# SESSION AT DIA CONFERENCE FOCUSES ON IMPROVING THE CLINICAL PROTOCOL

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The 40th annual conference of the Drug Information Association (DIA) was held on June 13-17, 2004, in Washington, DC. One of the sessions in the Medical/Scientific Writing interest areas was "Improving the Clinical Protocol: A Core Communication Tool." Helle-Mei Gawrylewski, MA, Director, Medical Writing, J & J Pharmaceutical Research and Development, LLC, served as chair of the session.

Clinical protocols, the foundation of clinical trials, must be clear and complete. Optimal protocol development is key to timely completion of a successful trial. The session included 3 presentations and covered recommendations and projects underway for improving the protocol language, content, development, and review.

Speaking first was Peter Schüler, MD, Vice President of Medical Affairs, PRA International. After pointing out that protocol amendments cost about $1,500 per site, Dr. Schüler made general and specific recommendations for improving protocols during development. General recommendations included using the most recent regulatory guidances, using precisely defined terms consistently, providing technical details in separate documents, giving consideration to medical monitoring requirements, providing clear directions and timelines, and explaining the reasons behind study requirements so that investigators are not forced to draw their own conclusions.

Dr. Schüler had detailed recommendations for specific protocol sections. For example, subject screening details that are often omitted in section 6.4.5 (Expected duration of subject participation, and description of the sequence and duration of all trial periods...) include use of a prescreening step; description of who should undergo more detailed screening; when (if ever) rescreening is allowed and which procedures (including re-signing the Informed Consent Form) would then need to be repeated; and a precise statement of when in the screening sequence a subject has consented.

Dr. Schüler emphasized that defining the patient population is key, that procedures must be detailed and reasoned, and that the statistical analyses should be planned early. The team should read the protocol together and discuss potential deviations, and the protocol should be tested with a dry run.

In the second presentation, Anne Tompkins, MSN, RN, Deputy Project Officer, Cancer Therapy Evaluation Program (CTEP), National Cancer Institute (NCI), summarized the Document management authoring review tracking (Docu-MART) system being implemented to facilitate development and review of the hundreds of protocols, revisions, and amendments received at CTEP each year. To overcome the challenges of processing protocols from a variety of institutions and investigators, Docu-MART uses Web/client-server-based software applications, a library of protocol templates with prepopulated fields, a commenting tool, and standardized workflows to assist in authoring, revising, and approving protocols.

The harmonized electronic templates, created in collaboration with colleagues and a Congressional committee, incorporate US Food and Drug Administration (FDA) regulations, International Conference on Harmonisation (ICH) guidelines, and common data elements. Template choice is dictated by the type of information input by the user into a series of dialog boxes. A template-based system benefits the users by clearly identifying required sections; providing suggested or boilerplate language, which reduces writing time; allowing reuse of information for new protocols; and, when the plan to expand templates to an XML backbone is implemented, allowing seamless transfer of information to the clinical study report.

The goal of CTEP in using this collaborative authoring and review system is to reduce the time from concept approval to protocol approval to 60 days. Templates for phase 3 protocols have been developed and meetings with users are ongoing; beta testing of the system is imminent.

The final presentation was given by Beverly Meadows, PhD(c), MS, RN, OCN, Nurse Consultant, Clinical Trials Development and Informatics, CTEP, NCI. Dr. Meadows described development of a standard protocol model. She explained that the Health Level 7 (HL7) vocabulary establishes standards for demographic information, units of measure, immunizations, and clinical encounters, and HL7 clinical document architecture (CDA) establishes standards for text-based reports. The HL7 Regulated Clinical Research and Information Management (RCRIM) Technical committee, under the co-leadership of representatives from HL7/Pharma, FDA, and the Clinical Data Interchange Standards Consortium (CDISC), develops common standards for clinical research and regulatory evaluation and ensures that other HL7 standards can be used in regulated clinical research. The RCRIM Protocol Representation (PR) group is building a human- and machine-readable protocol document which will incorporate regulatory requirements and HL7 standards.

With input from industry and government leaders, the

PR group developed a spreadsheet of essential concepts and topics, including high-level section headings and reference citations to the appropriate ICH sections and EudraCT. Separate expert project teams developed the detailed elements.

The initial protocol model uses HL7 CDA as the format. The goal is to create a flexible protocol model that has intuitive and understandable structure and content that will be accepted by industry stakeholders.

The next steps in the project include responding to comments that have been offered via the CDISC Web site and HL7 ballot, discussing the use of HL7 CDA as the appropriate protocol structure, integrating expertise from members of other committees (in RCRIM, FDA, etc.) which are developing related projects, increasing granularity of content by using input from content experts, and considering use of common data elements or other recognized vocabularies to standardize heading titles.

For more information on the CTEP project, see **http://ctep.cancer.gov**. For more information on CDISC, see **www.cdisc.org**, or the CDISC Glossary published at Applied Clinical Trials (**www.act.com**).

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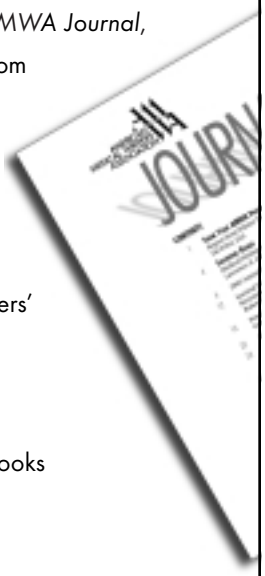

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