

PMDA's New Validation Rules

PMDA Validation Rule Version 2.0概要説明及び
Pinnacle 21 LLCの実装

中尾 親彰, Country Manager

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Presenter – 中尾 親彰



- › SAS Programmer / Data Manager since 2004 in CRO/Pharm
- › P21 Japan GK Country Manager since 2019

PMDAへのデータ申請

- › 現在は必須ではなく、選択制。
- › 2020年4月1日の申請より義務化
 - › 適応範囲については、基本的通知の2.2項を参照
- › PMDAの関連通知
 - › <http://www.pmda.go.jp/review-services/drug-reviews/about-reviews/p-drugs/0028.html>
 - › <https://www.pmda.go.jp/english/review-services/reviews/0002.html>
 - › <http://www.pmda.go.jp/review-services/drug-reviews/about-reviews/p-drugs/0026.html>
 - › <https://www.pinnacle21.com/useful-links>
 - › PMDA guidance documents
 - › PMDA presentations
 - › Industry experience with PMDA data submissions

審査関連業務

- ▣ [審査関連業務の概要](#)
- ▣ [相談業務](#)
- ▣ [治験関連業務](#)
- ▣ [承認審査業務\(申請、審査等\)](#)
- ▣ [申請等手続き](#)
- ▣ [審査等について](#)
- ▣ [医療用医薬品](#)
- ▣ [新医薬品](#)
- ▣ [次世代審査・相談体制\(申請時電子データ提出\)](#)
- ▣ [関連通知等](#)
- ▣ **申請電子データ提出に関する技術情報(FAQ、データ標準カタログ等)**
- ▣ [説明会・講演会等](#)
- ▣ [申請電子データ利用に関する](#)

申請電子データ提出に関する技術情報(FAQ、データ標準カタログ等)

申請電子データ提出に関する技術情報を掲載しております。

- [申請電子データ提出に際して利用可能な規格一覧](#) (2019年11月1日更新)
- [バリデーションルール一覧](#) (2019年9月27日更新)

バリデーションルール	受付期間(申請日)※
バージョン1.0(2015年11月18日)	2016年10月1日～ 2021年3月31日
バージョン2.0(2019年9月27日)	2020年4月1日～

※ 申請後に申請電子データを追加提出する場合は、申請時に選択したバージョンのバリデーションルールに基づいて提出してください。

- [バリデーション用ソフトウェア](#) (2019年9月27日更新)
- PMDAは申請電子データのバリデーションに『Pinnacle 21 Enterprise』を利用します。利用するソフトウェアのバージョン等は下表のとおりです。

ソフトウェアバージョン	バリデーションエンジンバージョン	稼働期間
Pinnacle 21 Enterprise 3.0.5	-	2016年10月1日～ 2020年2月21日
Pinnacle 21 Enterprise 4.0.2	1511.6(バリデーションルールバージョン1.0適用時)	2020年2月22日～
	1810.3(バリデーションルールバージョン2.0適用時)	

↑本ページの上部に移動する ↓

PMDA Data Submissions

PMDA Guidance Documentations

- [New Drug Review with Electronic Data](#)
- [Data Standards Catalog \(2019-11-01\)](#)
- [FAQs on Electronic Study Data Submission \(in Japanese\)](#)
- [FAQs on Electronic Study Data Submission \(Excerpt\) \(English version, January 2019\)](#)
- [Technical Conformance Guide \(English version, January 2019\)](#)
- [Study Data Validation Rules Version 1.0 \(2015-11-18\)](#)
- [Study Data Validation Rules Version 2.0 \(2019-09-27\)](#)
- [Attachment 8](#)

PMDA Presentations

- [Electronic Data Submission and Utilization in Japan](#)
- [CDISC標準準拠データの提出の現状と \(Current status of submission of CDISC standard compliant data\)](#)

Industry Experience with PMDA Edata Submissions

- [Understanding PMDA Engines](#)
- [Electronic Data Submission to PMDA : Our experiences and matters of concern](#)
- [Lessons Learned for Successful e-Study Data Submission to the PMDA toward the End of Transitional Period](#)
- [Challenges of Submitting Electronic Study Data to Two Authorities: the PMDA & FDA](#)
- [Process optimization for efficient and smooth e-data submissions to both FDA and PMDA](#)

- [Findings About: De-mystifying the when and how](#)
- [Considerations and Updates in the Use of Timing Variables in Submitting SDTM-Compliant Datasets](#)
- [Implementing CDISC Standards for Device-Drug Studies](#)

ADaM

- [Incremental Changes: ADaMIG v1.2 Update](#)
- [Timing is Everything: Defining ADaM Period, Subperiod and Phase](#)
- [Practical Guidance for ADaM Dataset Specifications and Define.xml](#)

