IMPLEMENTING CDISC STANDARDS IN IMAGING CLINICAL TRIALS CHALLENGES & LESSONS LEARNED

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CDISC

CLINICAL DATA INTERCHANGE STANDARDS CONSORTIUM

- Non-profit, vendor neutral, open standards development organization
- Develops and supports global data standards to improve medical research
- Established multiple foundational standards used throughout trial lifecycle

SDM-XML / ODM-XLM / DEFINE-XML

CDASH – Clinical Data Acquisition Standards Harmonization

SDTM – Study Data Tabulation Model

SEND – Standard For Exchange Of Nonclinical Data

ADaM – Analysis Data Model

TAUG – Therapeutic Area User Guides

CT – Controlled Terminology

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SDTM AND CT

STUDY DATA TABULATION MODEL

- Standardizes Study Data organization, formatting, and interchange
  - First proposed in 1999
  - Required per FDA Data Standards Catalogue effective December 2016

CONTROLLED TERMINOLOGY

- Standardizes terminology used at all levels of clinical trials (e.g. units, response assessments, criteria, body systems)
- Harmonizes across existing dictionaries
  - NCI EVS (provides starting definitions)
  - SNOMED CT, MedDRA, WHODD
  - Updates quaterly to keep pace with other standards updates

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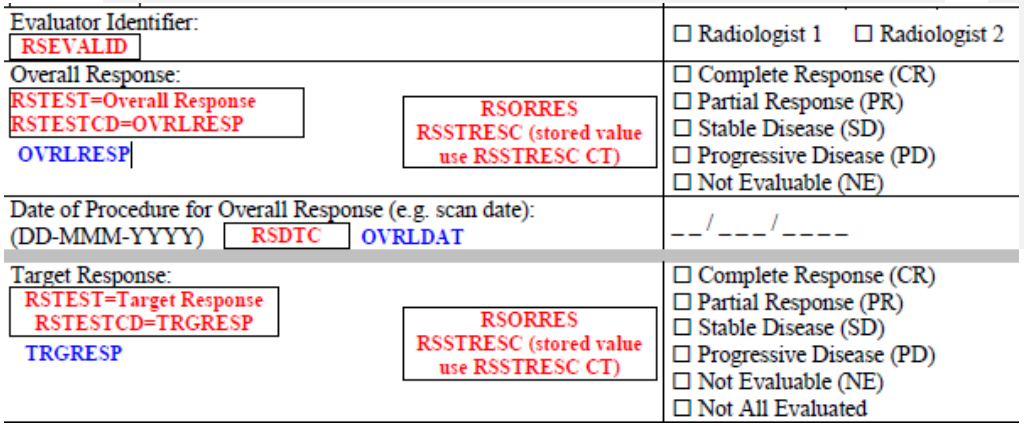
PAREXEL INFORMATICS MIPTS AND CDISC SDTM

SDTM AND CT IN INDEPENDENT IMAGING REVIEW

- CRF data capture design with CT
- Identification of required data at startup (DB creation), rather than when defining data transfer specifications
- Improved communication between stakeholders with common terminology



Evaluator Identifier: RSEVALID		☐ Radiologist 1 ☐ Radiologist 2
Overall Response: RSTEST=Overall Response RSTESTCD=OVRLRESP OVRLRESP	RSORRES RSSTRESC (stored value use RSSTRESC CT)	☐ Complete Response (CR) ☐ Partial Response (PR) ☐ Stable Disease (SD) ☐ Progressive Disease (PD) ☐ Not Evaluable (NE)
Date of Procedure for Overall Response (e.g. scan date): (DD-MMM-YYYY) RSDTC OVRLDAT		__/___/____
Target Response: RSTEST=Target Response RSTESTCD=TRGRESP TRGRESP	RSORRES RSSTRESC (stored value use RSSTRESC CT)	☐ Complete Response (CR) ☐ Partial Response (PR) ☐ Stable Disease (SD) ☐ Progressive Disease (PD) ☐ Not Evaluable (NE) ☐ Not All Evaluated

