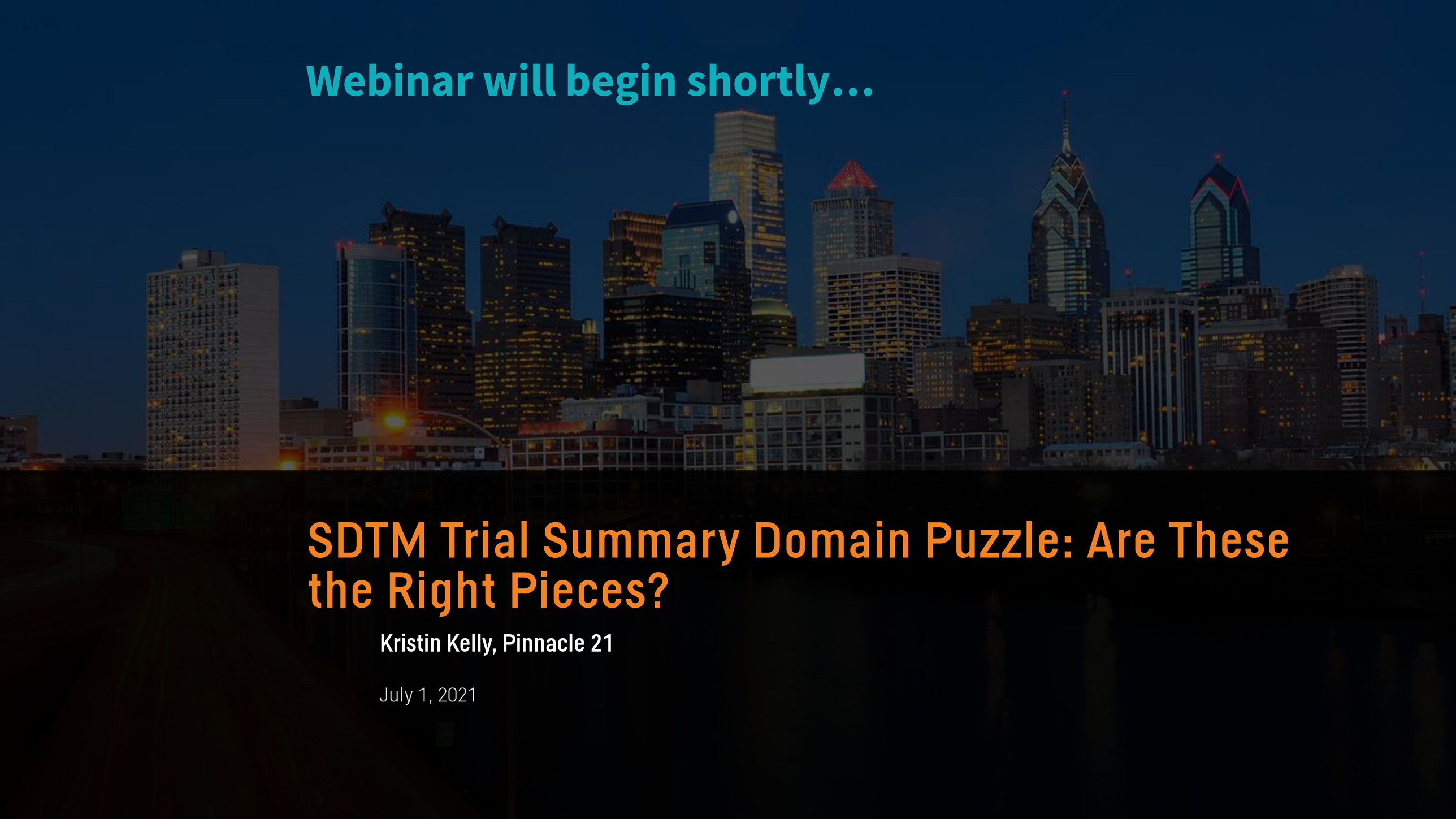

Webinar will begin shortly…

SDTM Trial Summary Domain Puzzle: Are These the Right Pieces?

Kristin Kelly, Pinnacle 21

July 1, 2021

SDTM Trial Summary Domain Puzzle: Are These the Right Pieces?

