



# eClinical Forum Meeting Report

## 4-6 May 2011

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# 1 Overview

On 4-6 May 2011, the eClinical Forum met in Banbury, UK to discuss how existing and emerging healthcare environments impact on clinical trials, and the future role of eClinical trial technologies.

The meeting was held at iSOFT's headquarters and was opened by iSOFT chief executive Andrea Fiumicelli who explained that despite the enormous progresses made, much needed to be done to improve the delivery of healthcare, and in particular improve safety through better use of information systems.

He said: "If you take the aviation industry, when a Boeing or an Air bus crashes and 300 people die 100s of officers take all the pieces of the plane and make sure that everything is reengineered to have zero defects. We as an industry do not have this zero defect mentality."

He predicted that there will be a tectonic shift in delivery systems, with management of long term conditions and personalised medicine driving innovation and improvements.

## 2 New generation software - Lorenzo

Dr. Michael Dahlweid, Chief Medical Officer iSOFT said this paradigm shift required a far more person centric and non-facility bound healthcare delivery process to integrate care and bridge the gap between different services and facilities.

iSOFT has created Lorenzo to do this. Lorenzo is a technical architecture that allows healthcare organisations to construct their solutions “like a lego system”, Dr. Dahlweid said. It includes a chronological data repository for patient record management, a service repository of around 3,000 care activities to select from, which fulfil demands from different environments.

Stephen Richardson, UKI Solutions office iSOFT said: “Lorenzo is the only purpose-built health care system in a generation. It is completely new code built from the floor up. We have over 100 products in the iSOFT portfolio, and Lorenzo is the path we are taking with every one of those products and applying across the continuum of health care.”

Data access within Lorenzo can be configured to an individual user, according to their responsibilities or assigned according to particular roles. A patient can also decide that certain information, such as their participation in a clinical trial, should be hidden from all but specific individuals. Lorenzo can be populated with data that is native to the institution, messaged from another application or be read from other parties' database.

The forms within Lorenzo hold structured data capture elements and the native data values are held within the database, so when a piece of data is input into one form or updated it automatically does so in the other forms. Forms can be prepared offline and then the data uploaded.

Lorenzo can be configured to dictate that particular forms need to be completed in a certain sequence or at specific times, and the completion of a form or other event can trigger a message out to a clinician or the patient. A sequence of appointments can be booked and the time between each specified both as a range and as an optimal number. “That could be, from a clinical trial perspective, a sequence of appointments over many months,” Mr Richardson explained. Information can be highlighted and tagged for the attention of a specific individual or team.

The system protocol can also specify what happens if a patient does not follow the desired sequence, which could be the clinical trial schedule. For example, if a patient misses a step, he or she could be sent back to the beginning, or skip onto the next step.

The decision support element of the system will suggest referral if a patient has a particular symptom or set of symptoms. Mr Richardson pointed out: “There is no reason why those questions and answers couldn't lead to referral to review for clinical trial research”

### 3 Improving identity of clinical trial candidates

Identifying eligible patients for clinical trials is a constant challenge, and 58 per cent of clinical trials fail to achieve their recruitment targets. Dr Joerg Kraenzlein, Director of Life Science at iSOFT described a system being developed to help investigators and pharmaceuticals companies conduct trials more easily. “We want to build a network for physicians to collaborate, foster the use of personalised medicine and the production of clinical trials, and speed up the process,” he explained. In the absence of formal research databases, recruitment relies on physicians being aware that a trial is taking place and putting a patient forward, or investigators trawling through thousands of records to find suitable patients. Some countries are building tumour registers storing data on patients who could be appropriate candidates for trials in oncology, but collecting this information is cumbersome and there are few incentives for hospitals to do it.

Dr Kraenzlein said the most accurate and comprehensive patient data is usually stored at physician level. “Billing data is optimised to ensure more accurate reimbursement,” he said, “whereas documents exchanged between physicians are usually a good source of information. Physicians have to understand what the other did and create very structured and standardised documentation, therefore it is very easy with a natural language processing tool to extract that language and transform it into a structured database.”

In the system under development, patient records are de-identified and medical terms extracted to create the AccelCDB™ (Clinical Database). The investigator can then use the AccelFind™ web base application to identify suitable patients for the trial by defining the inclusion and exclusion criteria. Both of these products are developed by our partner CliniWorks™. The system can apply different levels of security to the end data for different users ranging from simple access to the aggregate data (number of patients identified), lists of clinical terms identified, to processed text stripped of patient identifiers. Only an authorised investigator will be able to access patient identifiable material.

Dr Kraenzlein said the vision was to have multiple sites connected to this service platform and then run the AccelFind™ protocol identification application on a broader level. The efficiency of the system in identifying patients has been compared against physicians selecting patients manually by trawling through 10,000 records. “It is pretty obvious. It just takes 5 to 10 seconds to screen 10,000 medical records, whereas the physician has to work for weeks,” Dr Kraenzlein said, “and the hit rate is really very high.”