SDTM AND CT IN TRANSFER OF REVIEW RESULTS

- Transferring data in predefined SDTM datasets and expectations
- 'Intuitive' understanding of the data parameters and represented assessments
- Aligning terms with appropriate CT version
- Standardizing libraries, structures, and validation across trials

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PAREXEL IMAGING – SDTM EXPERIENCE

- Oncology related data (domains)
  - Solid Tumor Imaging (TU/TR/RS; RECIST 1.1)
  - Physical Exam/Clinical data (PE/MO/LB/CE; NHL-IWG)
- Other Indications
  - MSK (e.g. RA, OA, AS, SpA, soon in the MK domain)
  - Ophthalmology (soon in the OA domain)
- Specialized/Custom data (domains)
  - Nuclear Medicine (e.g. PC, soon in the TU/TR/RS domains)
  - Immune Response Criteria (RECIST/irRECIST)
- Extensive Experience with Special Purpose Domains
  - Comments Domain (CO), Data Relationships, Supplemental Qualifiers

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SDTM AND CT EXAMPLES

RS Domain: Disease Response

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	STUDYID	DOMAIN	USUBJID	RSTESTCD	RSTEST	RSCAT	RSORRES	RSNAM	RSEVAL	RSEVALID	VISITNUM	VISIT	RSDTC
2	ABC12345	RS	40912	TRGRESP	Target Response	RECIST 1.0	SD		INVESTIGATOR		3	Cycle 2 Week 4	2007-02-25
3	ABC12345	RS	40912	NTRGRESP	Non-target Response	RECIST 1.0	SD		INVESTIGATOR		3	Cycle 2 Week 4	2007-02-25
4	ABC12345	RS	40912	OVRLRESP	Overall Response	RECIST 1.0	SD		INVESTIGATOR		3	Cycle 2 Week 4	2007-02-25
5	ABC12345	RS	40912	TRGRESP	Target Response	RECIST 1.0	SD	ACME VENDOR	INDEPENDENT ASSESSOR	RADIOLOGIST	3	Cycle 2 Week 4	2007-02-25
6	ABC12345	RS	40912	NTRGRESP	Non-target Response	RECIST 1.0	SD	ACME VENDOR	INDEPENDENT ASSESSOR	RADIOLOGIST	3	Cycle 2 Week 4	2007-02-25
7	ABC12345	RS	40912	OVRLRESP	Overall Response	RECIST 1.0	SD	ACME VENDOR	INDEPENDENT ASSESSOR	RADIOLOGIST	3	Cycle 2 Week 4	2007-02-25
8	ABC12345	RS	40912	TRGRESP	Target Response	RECIST 1.0	SD		INVESTIGATOR		5	Cycle 4 Week 4	2007-04-22
9	ABC12345	RS	40912	NTRGRESP	Non-target Response	RECIST 1.0	SD		INVESTIGATOR		5	Cycle 4 Week 4	2007-04-22
10	ABC12345	RS	40912	NEWLPROG	New Lesion Progressi	RECIST 1.0	PD		INVESTIGATOR		5	Cycle 4 Week 4	2007-04-22