Kristin Kelly, Pinnacle 21

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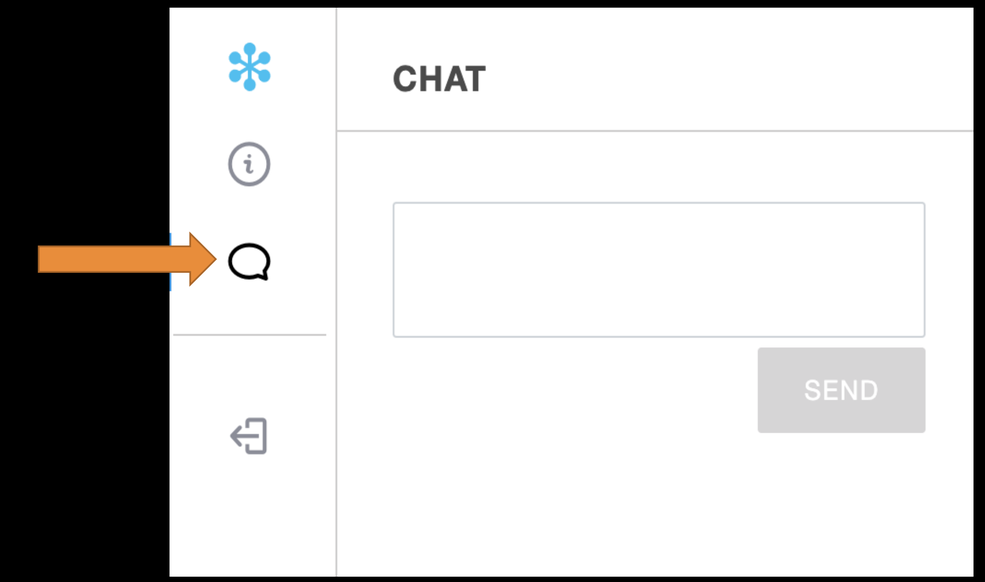
PRESENTER – KRISTIN KELLY

- Principal Consultant at Pinnacle 21
- More than 10 years experience at both Pharma and CROs
- SME for nonclinical and clinical FDA projects for CDER and CBER
- Incoming lead of CDISC SDS Team

QUESTIONS

- Ask a question at any time during the webinar
- Questions will be answered at the end



INTRODUCTION

- FDA requires that the Trial Summary domain (TS) (ts.xpt) be submitted for SDTM, SEND and legacy data
  - Soon to be implemented ‘FDA Technical Rejection Criteria’ will check for the presence of the ts.xpt dataset as well as the study start date (TSPARMCD = SSTDTC)

- At the validation level, several rules have been published that check the adherence to FDA expectations of the content of this dataset as well as rules to check conformance to the guidance in the SDTMIG

- Constructing an informative and complete TS domain can be challenging when interpreting guidance (e.g. SDTMIG, TCG) and using the correct reference terminologies

TRIAL SUMMARY DOMAIN DEFINITION

- The Trial Summary (TS) domain is a trial-level dataset that allows for the submission of a high-level view of a study in a structured format
  - Each record contains the value of a parameter or characteristic of the trial
  - Used to record basic information about the study such as trial phase, protocol title, and trial objectives
  - Contains both planned and actual aspects of the trial, e.g., number of subjects, study start/end dates

TRIAL SUMMARY DOMAIN DEFINITION

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
STUDYID	Study Identifier	Char		Identifier	Unique identifier for a study.	Req
DOMAIN	Domain Abbreviation	Char	TS	Identifier	Two-character abbreviation for the domain.	Req
TSSEQ	Sequence Number	Num		Identifier	Sequence number given to ensure uniqueness within a dataset. Allows inclusion of multiple records for the same TSPARMCD and can be used to join related records.	Req
TSGRPID	Group ID	Char		Identifier	Used to tie together a group of related records	Perm
TSPARMCD	Trial Summary Parameter Short Name	Char	TSPARMCD	Topic	TSPARMCD (the companion to TSPARM) is limited to 8 characters and does not have special character restrictions. These values should be short for ease of use in programming, but it is not expected that TSPARMCD will need to serve as variable names. Examples: AGEMIN, AGEMAX	Req
TSPARM	Trial Summary Parameter	Char	TSPARM	Synonym Qualifier	Term for the Trial Summary Parameter. The value in TSPARM cannot be longer than 40 characters. Examples Planned Minimum Age of Subjects, Planned Maximum Age of Subjects	Req
TSVAL	Parameter Value	Char	*	Result Qualifier	Value of TSPARM. Example: “ASTHMA” when TSPARM value is “Trial Indication”. TSVAL can only be null when TSVALNF is populated. Text over 200 characters can be added to additional columns TSVAL1-TSVALn.	Exp
TSVALNF	Parameter Null Flavor	Char	ISO 21090 NullFlavor enumeration	Result Qualifier	Null flavor for the value of TSPARM, to be populated if and only if TSVAL is null.	Perm
TSVALCD	Parameter Value Code	Char	*	Result Qualifier	This is the code of the term in TSVAL. For example; 6CW7F3G59X is the code for Gabapentin, C49488 is the code for Y. The length of this variable can be longer than 8 to accommodate the length of the external terminology.	Exp
TSVCDREF	Name of the Reference Terminology	Char		Result Qualifier	The name of the Reference Terminology from which TSVALCD is taken. For example; CDISC, SNOMED, ISO 8601.	Exp
TSVCDVER	Version of the Reference Terminology	Char		Result Qualifier	The version number of the Reference Terminology, if applicable.	Exp

