The International Society for CNS Clinical Trials, ISCTM, welcomes the opportunity to provide comment on the ***HL7 Version 3 Domain Analysis Model: Schizophrenia***. The ISCTM was chartered in the fall of 2004 as an international society charged with providing a commercial free forum where key stakeholders from academia, industry and regulatory branches can discuss/resolve challenges specific to the design and methodological issues in CNS clinical trials. Recognizing the importance of this document for our constituency, the ISCTM convened a working group to review and comment on the guidance.

For this response, the group has provided general comments and recommendations regarding the inclusion of scales/questionnaires in the Schizophrenia Data Standards.

Below are those who contributed to the ISCTM Working Group on *Response to HL7 Version 3 Domain Analysis Model: Schizophrenia*
Chair: Andrei Pikalov, MD, PhD, Sunovion
Larry Alphs, MD, PhD, Janssen
Vicki Davis, DrPH, NeuroCog Trials
Richard, Keefe, PhD, Duke University
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HL7 Version 3 Domain Analysis Model: Schizophrenia

General Comments
1) The overall objectives of this task and the final outcomes to be produced have not been well defined by the initiating sponsor, we suggest to include such information in the introductory statements.
2) It should also be clarified in the introduction of the document whether the collection of all data elements is required in each domain, or if the choice of domain is optional but the specific data elements within that domain are required and parameters (permissible values) should be explicitly defined as per this document. Discussion with the document owners clarified that the data elements will contain both core (i.e. required) elements such as past history, demographic features, disease characterization, etc. and optional elements that will be based on trial type, phase,

detail level and derived data as appropriate for the user.

3) The time to review this extensive document is very limited and may not be sufficient to perform a comprehensive review of all variables. ISCTM suggests to create a new opportunity for experts to comment. The document owners communicated that they will have another opportunity to comment in about one year's time when the consortium (CFAST) will ask for another round of comments. Furthermore, industry stakeholders will have an opportunity to comment on the research specific standard through CDISC.

4) Additional input is recommended from experts in the schizophrenia field who will be the ultimate end users of this document. The document owners communicated that two rounds of comments have been received from experts in the past year and additional future input from experts in the field is a reasonable request. ISCTM feels that the importance of this document and the amount of the amount of the information presented for review call for another round of comprehensive expert review.

5) A qualified rater performs the majority of testing, not a clinician. It is recommended to replace "clinician" with "rater" where appropriate.

Specific Comments

Page	Item	Comment
15, 16, 25, 27, 79, 96	Multiple items pertaining to DSM-IV diagnostic criteria	We recommend to replace "DSM-IV" with "DSM-5" which will impact multiple items in this document and raise several issues for further clarification: • How will DSM-5 changes in schizophrenia and schizoaffective diagnoses affect data elements? • How will the DSM-5 changes regarding negative symptoms impact data elements defining diagnosis of schizophrenia or schizoaffective disorder? In addition, there is the caveat that making this change to DSM-5 criteria may affect ongoing programs that are using the DSM-IV criteria.
21	Daily living situation	This data element is not sufficiently detailed. Suggest adding a specific living arrangement tool to better quantify this variable.
21	Duration of episode	Duration of episode is a subjective measure. Suggest changing this data field to "Date of hospital discharge" which follows the data field "Date of hospitalization for current episode" so that a more reliable quantitative duration can be recorded
22	Episode severity comparison	Severity comparison of current episodes with previous episodes cannot be recorded reliably. We recommend deleting this data element.
22	Episode symptom similarity to previous episodes classification	Classification comparison of current episodes with previous episodes cannot be recorded reliably. We recommend deleting this data element.
26	Mental Health Assessment	Currently, the mental health assessment fields only contain global clinical impression scales (i.e. CGI-I and CGI-S). It is proposed that additional mental health assessments

		measuring other parameters (e.g. psychiatric symptoms, functional ability, cognition, movement disorders, quality of life, etc.) also be considered for this section. o Please see the attached Excel spreadsheet with a list of scales to recommend for inclusion. Changes to the original list made are highlighted in red text. They include: ▪ Adding the abbreviated version of the Extrapyramidal Symptom Rating Scale. ▪ Adding the International Suicide Prevention Trial Plus ▪ Adding a separate "Diagnosis" category composed of the Structured Clinical Interview for DSM Disorders (RV) and Clinician-Rated Dimensions of Psychosis Symptom Severity (DSM 5 measure) ▪ Moving the following tests to the "Other" category: MacArthur competence assessment tools, UKU Side effect rating scale, Premorbid Adjustment Scale, Arizona Sexual Experiences Scale, Short Form (36) Health Survey o Concerns raised during the 11/12/13 meeting to discuss the list of scales included: ▪ By what criteria were people deciding on which tests to include vs. exclude? ▪ Adding tests to the list that were not included on the list. ▪ How to determine inclusion of test not well known, in particular, some of the quality of life scales.
26	Mental Health Assessments	There should be an effort to capture quantitative data (i.e. mean change from baseline or % change from baseline) rather than qualitative data (i.e. low, medium, high).
26	CGI rater different from last assessment	The CGI-I is a difficult assessment to perform accurately and consistently (especially in the study where multiple raters might see a patient as different evaluations). There should be an effort to ensure rater continuity throughout the study if current version of CGI-I is suggested or

		different measuring instrument should be used.
40	Birth time	Time of birth cannot reliably or consistently be recorded. We suggest deleting this data element.
82,83	Symptoms are similar/different from previous episodes	Severity comparison of current episodes with previous episodes cannot be recorded reliably. We suggest deleting this data element or defining the rules for such comparison (i.e. compare baseline PANSS or CGI-S rating at the baseline of the previous and current episode, etc.)

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