Of the 42 patients who met the trial criteria, the physician picked up 30 manually, while the system highlighted 65 patients as potentially suitable. When the system’s choices were analysed by a physician, 41 met the criteria fully.

Dr Ulrike Schwarz-Boeger, of the Technical University of Munich in Germany, said finding eligible patients from the hospital information system at her hospital was not possible at the moment and tools like this would be very helpful.

At her hospital doctors have to input the same patient data into the hospital information system several times for billing, quality management and research purposes, because strict privacy laws make it difficult to access data already in the system for another purpose. This is frustrating and time consuming for the doctors. Estimates for double entry of data vary from 17 per cent to 80 per cent according to the health system.

The university hospital has 35 trials running, mostly in oncology, and recruitment is discussed at interdisciplinary meetings, and suitable patients are also referred on an ad hoc basis as doctors come across them in clinic. “,” Ms Dr Schwarz-Boeger said.

Data from the hospital system has been used to identify patients for two clinical trials as part of a direct data capture pilot in conjunction with Siemens. The data was put through a validated integration engine which assigned possible patients to the clinical trials. Privacy laws still caused some difficulties

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because the ban on patient data from being transferred through the internet hampered communication with other department which is essential to ensure serious side effects are reported within 24 hours.

The solution improved data quality and meant much less time and effort was required from the clinicians and study nurses, but unfortunately there was no money to fund roll out of the system, she said.

## 4 Bid for EU funding for ClinHealthCloud

The European Union has a budget of €50 billion between 2007 and 2013 for projects that strengthen the technology and scientific research base in the EU and help make the EU more competitive. In October last year bids were invited for €35 million under framework programme 7, challenge five.

The outcomes project had to meet to be successful included integrating healthcare in clinical research, solving the issue of double data entry, enhancing recruitment into clinical trials, ensuring interoperability (EN 136060), privacy, and contributing to research knowledge on epidemiology and patient safety.

A proposal team was put together to bid for €4 million to develop the ClinHealthCloud concept, and a 96 page document submitted by the 18 January deadline. Richard Perkins said that the aim was to bring together information from an electronic data capture system together with information from the electronic healthcare records systems in a data cloud environment. This would help avoid double entry, and information could be populated back into the EHR system. A copy would also be left in the cloud for future research on epidemiology or safety issues.

Extraction servers would take data from the EHR and EDR systems, de-identify it and load into onto a mediation server in the cloud, where querying servers would enable the data to be probed for research purposes.

Mr Perkins said: "We got a letter back from the European Commission on 12 April which was very positive. It confirmed that our submission had been reviewed by a panel of independent external experts. They confirmed that we had met all of the criteria for the proposal."

The proposal had been scored in three categories: scientific technical excellence, quality and efficiency of the implementation management, and the potential impact through the development and dissemination and use of the project itself. Each category was worth up to 5 points and the proposal had scored 12 out of 15 overall.

There were 12 applicants and a final decision on whether the project will be one of the five to be awarded funding. "If we don't get funding, we might come back to this and say 'can we still do something with the goodwill of all the consortium members?' May be scaled down, but still do something in terms of delivering this project," Mr Perkins said.

## 5 Update on progress with EHR4CR

EHR4CR is a large four to five year project funded by the Innovative Medicines Initiative (jointly funded by the European Commission and pharmaceutical industry). While the ClinHealthCloud is on technology, EHR4CR is about the processes and business models needed to make technology a success.

EHR4CR is focusing on four key areas: how to use healthcare data to evaluate patient populations, how to use healthcare data to accelerate patient recruitment, how to exchange clinical trials data, and how this data can be used to improve patient safety.

Ian Hamilton, Lilly, said resolving these issues involved improving feasibility, inclusion and exclusion criteria, and protocols. There are two key components the platform and the business model. The platform is the technology that is going to be offering certain services and this needs to be able to lots of different data complying with different standards (HL7, EN 13 606, and EDIFACT), be integrated and interoperable. Mr Hamilton said: "There is a lot of political pressure to achieve EHR. Politicians see clinical research needs as being one of the potential drivers to make that happen." The business model is about describing how this platform will be used, the role of the ethics committees and how it will be integrated with trusted third parties.

There are 31 different partners in the project and the eClinical Forum is leading on two tasks: defining the scenarios for the project and evaluating the pilots based on the business model.

The deadline for scenario development is March 2012. The core management processes, from protocol feasibility and patient recruitment to collecting and exchanging clinical trial data and adverse events detection and reporting, have been identified and are being worked through. Mr Hamilton said the focus has been the needs of clinical trials and the pharmaceutical industry, but that the needs of customers, vendors and technology providers would be taken into account by reality checking the concept.

Mr Hamilton said what was envisaged was a transformed anonymised dataset which is not just located at the site but federated in some way so that the investigator's query goes out to lots of different sites. An authorised investigator would then run the query again in a non-transformed set of data to identify named patients who potentially fit that profile.