TRIAL SUMMARY DOMAIN RESOURCES

- In the SDTMIG (Appendix C1), there is a minimum set of parameters that should be included in TS
  - Those listed as 'Required' means that a record for that parameter should be present
  - 'Conditionally Required' parameters should be included based on some condition
  - 'If Applicable' can be included as needed

TSPARMCD	TSPARM	TSVAL (Codelist Name or Format)	Record with this Parameter	Notes
ADDON	Added on to Existing Treatments	No Yes Response	Required	
AGEMAX	Planned Maximum Age of Subjects	ISO 8601	Required	If there is no maximum age, TSVALNF = "PINF".
AGEMIN	Planned Minimum Age of Subjects	ISO 8601	Required	If there is no minimum age, populate TSVAL with "P0Y".
LENGTH	Trial Length	ISO 8601	Required	
PLANSUB	Planned Number of Subjects	number	Required	
RANDOM	Trial Is Randomized	No Yes Response	Required	
SEXPOP	Sex of Participants	Sex of Participants	Required	
STOPRULE	Study Stop Rules	text	Required	Protocol-specified stopping rule. If there is no stopping rule, record "NONE" in this field.
TBLIND	Trial Blinding Schema	Trial Blinding Schema	Required	
TCNTRL	Control Type	Control Type	Required	
TDIGRP	Diagnosis Group	SNOMED CT	Conditionally Required	If the study population is healthy subjects (i.e., healthy subjects flag is "Y"), this parameter is not expected. If the healthy subject flag is "N", then this parameter would contain the diagnosis/medical problem of the study population. [Validation rule: IF healthy volunteers = "N" then TDIGRP must be present and not null.]
INDIC	Trial Disease/Condition Indication	SNOMED CT	If Applicable	If applicable. Don't include if the sole purpose is to collect PK data. See TS Assumption 13. Use as many rows as needed.

TRIAL SUMMARY DOMAIN RESOURCES

- CDISC also maintains a TS Codetable that provides detailed information on TS parameters that are subject to CDISC Controlled Terminology

C-code (Concept Code)	Trial Summary Parameter Test Code (TSPARMCD) (codelist code = C66738)	Trial Summary Parameter Test Name (TSPARM) (codelist code = C67152)		C-code (Concept Code)	No Yes Response (NY) (codelist code = C66742)		C-code (Concept Code)	Observational Study Biospecimen Retention (OBSSBSR) (codelist code = C127258)		C-code (Concept Code)	Intervention Model Response (INTMODEL) (codelist code = C99076)
C98746	INTMODEL	Intervention Model								C82637	CROSS-OVER
C98746	INTMODEL	Intervention Model								C82638	FACTORIAL
C98746	INTMODEL	Intervention Model								C82639	PARALLEL
C98746	INTMODEL	Intervention Model								C82640	SINGLE GROUP

https://www.cdisc.org/system/files/members/standard/terminology/TS_Codetable_Mapping_2020-09-25.xlsx

TRIAL SUMMARY DOMAIN RESOURCES

- In the FDA TCG (Appendix B), a list of requested TS parameters for clinical studies is provided
  - Some of these are not listed in Appendix C1 of the SDTMIG but are in NCI CT
  - Minimal requirements provided in the TCG Appendix vs SDTMIG (e.g. codelist references)

FDA Desired - Clinical	TSPARMCD	TSPARM	FDA Notes
Y	ACTSUB	Actual Number of Subjects	
Y	ADAPT	Adaptive Design	
Y	ADDON	Added on to Existing Treatments	
Y	AGEMAX	Planned Maximum Age of Subjects	
Y	AGEMIN	Planned Minimum Age of Subjects	
Y	COMPTRT	Comparative Treatment Name	
Conditional	CRMDUR	Confirmed Response Minimum Duration	If applicable.
Conditional	CTAUG	CDISC Therapeutic Area User Guide	If applicable. the value should be the exact listing as in section 5.2 of the Technical Conformance Guide. Use as many rows as needed.
Conditional	CURTRT	Current Therapy or Treatment	Where ADDON = 'Y'. Use as many rows as needed.
Y	DCUTDESC	Data Cutoff Description	GRPID relates DCUTDTC to DCUTDESC.
Y	DCUTDTC	Data Cutoff Date	GRPID relates DCUTDTC to DCUTDESC.

