CDASH:
A MUST FOR EDC TRIALS

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CDISC and EDC are 2 acronyms that hardly need an introduction these days. EDC (Electronic Data Capture) is a widely accepted alternative for paper trials, and has numerous advantages such as: immediate access to both trial data and trial status reports via the web, improved data quality by auto-queries that are sent by the EDC system as soon as data is entered, full control over the time point that trial changes are activated allowing adaptive trial design, etc. CDISC (Clinical Data Interchange Standards Consortium) provides a set of standards that support the acquisition, exchange, submission and archive of clinical research data and metadata.

The ultimate goal for all clinical trials is to evaluate the safety and efficacy of the investigational medication and to prepare for registration afterwards. This process has always been subject to business pressure that is trying to move the product to the market faster while spending less money. It's therefore very important to take advantage of all business benefits that are provided by EDC vendors and the CDISC models that are used when submitting data. Now the question becomes: "What about CDASH (Clinical Data Acquisition Standards Harmonization)?"

CDISC & EDC: SHAKING HANDS

Both CDISC and EDC have offered process efficiency to the industry with the goal of reducing time to market and limiting the development cost of new drugs.

The EDC vendors have contributed to this efficient process by bringing in the tools that make the complete trial more transparent to all of the parties involved in the clinical trial. Increased data visibility not only allows faster query resolution but it also allows project managers to respond quicker to any trend in the trial (e.g. inaccurate completion of CRF pages) which, in the end, leads to a faster database lock.

CDISC contributed to trial efficiency by offering a number of standards that are all vendor-neutral and platform-independent. These standards allow the FDA to run their review-tools on the submitted data, leading to far fewer questions about the data structure and therefore shorter review cycles with faster approval. In addition, data standards simplify the data transfer between data providers (Lab, ECG, IVRS, etc) and data receivers (data management and statistics teams) while the trial is ongoing.

CDISC and EDC have offered real benefits to the clinical research industry over the past decade, but there has never been a real 'link' between them until recently. CDASH is a new standard in the CDISC portfolio that integrates the SDTM requirements into the CRF. The SDTM model has always been the CDISC standard that received the most attention and EDC has been working for years on improving data acquisition. CDASH is therefore the standard that brings the CDISC and EDC worlds together.

CDASH: NOW WHAT?

The CDASH team released the CDASH v1.1 specifications in January 2011. These specifications include 16 domains that are all therapeutic area agnostic. More extensive CDASH specifications via a CDASH User Guide are expected to be published in Q3 2011. CDASH is at the moment still a work-in-progress. However, a lot of work has been done by the CDASH team which is already providing a number of benefits:

1. The standard CDASH Case Report Forms allow efficient data acquisition and efficient data monitoring at the sites.

Sites have always been asked to complete non-standard CRFs while patients are performing daily assessments and CRFs are expected to be completed on time and accurately by the site. On the other hand, the variety of CRF questions and lay-outs is almost unlimited at the moment. Replacing non-standard CRFs by the 16 CDASH Case Report Forms already significantly improves the situation at the site.

2. The standard CDASH Case Report Forms lead to more standard SDTM datasets.

The SDTM model is widely accepted as 'the' submission standard for clinical trials. The reality is that companies around the world are all implementing slightly different variants of the SDTM standard. This spectrum of implementations originates from the diversity of CRFs that exist today. Non-standard CRFs are capturing similar information in different ways leading to different controlled terminology for the same data across companies. It even occurs that similar information is captured in different SDTM domains because of the non-standard CRFs. The current 16 CDASH Case Report Forms are associated with standard SDTM mappings and standard CDISC controlled terminology which is already reducing the spectrum of SDTM implementations that exists today.