SEND

- [The Benefits, Challenges and Myths of SEND](#)

Define-XML

- [Using Pinnacle 21 Enterprise for define.xml Creation: Tips and Tricks from a CRO Perspective.](#)
- [Do's and Don'ts of Define.xml](#)
- [How to use SUPPQUAL for specifying natural key variables in define.xml?](#)

BIMO

- [Clinical Development Standards for FDA Bioresearch Monitoring \(BIMO\) Submissions](#)
- [Sponsor Considerations for Building a Reviewer's Guide to Facilitate BIMO \(Bioresearch Monitoring\) Review](#)

最近更新された通知など

› (2019-01-24)

- › -承認申請時の電子データ提出に関する基本的考え方について
- › -承認申請時の電子データ提出に関する実務的事項について
- › -「承認申請時の電子データ提出に関する基本的考え方について」に関する質疑応答集(Q&A) について

› (2019-04-10)

› 申請電子データに関するFAQ

› (2019-09-27)

› バリデーションルール

PMDAへのデータ申請プロセス

- › 段階的なPMDAとの相談
 - › 治験相談
 - › 方法相談
 - › 確認相談
- › 他の文書(eCTD)とは別での申請
- › 申請日の数週間前から提出可能
- › バリデーション結果の確認（比較）

バリデーション結果の確認（比較）

- › PMDAはP21 Enterpriseで検証します。
- › 申請企業から提出された検証結果と比較します
- › RejectとErrorが議論の中心になります。
- › 報告内容に過不足があった場合調査が必要
 - › ソフトウェアの環境設定の不具合
 - › define.xmlをバリデーションしていない
 - › Xportファイルと一緒にdefine.xmlをバリデーションしていない
 - › False Positiveの内容を記載していない。
- › Note:別紙8の内容と申請データパッケージの梱包物が一致していることが前提です。

Severity (問題点の深刻さ)

> *Reject*

- > 申請電子データ受け入れプロセスが一旦ストップするルール。メタデータもしくはデータの修正が必要。

> *Error*

- > いずれかの”Reviewer’s Guide”で説明がなされるべきルール。確認相談などで事前の説明がされていない場合、プロセスの遅延につながる場合がある。

> *Warning*

- > 必ずしも説明を必要としないルール。（ミス防止のためのアラート）

PMDA Validation Rule 履歴

- › Version 1.0
 - › 2015年発効
 - › Enterprise V3.0.5(Community V2.1.3) 2020年2月21日まで
 - › Engine 1511.6として、2021年3月31日まで稼働
- › Version 2.0
 - › 2019年9月27日発効
 - › 2020年2月22日以降 Engine 1810.3として稼働

Validation Rulesの文書構成

- › エクセル形式
- › 列の構成
 - › Rule ID :Pinnacle IDと一致したもの
 - › Message, Description
 - › Domains, PMDA Severity
 - › Standards, PMDA Notes

PMDA Study Data Validation Rules Change History

Date (YYYY/MM/DD) ▾	Sheet Name ▾	Version # ▾	Description ▾
2015/11/18	SDTM Rules	1.0	Initial version.
2015/11/18	ADaM Rules	1.0	Initial version.
2015/11/18	Define-XML Rules	1.0	Initial version.
2019/09/27	SDTM Rules	2.0	Updated with consideration for the conformance rules by CDISC, system update, etc.
2019/09/27	ADaM Rules	2.0	Updated with consideration for the conformance rules by CDISC, system update, etc.
2019/09/27	Define-XML Rules	2.0	Updated with consideration for system update, etc.

Severity:

Reject : Rules which, if violated, will cause the review to be suspended until corrections have been made.

Error : Rules which, if violated without any prior explanation, will cause the review to be suspended until corrections have been made.

Warning : Rules which, even when violated, will not necessarily require any explanation.

SDTM Rules v2.0

RULE ID	MESSAGE	DESCRIPTION	DOMAINS	PMDA Severity	3.1.2	3.1.3	3.2	PMDA NOTES
CT2001	<Variable Name> value not found in '<Codelist Name>' non-extensible codelist	Variable must be populated with terms from its CDISC controlled terminology codelist. New terms cannot be added into non-extensible codelists.	ALL	Reject	X	X	X	Violation of CT2001 for the following variable/codelist pairs will be considered part of Rejection criteria. All others will be considered Errors. <Variable Name (Codelist Name)> AGEU (AGEU) COUNTRY (COUNTRY) IECAT (IECAT) RELTYPE (RELTYPE) SEX (SEX) --BLFL (NY) --DRVFL (NY) --FAST (NY) --OCCUR (NY) --PRESP (NY) AESER (NY) AESCONG (NY) AESDISAB (NY) AESDTH (NY) AESHOSP (NY) AESLIFE (NY) AECONTRT (NY) AESCAN (NY) AESMIE (NY) AESOD (NY) IEORRES (NY) IESTRESC (NY)
CT2002	<Variable Name> value not found in '<Codelist Name>' 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.	ALL	Warning	X	X	X	
CT2003	<Variable Name> and <DecodedVariable Name> 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.	ALL	Error	X	X	X	
CT2004	<Variable Name> value not found in '<Codelist Name>' non-extensible codelist	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.	QS, TS	Reject	X	X	X	Violation of CT2004 for the following variable/codelist pairs will be considered part of Rejection criteria. All others will be considered Errors. <Variable Name (Codelist Name)> TSVAL when TSPARMCD value is SEXPOP (SEXPOP) TSVAL when TSPARMCD value is ADDON (NY)
CT2005	<Variable Name> value not found in '<Codelist Name>' extensible codelist	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	DS, SC, TS, VS	Warning	X	X	X	