TRIAL SUMMARY PARAMETER VALIDATION RULES

- Many validation rules that check for the presence of ‘Required’ and ‘Conditionally Required’ parameters based on the list in Appendix C1

Rule ID	Message
SD2219	Missing TRT Trial Summary Parameter
SD2221	Missing REGID Trial Summary Parameter
SD2222	Missing OUTMSPRI Trial Summary Parameter
SD2223	Missing PCLAS Trial Summary Parameter
SD2224	Missing FCNTRY Trial Summary Parameter
SD2225	Missing ADAPT Trial Summary Parameter
SD2226	Missing DCUTDTC Trial Summary Parameter
SD2227	Missing DCUTDESC Trial Summary Parameter
SD2228	Missing INTMODEL Trial Summary Parameter
SD2229	Missing NARMS Trial Summary Parameter
SD2230	Missing STYPE Trial Summary Parameter
SD2231	Missing INTTYPE Trial Summary Parameter
SD2232	Missing SSTDTC Trial Summary Parameter
SD2233	Missing SENDTC Trial Summary Parameter
SD2234	Missing ACTSUB Trial Summary Parameter
SD2235	Missing HLTSUBJI Trial Summary Parameter
SD1308	TSVAL is missing for the CURTRT Trial Summary Parameter, when ADDON parameter equals 'Y'
SD1309	TSVAL is missing for the TRT Trial Summary Parameter, when STYPE parameter equals 'INTERVENTIONAL'

TRIAL SUMMARY PARAMETER VALIDATION RULES

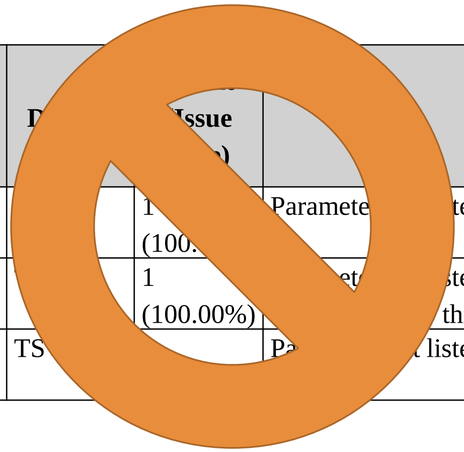
- New validation rules added that check for the presence of ‘FDA Desired’ parameters listed in the TCG that are not in the SDTMIG

Rule ID	Message	Description
SD2273	Missing EXTTIND Trial Summary Parameter	'Extension Trial Indicator' (EXTTIND) record must be populated in Trial Summary (TS) domain. It is an 'FDA Desired' parameter listed in the Technical Conformance Guide (TCG).
SD2274	Missing NCOHORT Trial Summary Parameter	'Number of Groups/Cohorts' (NCOHORT) record must be populated in Trial Summary (TS) domain. It is an 'FDA Desired' parameter listed in the Technical Conformance Guide (TCG).
SD2275	Missing OBJSEC Trial Summary Parameter	'Trial Secondary Objective' (OBJSEC) record must be populated in Trial Summary (TS) domain. It is an 'FDA Desired' parameter listed in the Technical Conformance Guide (TCG).
SD2276	Missing PDPSTIND Trial Summary Parameter	'Pediatric Postmarket Study Indicator' (PDPSTIND) record must be populated in Trial Summary (TS) domain. It is an 'FDA Desired' parameter listed in the Technical Conformance Guide (TCG).
SD2277	Missing PDSTIND Trial Summary Parameter	'Pediatric Study Indicator' (PDSTIND) record must be populated in Trial Summary (TS) domain. It is an 'FDA Desired' parameter listed in the Technical Conformance Guide (TCG).
SD2278	Missing PIPIND Trial Summary Parameter	'Pediatric Investigation Plan Indicator' (PIPIND) record must be populated in Trial Summary (TS) domain. It is an 'FDA Desired' parameter listed in the Technical Conformance Guide (TCG).
SD2279	Missing RDIND Trial Summary Parameter	'Rare Disease Indicator' (RDIND) record must be populated in Trial Summary (TS) domain. It is an 'FDA Desired' parameter listed in the Technical Conformance Guide (TCG).
SD2280	Missing SDTIGVER Trial Summary Parameter	'SDTM IG Version' (SDTIGVER) record must be populated in Trial Summary (TS) domain. It is an 'FDA Desired' parameter listed in the Technical Conformance Guide (TCG).
SD2281	Missing SDTMVER Trial Summary Parameter	'SDTM Version' (SDTMVER) record must be populated in Trial Summary (TS) domain. It is an 'FDA Desired' parameter listed in the Technical Conformance Guide (TCG).
SD2282	Missing THERAREA Trial Summary Parameter	'Therapeutic Area' (THERAREA) record must be populated in Trial Summary (TS) domain. It is an 'FDA Desired' parameter listed in the Technical Conformance Guide (TCG).

