“Ask the Expert” session of the CDISC European Interchange 2012 was quite remarkable. Stimulating questions related to the CDISC achievements and other issues grabbed the attention of the audience. In fact, this was arguably the best session of 2012 CDISC Interchange since the two excellent Plenary Sessions had not allowed time for Q&A, while this session gave the audience plenty of opportunity to ask many of these Plenary speakers about issues they really wanted to understand.

The panel was formed of international experts in the healthcare/research industry: Charles Cooper of FDA, Bernard De Bono of the European Bioinformatics Institute, Bron Kisler and Wayne Kubick of CDISC and Pierre-Yves Lastic of Sanofi and the E3C answered inquiries from the attendees.
1. **Does the FDA expect the community to use the latest SDTM Implementation Guide and how is this going to be approached?**

Dr. Charles Cooper indicated that FDA is still trying to incorporate data validation into SDTM. He stated that they are trying to understand how to relate validation errors with impact in the review process. FDA is building an environment that leverages data standards. Dr. Cooper mentioned that the enterprise version of OpenCDISC easily allows customizing and has a database on the back-end, allowing them to immediately identify difficulties and challenges.

“We like this open sharing platform, and we would like to take the exact checks and share with the industry. We are in an early phase of the development process; we just installed a version for development within the last month. It will most likely require a period of ~2 years to get to a point where we will be able to share our files and specifications”, he stated.

2. **It is not always possible to use the latest version of a standard. Can you please advise us?**

“To clarify the Technical Roadmap – SDTM Version 3.1.3 will be 3.1.2 (current) plus a number of pieces that have already been reviewed and posted (e.g. Trial Summary, Amendment 1). Version 3.1.4 will add more domains such as those for TA standards. These versions will make it easier to reference and will augment but not change Version 3.1.2”. Wayne Kubick, CDISC CTO.

3. **How can we distinguish between standards to be submitted and the tools we use? Is that fixed with v 3.1.3?**

Charles Cooper of FDA indicated that there is a new PhUSE-FDA workgroup that has been charged with developing validation checks, including identifying validation checks that are too sensitive and that may cause confusion. He requested more participation from the global community for this effort.

4. **Philippe Verplancke from X-Clinical asked if FDA will impose a regulation requiring the use of thousands of variable definitions that will be published with the upcoming therapeutic standards.**

Charles Cooper of FDA clarified that there are specific items that will result in the requirement of submission of data with PDUFA 5; and Therapeutic Area Standards will be considered part of the standard electronic data. “One of the challenges that we will face is to ensure that we are not excluding main research communities from different parts of the world. We have to balance between quick progress and involving as many international groups as we can” stated Dr. Cooper.

Wayne Kubick, CTO of CDISC, announced the new Online Comment tool that CDISC will be using. CDISC has been able to license this tool from ANSI and it is now installed within the CDISC SharePoint portal, which allows receiving comments on the standards under production. Wayne encouraged everyone to begin using that tool for all the standards packages within the next three months. Testing has already begun with the CDISC Technical Leadership Committee (TLC). The tool enables everyone to see all comments and to sort and search on these comments.
Bron Kisler, VP of Strategic Alliances of CDISC, declared that the Therapeutic Area projects have emerged quickly at the end of 2011. Now we have a clear list from the FDA that is open for discussion and for feedback from the industry. CDISC wants to make sure to plan out these projects and make them available to the community through the appropriate communications.

5. Pierre-Yves Lastic of Sanofi asked where do the Oncology standards stand at this point? How do we help the cancer community to come up with the appropriate tools for people running clinical trials?

Bron Kisler said that CDISC looked at cardiovascular disease as a ‘program’ and then broke it down to look at the common layers and various diseases in an attempt to come up with domains for the cardiovascular area. Oncology domains would presumably require a similar process.

Bernard De Bono of the European BioInformatics Institute indicated that we need to think carefully that there are already terminology and oncology domains out there. We owe it to the community to check whether a specific term already exists or not; the community must be mapping data. We should be asking: is there really a purpose to create a term and is it easy to create? We also need to maintain our terminology; the more you create the more you have to maintain. There is no need to ‘reinvent the wheel’. A composite of complex concepts and elements is not new.

From inception these complex concepts should be semantically interoperable. Having a large set of terms is not an index of achievement; it is an index of activity. We need to have a strategy to build our terms. CDISC has a huge task ahead, which could benefit by reusing the existing ontologies (we should be able to map to the existing domains). A list of terms is not enough – one must have the knowledge representation.

Bron Kisler stated that the idea of existing ontologies must take place with respect to the CDISC Shared Health and Clinical Research Electronic Library (SHARE) http://www.cdisc.org/cdisc-share.

Wayne Kubick reinforced that our goal within CDISC (and for SHARE) is not to create new terms; part of our process is to check every term and make sure that it is part of the existing process. As for the Therapeutic Area Standards, the proliferation of these new terms will be happening within these seven years; CDISC also must make sure to get new input from the global community in that regard. We start with a charter and break it down into pieces, Wayne said. Then, we must define the scoping document and part of that process is to examine existing ontologies. Wayne stated that he agrees with Bernard de Bono and that we have to incorporate the ontology domains within SHARE.

Pierre-Yves Lastic indicated the need for a huge amount of training to get people understand the CDISC Therapeutic Area standards process, including ontologies.

6. We have talked about the ongoing CDISC projects and provided feedback and discussions; now, a valuable question we should ask ourselves is to list the recent accomplishments of CDISC.

Pierre-Yves: in 15 years we have come so far, 15 years ago there was nothing.
Bron Kisler: Therapeutic Area projects have pleased me last year. These projects brought along whole new communities that CDISC had not touched before; I got messages from clinicians who brought patient advocates to the table. Keeping the patients in mind is extremely important and stimulating. Another success for CDISC is in the European market place; we have a legal entity established in Brussels, which helped us create better collaboration with IMI.

Wayne Kubick: Looking back (I have been with CDISC since 1998), we said ‘Why don’t we do something to describe what FDA would like to see with the data?’ We were certain that we can accomplish that. The Genzyme GetSmart case study, with the Protocol Representation Standard; FDA converted data to SDTM; also, what C-path has done with the Alzheimer--putting the data into SDTM format, C-Path is doing disease models that inform the community to help find better therapies for this disease. We should identify and communicate and celebrate success with these stories.

Dr. Chuck Cooper of FDA stated that CDER needs standards activities to leverage and improve the review process, having dealt with various previous reviews. With my first review in July 2000, when I received my first NDA, my team asked me to pick three reviewers to look at their reviews. So, I picked three well-respected experienced reviewers, and I was shocked to find all three reviews were different. We have experiences that were dictated with the skills of each specific reviewer. In order to ensure predictability and consistency, and to communicate our processes, we are building a review process based on a new technology that has not been achieved by reviewers before. With the transparency of reviews that relate to CDISC data, we can start to see modernized processes. And, with the FDA Computational Science Center activities, in addition to PDUFA and CDISC Standards, the rate of submissions using standards has increased 50%. Dr. Cooper added that the quality of data submitted for review is much better now, given that sponsors are adhering to the CDISC standards.

De Bono: I was dealing with IMI and the DDMore project. This project should make direct efforts in terms of semantic interoperability (EHR4CR), but it was not easy to convince some that we need to have semantic interoperability; people started listening when I said the word CDISC. When I explained how useful it is to have semantic mappings, pharmaceutical companies started to listen more. There is much to celebrate in CDISC! CDISC is a growing influence and it makes life easier for FDA to compare several studies.