Severity:

Reject : Rules which, if violated, will cause the review to be suspended until corrections have been made.

Error : Rules which, if violated without any prior explanation, will cause the review to be suspended until corrections have been made.

Warning : Rules which, even when violated, will not necessarily require any explanation.

SDTM Rules v2.0

RULE ID	MESSAGE	DESCRIPTION	DOMAINS	PMDA Severity	3.1.2	3.1.3	3.1.4	PMDA NOTES
CT2001	<Variable Name> value not found in '<Codelist Name>' non-extensible codelist	Variable must be populated with terms from its CDISC controlled terminology codelist. New terms cannot be added into non-extensible codelists.	ALL	Reject	X	X	X	Violation of CT2001 for the following variable/codelist pairs will be considered part of Rejection criteria. All others will be considered Errors. <Variable Name (Codelist Name)> AGEU (AGEU) COUNTRY (COUNTRY) IECAT (IECAT) RELTYPE (RELTYPE) SEX (SEX) --BLFL (NY) --DRVFL (NY) --FAST (NY) --OCCUR (NY) --PRESP (NY) AESER (NY) AESCONG (NY) AESDISAB (NY) AESDTH (NY) AESHOSP (NY) AESLIFE (NY) AECONTRT (NY) AESCAN (NY) AESMIE (NY) AESOD (NY) IEORRES (NY) IESTRESC (NY)
CT2002	<Variable Name> value not found in '<Codelist Name>' 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.	ALL	Warning	X	X	X	
CT2003	<Variable Name> and <DecodedVariable Name> 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.	ALL	Error	X	X	X	
CT2004	<Variable Name> value not found in '<Codelist Name>' non-extensible codelist	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.	QS, TS	Reject	X	X	X	Violation of CT2004 for the following variable/codelist pairs will be considered part of Rejection criteria. All others will be considered Errors. <Variable Name (Codelist Name)> TSVAl when TSPARMCD value is SEXPOP (SEXPOP) TSVAl when TSPARMCD value is ADDON (NY)
CT2005	<Variable Name> value not found in '<Codelist Name>' extensible codelist	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	DS, SC, TS, VS	Warning	X	X	X	

RULE ID	MESSAGE	PMDA Severity	3.1.2	3.1.3	3.2	PMDA NOTES
CT2001	<Variable Name> value not found in '<Codelist Name>' non-extensible codelist	Reject	X	X	X	<p>Violation of CT2001 for the following variable/codelist pairs will be considered part of Rejection criteria. All others will be considered Errors.</p> <p><Variable Name (Codelist Name)> AGEU (AGEU) COUNTRY (COUNTRY) IECAT (IECAT) RELTYPE (RELTYPE) SEX (SEX) --BLFL (NY) --DRVFL (NY) --FAST (NY) --OCCUR (NY) --PRESP (NY) AESER (NY)</p>

Pinnacle 21 support for PMDA rules

> Version 1.0

- > P21 Enterprise v3.0.5 or [engine 1511.6](#) in v4+
- > P21 Community v2.1.3 or [engine 1511.6](#) in v3+
- > *“PMDA Legacy (1511.6)”*

> Version 2.0

- > P21 [engine 1810.3](#) in both Enterprise v4+ and Community v3+
- > *“PMDA (1810.3)”*

ALL FDA PMDA 1511.6 PMDA 1810.3



Rule ID ▲	Publisher ID ▲	Message	Description	Domains	FDA	PMDA 1511.6	PMDA 1810.3	FDA Severity	PMDA Severity	3.1.2	3.1.3	3.2	Notes
CT2001	CG0020, CG0085, CG0131, CG0232-CG0235, CG0387-CG0396	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.	ALL	X	X	X	Reject		X	X	X	🗨️
CT2002	CG0021	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.	ALL	X	X	X	Warning		X	X	X	
CT2003	CG0021	Coded and Decoded 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.	ALL	X	X	X	Error		X	X	X	
CT2004	CG0021	Variable value not found in non-extensible codelist when value-level condition occurs	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.	QS, TS	X	X	X	Reject		X	X	X	🗨️
			Variable should be populated with terms from its CDISC										