TRIAL SUMMARY PARAMETER VALIDATION RULES

- In general, sponsors have been adding these TS parameters listed in the TCG but there are still many that do not include them
  - Example from the cSDRG:

Check ID	Diagnostic Message	FDA Severity	D	Issue	Explanation
SD2280	Missing SDTIGVER Trial Summary Parameter	Warning		1 (100.	Parameter listed in the SDTMIG, thus not required to be included.
SD2281	Missing EXTTIND Trial Summary Parameter	Warning		1 (100.00%)	Parameter listed in the SDTMIG, thus not required to be included. This study is not this parameter is not applicable for the study.
SD2282	Missing THERAREA Trial Summary Parameter	Warning	TS		Parameter listed in the SDTMIG, thus not required to be included.



  - These are TS parameters expected by the FDA. It is not ‘optional’ to include them when FDA Desired = ‘Y’ in TCG’s Appendix B
  - Parameters should be added to TS so the validation rules no longer fire. These rules should not be explained in the cSDRG

TRIAL SUMMARY PARAMETER VALIDATION RULES

- Validation rules that check TSVAL against CDISC CT at the value/parameter level as well as TSPARMCD/TSPARM

Rule ID	Message	Description
CT2001	Variable value not found in non-extensible codelist	Variable must be populated with terms from its CDISC controlled terminology codelist. New terms cannot be added into non-extensible codelists.
CT2002	Variable value not found in extensible codelist	Variable should be populated with terms from its CDISC controlled terminology codelist. New terms can be added as long as they are not duplicates, synonyms or subsets of existing standard terms.
CT2003	Variable and Variable Decode values do not have the same Code in CDISC CT	Paired variables such as TEST/TESTCD must be populated using terms with the same Codelist Code value in CDISC control terminology. There is one-to-one relationship between paired variable values defined in CDISC control terminology by Codelist Code value.
CT2004	Variable value not found in non-extensible codelist when value-level condition is met	Variable must be populated with terms from its CDISC controlled terminology codelist, when its value level condition is met. New terms cannot be added into non-extensible codelists.
CT2005	Variable value not found in extensible codelist when value-level condition is met	Variable should be populated with terms from its CDISC controlled terminology codelist, when its value level condition is met. New terms can be added as long as they are not duplicates, synonyms or subsets of existing standard terms.
CT2006	Variable and Variable Decode values do not have the same Code in CDISC CT when value-level condition is met	Paired variables such as TEST/TESTCD must be populated using terms with the same Codelist Code value in CDISC control terminology. There is one-to-one relationship between paired variable values defined in CDISC control terminology by Codelist Code value within the same value level condition.

TRIAL SUMMARY PARAMETER VALIDATION RULES

- CT2003

Rule ID	Message	Description
CT2003	Variable and Variable Decode values do not have the same Code in CDISC CT	Paired variables such as TEST/TESTCD must be populated using terms with the same Codelist Code value in CDISC control terminology. There is one-to-one relationship between paired variable values defined in CDISC control terminology by Codelist Code value.

- Rule will fire when paired values that share the same C-code have a submission value that matches CDISC CT but the other does not
  - TSPARMCD/TSPARM – Both have a ‘Submission Value’ with the same C-code

Code	Codelist Code	Codelist Extensible (Yes/No)	Codelist Name	CDISC Submission Value	CDISC Synonym(s)	CDISC Definition
C156602	C66738		Trial Summary Parameter Test Code	CTAUG	CDISC Therapeutic Area User Guide	The name and version of the CDISC therapeutic area user guide that is being used in the study submission.
C156602	C67152		Trial Summary Parameter Test Name	CDISC Therapeutic Area User Guide	CDISC Therapeutic Area User Guide	The name and version of the CDISC therapeutic area user guide that is being used in the study submission.

TRIAL SUMMARY PARAMETER VALIDATION RULES

- CT2003 Example:

Dataset	Record	Count	Variables	Values	Rule ID	Publisher ID	Message	Category	FDA
TS		1	TSPARMCD, TSPARM	OBJEXP, Trial Explortory Objective	CT2003	FDAB009, CG0021	TSPARMCD and TSPARM values do not have the same Code in CDISC CT	Terminology	Error
TS		1	TSPARMCD, TSPARM	EPDEMIC, Name of Epi/Pandemic	CT2003	FDAB009, CG0021	TSPARMCD and TSPARM values do not have the same Code in CDISC CT	Terminology	Error

- CT2002 will fire in this instance as well so it is relatively easy to determine the value that does not match CDISC CT
- cSDRG explanation:

Check ID	Diagnostic Message	FDA Severity		Count (Rate)	Explanation
CT2003	TSPARMCD and TSPARM values do not have the same Code in CDISC CT	Error	T	7%)	se positive errors within P21 tool. The values below were populated correctly as own: SPARMCD – 'OBJEXP' and 'EPDEMIC' TSPARM – 'Trial Explortory Objective' and 'Name of Epi/Pandemic'