3. The standard CDASH Case Report Forms allow faster go-live of EDC trials.

The eCRF design tools that are on the market today come with a number of time-saving features, such as: extensive library capabilities and collaboration functionalities that allow multiple eCRF designers to work on the same trial at the same point in time. EDC applications can have an earlier go-live date because:

- The eCRF design time is shortened since CDASH eCRF forms can be pulled out of the EDC library on the fly.
- The CDASH forms can be created in the library with edit checks. These edit checks are available in the new trial as soon as the eCRF form has been added. This functionality significantly reduces the current development time for programming edit checks.
- CDASH eCRF forms with associated edit checks that are selected from a validated library guarantee shorter User Acceptance Testing cycles for EDC trials.

The CDISC ODM (Operational Data Model) standard even allows the transfer of CDASH EDC-library forms from one tool to another. As a consequence, a company is never limited to a single EDC application when using a CDASH EDC-library.

EDC-CDASH-CDISC: END-TO-END

A streamlined EDC-CDASH-CDISC end-to-end implementation guarantees the highest quality in the shortest time for the full life cycle of the trial. Streamlining the complete process flow is really the key to ensuring that the benefits of each standard ripple through the next standard in the process flow as illustrated in figure 1:

- Standard CDASH Case Report Forms can be transformed to standard SDTM datasets using standard ETL (Extract Transform Load) code.
- Standard CDASH Case Report Forms are easier to complete and therefore generate less data queries. Furthermore, EDC applications are firing data queries as soon as data is entered. This all leads to an earlier database lock date.
- The statistical analysis can be performed much faster on a locked SDTM database that is compliant with the CDASH-SDTM mapping and that employs CDISC controlled terminology. As a consequence, the safety and efficacy results will be available sooner. Furthermore, the creation of the ADaM datasets on top of fully compliant SDTM datasets will go much smoother and validation can be done more efficiently.

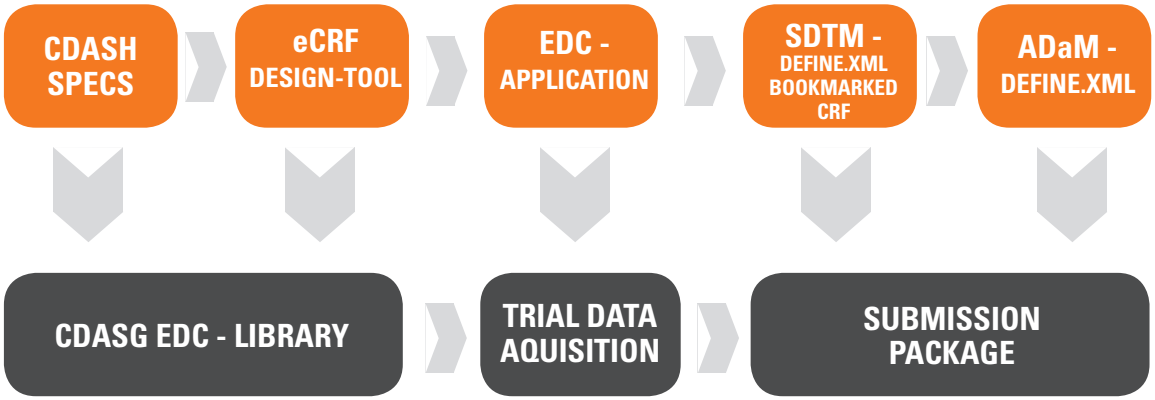
These EDC-CDASH-CDISC integration benefits and the generally accepted benefits of EDC and CDISC help to ensure that clinical trials can be completed on time, on budget and in scope.

CONCLUSION

The library capabilities of current eCRF design tools already allow the industry to implement the current CDASH standard, while still leaving all options open for the implementation of therapeutic area specific domains when released by the CDASH team in the future. From an eCRF application design point of view, the cost savings of using standard eCRF forms are obvious. Furthermore, the positive impact of CDASH on SDTM cannot be underestimated. The existence of the ODM standard even allows uploading CDASH CRF pages from one design tool to another with no re-work at all.

In time, CDASH with standard controlled

FIGURE 1: EDC-CDASH-CDISC: END-TO-END IMPLAMENTAION FLOW



terminology will be the foundation of a turnkey EDC-CDISC solution.

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