Controlled Terminology: Resonse Assessment Category

	A	B	C	D
1	Codelist Name	CDISC Submission Value	CDISC Definition	NCI Preferred Term
2	Category of Oncology Response Assessment	CHESON CLL 2006	CLL response criteria. (Cheson BD. CLL response criteria.Clin Adv Hematol Oncol. 2006 May;4(5):4-5; discussion 10; suppl 12.)	Cheson CLL 2006 Oncology Response Criteria
3	Category of Oncology Response Assessment	CHESON CLL 2012	Novel targeted agents and the need to refine clinical end points in chronic lymphocytic leukemia. (Cheson BD, Byrd JC, Rai KR, Kay NE, O'Brien SM, Flinn	Cheson CLL 2012 Oncology Response Criteria
4	Category of Oncology Response Assessment	CHESON MALIGNANT LYMPHOMA 2007	Revised response criteria for malignant lymphoma. (Cheson BD, Pfistner B, Juweid ME, Gascoyne RD, Specht L, Horning SJ, Coiffier B, Fisher RI, Hagenbeek A,	Cheson Malignant Lymphoma 2007 Oncology Response Criteria
5	Category of Oncology Response Assessment	IWC HALLEK CLL 2008	Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating	IWC Hallek CLL 2008 Oncology Response Criteria
6	Category of Oncology Response Assessment	LUGANO CLASSIFICATION	Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification. (Cheson BD,	Lugano Classification Oncology Response Criteria
7	Category of Oncology Response Assessment	RANO	Updated Response Assessment Criteria for High-Grade Gliomas: Response Assessment in Neuro-Oncology Working Group. (Wen PY, Macdonald DR,	Response Assessment in Neuro-Oncology Criteria
8	Category of Oncology Response Assessment	RECIST 1.0	Response Evaluation Criteria in Solid Tumors (RECIST) version 1.0 (Therasse P, Arbuck SG, Eisenhauer EA, Wanders J, Kaplan RS, Rubenstein L, Verweij J, Van	Response Evaluation Criteria in Solid Tumors Version 1.0
9	Category of Oncology Response Assessment	RECIST 1.1	Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 (E.A. Eisenhauer, P. Therasse, J. Bogaerts, L.H. Schwartz, D. Sargent, R. Ford, J.	Response Evaluation Criteria in Solid Tumors Version 1.1

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ADVANTAGES OF CDISC IMPLEMENTATION

- Communication and Transparency
  - Better communication between operational, medical, and technical team members
  - Common language on multi-institution teams across therapeutic areas and indications
  - Consistent data validation rules independent of sponsor, indication, or trial history
- Trial Component Reuse
  - Development of internal documentations templates to ease start-up
  - Centralized standards being updated synchronously
  - Knowledge and ‘lessons learned‘ apply beyond the scope of a single trial
- Robust data relationships throughout trials

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REQUIREMENTS FOR NEW SDTM IMPLEMENTATION

- Proactive close contact with CDISC teams for detailed guidance
- Processes required for sharing interpretations and ‘lessons learned‘
  - Distributing information regarding pending updates and incoming terms
  - Creating and maintaining central documentation templates/libraries
- Mapping various legacy systems to SDTM
- Experience with extensive implementation alternatives
  - Selection of appropriate domains for crossover data
  - Record and domain relationships
  - Structuring of non-standard values

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CHALLENGES OF SDTM IMPLEMENTATION

- Variation in implementation
- Need to compensate for Legacy Data Structures
- Differing interpretations of new and evolving standards
- Working with older (or newer) standards versions
  - Extensive and ongoing training required
- Study data not yet covered by CDISC
  - Volunteering in CDISC workgroups for new Therapeutic Areas
  - Reviewing and requesting new Terminology
  - Defining robust Custom Domains in the interim
- Representation of complex review designs and required non-conformity

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CHALLENGES OF SDTM IMPLEMENTATION II

- Difficult to obtain information and guidance
  - Problematic access and navigation of various sites and accounts
- Limited channels of communication
  - Volunteer groups
  - Public and Member Reviews of Draft Standard Versions
- User Groups
  - Non-specialized, location based
  - Few common structures or interplay
  - Little to no support from CDISC

PINTAD SUBGROUP FOR IMAGING SPECIFIC CDISC STANDARDS IMPLIMENTATION

- Organized by PAREXEL Informatics
- Mailing list for CDISC Implementation Questions and Answers
  - Initally limited to SDTM until colleagues of broader expertise join the group
- Regular teleconferences for updates and discussions
- Collection of feedback and questions for CDISC and Agencies
- Can be migrated to an offical CDISC imaging-specifc user group once fully established

Interested?

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THANK YOU

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