TRIAL SUMMARY PARAMETER VALIDATION RULES

- Validation rules that check the format and datatype in TSVAL at the parameter level

Rule ID	Message	Description
SD2246	Invalid TSVAL value for NARMS	TSVAL variable value must be numeric, when TSPARMCD='NARMS'.
SD2247	Invalid TSVAL value for SSTDTC	TSVAL variable value must be in ISO 8601 format, when TSPARMCD='SSTDTC'.
SD2248	Invalid TSVAL value for SENDTC	TSVAL variable value must be in ISO 8601 format, when TSPARMCD='SENDTC'.
SD2249	Invalid TSVAL value for ACTSUB	TSVAL variable value must be numeric, when TSPARMCD='ACTSUB'.
SD2245	Invalid TSVAL value for DCUTDTC	TSVAL variable value must be in ISO 8601 format, when TSPARMCD='DCUTDTC'.
SD1323	Invalid TSVAL value for FCNTRY	TSVAL for FCNTRY record must be a valid term from ISO 3166.

TRIAL SUMMARY PARAMETER VALIDATION RULES

- Validation rules that check TSVAL and TSVALCD against external dictionaries (e.g. SNOMED, MED-RT, UNII)
  - Rules that check against SNOMED for TSPARMCD = INDIC and TDIGRP

Rule ID	Message	Description
SD2257	Invalid TSVAL value for INDIC	TSVAL for INDIC record must be a valid term from SNOMED CT.
SD2258	Invalid TSVALCD value for INDIC	TSVALCD for INDIC record must be a valid concept ID from SNOMED CT.
SD2259	TSVAL/TSVALCD value mismatch for INDIC	TSVAL and TSVALCD values must be populated from the same concept description record in SNOMED CT.
SD2267	Invalid TSVAL value for TDIGRP	TSVAL for TDIGRP record must be a valid term from SNOMED CT.
SD2268	Invalid TSVALCD value for TDIGRP	TSVALCD for TDIGRP record must be a valid concept ID from SNOMED CT.
SD2269	TSVAL/TSVALCD value mismatch for TDIGRP	TSVAL and TSVALCD values must be populated from the same concept description record in SNOMED CT.

  - Rules that check against MED-RT for TSPARMCD = PCLAS

Rule ID	Message	Description
SD2263	Invalid TSVAL value for PCLAS	TSVAL for PCLAS record must be a valid term from MED-RT or NDF-RT (Note: Any version 2018-02-05 or earlier uses NDF-RT, and any version after is MED-RT).
SD2264	Invalid TSVALCD value for PCLAS	TSVALCD for PCLAS record must be a valid code from MED-RT or NDF-RT (Note: Any version 2018-02-05 or earlier uses NDF-RT, and any version after is MED-RT).
SD2265	TSVAL/TSVALCD value mismatch for PCLAS	TSVAL and TSVALCD values must be populated from the same record in MED-RT or NDF-RT (Note: Any version 2018-02-05 or earlier uses NDF-RT, and any version after is MED-RT).

TRIAL SUMMARY PARAMETER VALIDATION RULES

- UNII (FDA Unique Ingredient Identifier) rules

Rule ID	Message	Description
SD2250	Invalid TSVAL value for CURTRT	TSVAL for CURTRT record must be a valid preferred term from FDA Substance Registration System (SRS).
SD2251	Invalid TSVALCD value for CURTRT	TSVALCD for CURTRT record must be a valid unique ingredient identifier from FDA Substance Registration System (SRS).
SD2252	TSVAL/TSVALCD value mismatch for CURTRT	TSVAL and TSVALCD values must be populated from the same name record in FDA Substance Registration System (SRS).
SD2253	Invalid TSVAL value for COMPTRT	TSVAL for COMPTRT record must be a valid preferred term from FDA Substance Registration System (SRS).
SD2254	Invalid TSVALCD value for COMPTRT	TSVALCD for COMPTRT record must be a valid unique ingredient identifier from FDA Substance Registration System (SRS).
SD2255	TSVAL/TSVALCD value mismatch for COMPTRT	TSVAL and TSVALCD values must be populated from the same name record in FDA Substance Registration System (SRS).
SD2260	Invalid TSVAL value for TRT	TSVAL for TRT record must be a valid preferred term from FDA Substance Registration System (SRS).
SD2261	Invalid TSVALCD value for TRT	TSVALCD for TRT record must be a valid unique ingredient identifier from FDA Substance Registration System (SRS).
SD2262	TSVAL/TSVALCD value mismatch for TRT	TSVAL and TSVALCD values must be populated from the same name record in FDA Substance Registration System (SRS).