"Our next challenge is to go into the detail of how all this would work, knowing that the project rejected using natural language processing and knowing that there are certain constraints imposed on us about what that transformed dataset should look like what data standards we should use," he said. A website is also to be set up to help investigational sites determine whether their EHR system conforms with the requirements for clinical research and to provide them with some advice on how to close any gaps.

Mr Hamilton said: "We could start to build a database of hospital sites investigational sites which are interested in doing clinical research and have already pre-validated their environment, even though they've done it themselves."

## 6 Accreditation of EHR systems

The eClinical Forum has sponsored a research project to develop minimum requirements for electronic healthcare records system to enable source data to be taken for clinical research purposes. There are two regulatory standards prominent in this area: HL7 in the US and EuroRec in Europe. "To make sure that our work would get recognised, really no matter where it was in the world, we went down both avenues with our user requirements," Suzanne Bishop, said. "We started with the HL7 functional profile and that was approved in 2009 and it quickly became ANSI standard (American National Standard Institute).

"We took those same exact requirements and made them into EuroRec profile. The only difference really is the nomenclature of how the two profiles are described."

The guidelines have CCH certification in the US, which is the certification by the body that certifies record systems. CCH is now in the process of adding clinical research requirements and this should be in place by July.

Ms Bishop said: "We are in the process of finishing a paper that will get rolled out with that on the practical considerations, explaining the extra things that a site needs to do to make sure that it can be used for clinical research." For example that a system is in place to ensure that the audit trail is turned on and that passwords are not shared. "The end goal is hopefully that your sites could be using software that has a stamp that basically says it is ready for clinical research," she explained.

A mock certification process on the profile to test it works in the way that it is expected to, contains information and that systems can be certified has already taken place in the US with the help if iSOFT and the next step is to do the same in Europe, said Alan Yeomans, Neptune.

In Europe the profile was approved by EuroRec and has been considered/approved by CEN/ISO, and the next step is to get some kind of certification procedure in Europe. Mr Yeomans added that a self certification process, which is commonplace in other industries, has already been piloted: "If you want to make a telephone with 3G technology you are responsible for making sure that you follow all the regulations and requirements. If you don't, then your telephone gets banned."

One question to be resolved is whether a formal certificate should be issued following self-certification or whether that should a separate process. Mr Yeomans asked; "Should step 1 be self-certification and then there is some sort of examination of that before we produce a formal certificate, or should it be an automatic: if you've done the self-certification you should get the formal certificate, which to me sounds a bit like these mail order universities in the States, and I'm not sure that is something that our industry would accept?"

## **7      Should clinical trial software be Open Source?**

Jens Thuesen of Business System Integration revealed that there are 19 vendors that make ePortal software, which help reduce paperwork and allow secure information exchange, and only a few hundred of potential clients.

A lot of this technology is quite old and expensive and Mr Thuesen predicted that not all would survive. "If I was a pharmaceutical company I would be very reluctant to buy a piece of software from a small company if I don't know the whether this company will survive in the future." He proposed that it would make sense to make ePortal software Open Source. "When you have an Open Source everyone can contribute to your source code. Everybody can say I can improve this they can send it back to you and say please include this."

He explained why big companies like Boeing and Airbus need to use Open Source software. "They have to be able to recompile what happens to an Airbus that crashes somewhere in the mid-Atlantic. They have to be able to recompile and reverse engineer, so they need the source code. It might be the same with pharmaceutical companies."

## **8 The benefits and challenges of Electronic Patient Reported Outcomes**

An electronic patient-reported outcome (ePRO) is a patient-reported outcome that is collected by electronic methods, such as a handheld devices, tablet or digital pen. ePRO methods are most commonly used in clinical trials, but they are also used elsewhere in health care.

Data is input into the device by the patient and hosted by the vendor. The advantages of using ePRO in clinical trials include that the research team don't have to input data manually and it is possible to ensure that the patient is inputting the data at the time specified by the protocol, something that cannot be confirmed when data is collected on paper.

Maria Luisa Alamillo, Lilly said Lilly had surveyed data managers with and without experience of utilising ePRO within clinical trials to determine potential barriers to the technology. Cost was the most common barrier to managers with no hands on experience of ePROs (45 per cent). Unfamiliarity with processes and technology was a barrier for 34 percent; insufficient time to implement for 18 percent, and 3 per cent said they preferred using a paper method.

However, perceptions changed once managers had used ePRO technology for two or three studies, insufficient time to implement was the main barrier, cited by two thirds of managers; cost was a barrier for just 26 per cent, and unfamiliarity with processes and technology for 7 per cent.

Ms Alamillo emphasised that it was important to plan ahead if ePROs was to be used because a lot of time is needed up front for copyright approval of the questions, the translations and their validation. "There might be a copyright approval for paper, but you are going to use a device so you need to have the copyright approval for that device and that takes time," she explained.