaires are answered (13).

According to the responses of the PIs, the FPT decides which sites are included in the study (14) and finalizes the feasibility phase with the creation of the final recruitment plan and feasibility assessment (15).

2.3. To-be PF process using the EHR4CR system

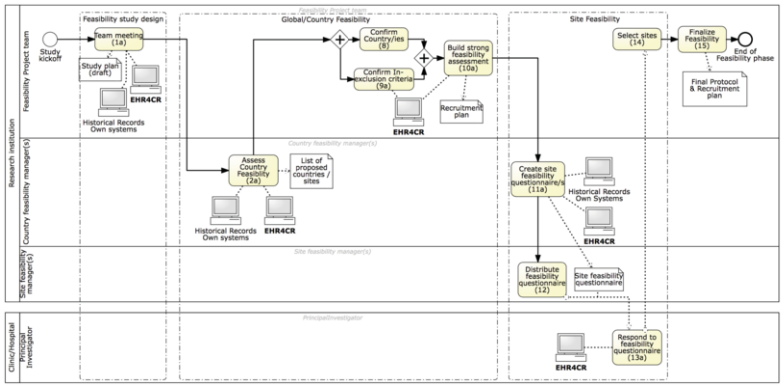

Figure 2. To-be PF process using the EHR4CR system.

The to-be PF basically includes the same process steps as the as-is PF. Out of the 15 initial steps, 5 could be deleted, because the country feasibility assessment is entirely performed by the CFM(s) now. Task numbers stayed the same to ease diagram comparison. Tasks that have changed due to additional support of the EHR4CR system are enriched by an 'a' in their task number.

In the proposed process, the FPT creates the study plan using historical records and their own systems as well as the EHR4CR query builder and historical records stored in the EHR4CR system (1a). Then, as explained above, the CFM(s) assess(es) country feasibility running queries through the EHR4CR system (2a) and create(s) a list of potentially eligible countries.

The EHR4CR system supports the determination of criteria (8, 9a) and the design of the recruitment plan (10a) with the execution of queries and the extraction of the query criteria in a human readable way [10].

The CFM(s) then create(s) the feasibility questionnaire using the recruitment plan, historical records, company-owned systems, and the EHR4CR system (11a), which is still distributed by the SFM following the as-is process (12). The PIs respond to this questionnaire now with the help of the EHR4CR system, from which they can retrieve information about historic patient counts by running selected criteria for their own site (13a).

Similar to the current process, the FPT decides which sites must be included in the study based upon the responses of the PIs to the questionnaires, (14) and finalizes the feasibility phase with the creation of the final recruitment plan and feasibility assessment (15).

3. Discussion

Our study demonstrates that EHR4CR can strongly support the PF phase of clinical trials by providing a tool that facilitates the design of feasibility queries and automatizes the country selection phase. Besides, we have identified interesting features not initially addressed in the EHR4CR project plan: To store results from executed trials and generate analytics from them, the possibility to send feasibility questionnaires through EHR4CR and eventually the creation of these questionnaires through the platform. This is relevant since experts interviewed emphasized the fact that approaching the local staff is both laborious and delaying.

By including the EHR4CR platform, the design of clinical trials, especially the eligibility criteria, can be based more on precise data than on experience and estimations. This might lead to a lesser number of protocol amendments needed.

The EHR4CR system is in a pilot stage and an evaluation of the system is still required, therefore it is soon to perform a substantial change of the current PF workflow. Nevertheless, with the modifications and additional features we have identified, EHR4CR could go from a country/site feasibility information tool to an ultimate feasibility system that covers all the steps of the process.

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