VALIDATION RULES CHECKING AGAINST UNII DICTIONARY

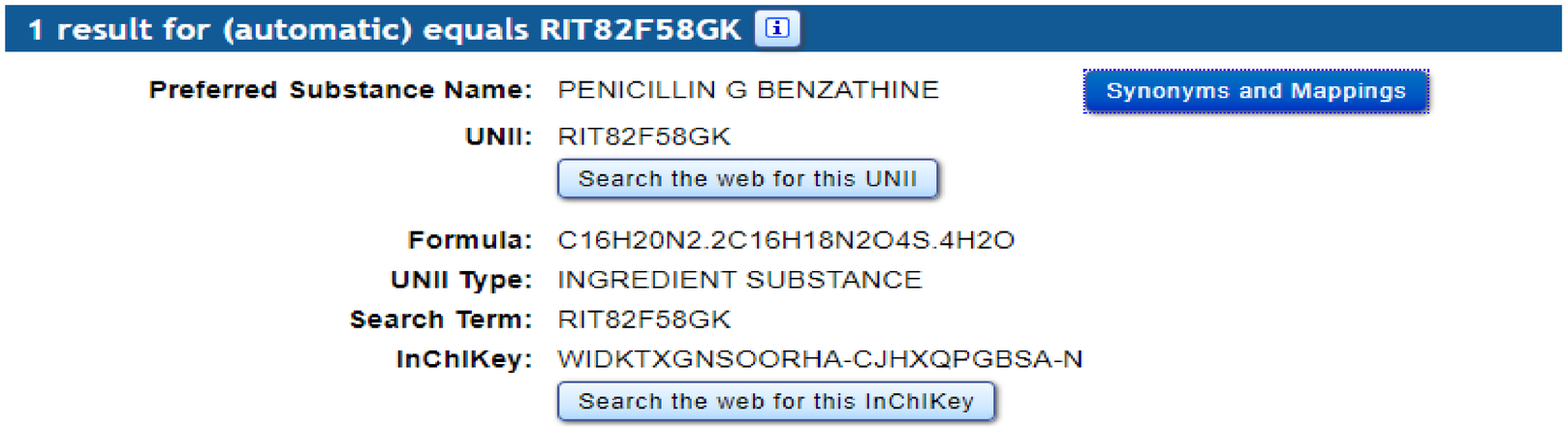
- SD2260, SD2261, and SD2262

Rule ID	Message	Description
SD2260	Invalid TSVAL value for TRT	TSVAL for TRT record must be a valid preferred term from FDA Substance Registration System (SRS).
SD2261	Invalid TSVALCD value for TRT	TSVALCD for TRT record must be a valid unique ingredient identifier from FDA Substance Registration System (SRS).
SD2262	TSVAL/TSVALCD value mismatch for TRT	TSVAL and TSVALCD values must be populated from the same name record in FDA Substance Registration System (SRS).

- UNII places substances into 5 discrete categories with a corresponding term and code for each:
  - of - Official Status (formerly ‘PT’/’Preferred Term’)
  - cn - Common Name
  - sys - Systemic Name
  - cd - Code
  - bn - Brand Name

VALIDATION RULES CHECKING AGAINST UNII DICTIONARY

- Prior to 09-2019, these rules only looked for the ‘of’ or ‘Official Status’ term/code based on FDA feedback
  - Over time, these rules (SD2250-55, SD2260-62) returned false positives for those drugs that did not have a term/code in the ‘of’ category
  - Terms/codes for these drugs were still available in the UNII dictionary: https://fdasis.nlm.nih.gov/srs/srs.jsp



VALIDATION RULES CHECKING AGAINST UNII DICTIONARY

- TS Dataset Snippet

STUDYID	DOMAIN	TSSEQ	TSPARMCD	TSPARM	TSVAL	TSVALNF	TSVALCD	TSVCDREF	TSVCDVER
ABC123	TS	1	TRT	Investigational Therapy or Treatment	PENICILLIN G BENZATHINE		RIT82F58GK	UNII	2019-07-12

- SD2260, SD2261, and SD2262 were triggered

Rule ID	Message	Description
SD2260	Invalid TSVAL value for TRT	TSVAL for TRT record must be a valid preferred term from FDA Substance Registration System (SRS).
SD2261	Invalid TSVALCD value for TRT	TSVALCD for TRT record must be a valid unique ingredient identifier from FDA Substance Registration System (SRS).
SD2262	TSVAL/TSVALCD value mismatch for TRT	TSVAL and TSVALCD values must be populated from the same name record in FDA Substance Registration System (SRS).

VALIDATION RULES CHECKING AGAINST UNII DICTIONARY

- After confirmation with FDA CDER eData team, there is no preference at this time as to which term type should be submitted
  - Filter for these rules that only looked for ‘of’ (‘Official Status’) terms/codes was removed to look at all categories

- SD2250-SD2255, SD2260-SD2262 should no longer be triggered as long as the term/code in TSVAL and TSVALCD matches a term in the UNII dictionary
  - Reducing false positives!

VALIDATION RULES CHECKING AGAINST DEFINE.XML

- Validation rules that check the consistency between the TS dataset and the define.xml

Rule ID	Message	Description
SD1228	Variable value not found in user-defined codelist when value-level condition occurs	Variable value must be populated with terms from user-defined value level codelist as specified in define.xml file.
SD1229	Variable value is null when value-level condition occurs	Variable value must be populated when value level attribute Mandatory='Yes' as specified in define.xml file.
SD1230	Variable datatype is not correct datatype when value-level condition occurs	Value level datatype must match the datatype described in define.xml.
SD1231	Variable value is longer than defined max length when value-level condition occurs	Value level length must not exceed the length as specified define.xml.

VALIDATION RULES CHECKING AGAINST DEFINE.XML

- SD1229 – Variable value is null when value level condition occurs
  - This rule is triggered when the variable is null at the value level in the dataset but the ‘Mandatory’ attribute in the define.xml code is set to ‘Yes’
  - Define-XML v2.0 guidance for the Mandatory element within ItemRef element for variable or value level metadata
    - SDTM: For SDTM based variables where Core is “Req” (Required), the value of Mandatory should be set to “Yes”
    - For variables where Core is “Exp” (Expected) or “Perm” (Permissible) and the sponsor does not require a more restrictive condition, Mandatory should be set to “No”
    - Variables where Mandatory=”Yes” must not have a null value

VALIDATION RULES CHECKING AGAINST DEFINE.XML

- In TS, SD1229 appears most often for TSVAL when TSVAL is null, TSVALNF is populated, and Mandatory = ‘Yes’ in the define.xml

STUDYID	DOMAIN	TSSEQ	TSPARMCD	TSPARM	TSVAL	TSVALNF	TSVALCD	TSVCDREF	TSVCDVER
ABC123	TS	1	PCLAS	Pharmacological Class of Invest. Therapy		NAV			

- Define.xml Code Snippet:

```
<ItemRef ItemOID="IT.TS.TSVAL.TS.TSPARMCD.EQ.PCLAS"
         OrderNumber="15"
         Mandatory="Yes">
   <def:WhereClauseRef WhereClauseOID="WC.TS.TSPARMCD.EQ.PCLAS"/>
</ItemRef>
```

- P21 Report:

Dataset	Rule ID	Publisher ID	Message	FDA
TS	SD1229	TCG 4.1.4.5	TSVAL value is null when TSPARMCD == 'PCLAS'	Error

VALIDATION RULES CHECKING AGAINST DEFINE.XML

- Per the SDTMIG, since TSVAL can be null when a value cannot be provided for a specific parameter, the ‘Mandatory’ attribute should be set ‘No’ in the define.xml and this rule will no longer fire
  - PLEASE NOTE: All define.xml structural issues as well as issues with consistency between the datasets and the define.xml should be rectified!
    - No define.xml related issues should remain prior to submission and thus, should not appear with explanations in the reviewer’s guide!!

FUTURE PLANS FOR TRIAL SUMMARY DOMAIN RESOURCES

- Currently, guidance for creating a comprehensive TS domain is found in the TCG, the SDTMIG including Appendix C1, and the TS Codetable
  - Beginning in SDTMIG v3.4, Appendix C1 will be removed and the following assumption added:
    - *Recipients may specify their requirements for which trial summary parameters should be included under which circumstances. For example, the US FDA includes such information in their Study Data Technical Conformance Guide.*
  - In addition to the TS Codetable, CDISC recently published resources that are similar to the TS Codetable and Appendix C1 to provide the linkage between variables and value-level metadata and the associated codelists including TS based on SDTMIG v3.2
    - CDISC CT Relationships v1.0 for SDTM v1.4 and SDTMIG v3.2: https://www.cdisc.org/standards/foundational/sdtmig/controlled-terminology-relationships-v1-0-sdtm-v1-4-and-sdtmig-v3-2

CONCLUSION

- It is well known within industry that a TS dataset is required for all submissions regardless of whether the data is submitted using CDISC standards or legacy
- It can be difficult to create an informative and complete Trial Summary domain due to many sources of guidance in the SDTMIG, the TCG etc.
- Hundreds of validation rules have been implemented for TS to aid sponsors in order to ensure submission of a comprehensive and conformant TS dataset
- Following all the regulatory and standards guidance is necessary to facilitate expedient review of the data in an effort to get drugs to patients faster


QUESTIONS?