Search

- ALL
- FDA
- PMDA 1511.6
- PMDA 1810.3

Rule ID	Publisher ID	Message	Description	Domains	FDA	PMDA 1511.6	PMDA 1810.3	FDA Severity	PMDA Severity	3.1.2	3.1.3	3.2	Notes
CT2001	CG0020, CG0085, CG0131, CG0232-CG0235, CG0387-CG0396	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.	ALL	X	X	X		Reject	X	X	X	🗨️
CT2002	CG0021	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.	ALL	X	X	X		Warning	X	X	X	
CT2003	CG0021	Coded and Decoded 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.	ALL	X	X	X		Error	X	X	X	
CT2004	CG0021	Variable value not found in non-extensible codelist when value-level condition occurs	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.	QS, TS	X	X	X		Reject	X	X	X	🗨️
			Variable should be populated with terms from its CDISC										

ALL FDA PMDA 1511.6 PMDA 1511.7

Rule ID	Publisher ID	Message	CDISC CT	3.1.2	3.1.3	3.2	Notes
CT2001	CG0020, CG0085, CG0131, CG0232, CG0235, CG0387, CG0396	Variable value not found in non-extensible codelist		Reject	X	X	X
CT2002	CG0021	Variable value not found in extensible codelist		Warning	X	X	X
CT2003	CG0021	Coded and Decoded values do not have the same Code in CDISC CT		Error	X	X	X
CT2004	CG0021	Variable value not found in non-extensible codelist when value-level condition occurs	QS, TS	Reject	X	X	X
CT2005	CG0021	Variable value not found in extensible codelist when value-level condition occurs	DS, SC, TS, VS	Warning	X	X	X

Rule Notes for CT2001

PMDA: Violation of CT2001 for the following variable/codelist pairs will be considered part of Rejection criteria. All others will be considered Errors.

<Variable Name (Codelist Name)>

- AGEU (AGEU)
- COUNTRY (COUNTRY)
- IECAT (IECAT)
- RELTYPE (RELTYPE)
- SEX (SEX)
- BLFL (NY)
- DRVFL (NY)
- FAST (NY)
- OCCUR (NY)
- PRESP (NY)
- AESER (NY)
- AESCONG (NY)
- AESDISAB (NY)
- AESDTH (NY)
- AESHOSP (NY)
- AESLIFE (NY)
- AECONTRT (NY)
- AESCAN (NY)
- AESMIE (NY)
- AESOD (NY)
- IEORRES (NY)
- IESTRESC (NY)
- STAT (ND)

CLOSE

ALL FDA PMDA 1511.6 PMDA 1810.3

Rule ID ▲	Publisher ID	Message	Description	Domains	FDA	PMDA 1511.6	PMDA 1810.3	FDA Severity	PMDA Severity	3.1.2	3.1.3	3.2	Notes
SD0004	CG0413	Inconsistent value for DOMAIN	Domain Abbreviation (DOMAIN) variable should be consistent with the name of the dataset.	ALL	X	X	X	Warning		X	X	X	
SD0005	CG0028	Duplicate value for --SEQ variable	The value of Sequence Number (--SEQ) variable must be unique for each record within a domain and within each Unique Subject Identifier (USUBJID), Pool Identifier (POOLID) or Sponsor Device Identifier (SPDEVID) variables value when they are present in the domain.	ALL	X	X		Error		X	X	X	
SD0005	CG0028	Duplicate value for --SEQ variable	The value of Sequence Number (--SEQ) variable must be unique for each record within a domain and within each Unique Subject Identifier (USUBJID) or Pool Identifier (POOLID) variables value when they are present in the domain.	ALL	X	X		Error		X	X	X	
SD0006	FDAB013	No baseline flag record in Domain for subject	All subjects should have at least one baseline observation (--BLFL = 'Y') in EG, LB, MB, MS, PC and VS domains, except for subjects who failed screening (ARMCD = 'SCRNFAIL') or were not fully assigned to an Arm (ARMCD = 'NOTASSGN') or were not treated (ACTARMCD = 'NOTTRT').	EG, LB, MB, MS, PC, VS	X	X	X	Warning		X	X	X	
SD0007	FDAB030	Inconsistent value for Standard Units	Standard Units (--STRESU) must be consistent for all records with the same Short Name of Measurement, Test or Examination (--TESTCD), Category (--CAT), Subcategory (--CAT2), or Unit (--UNIT).	FINDINGS	X	X	X	Warning		X	X	X	

Rules v2.0 変更点

- › 新規発効のルール
- › ルールの修正
- › 適応範囲の変更
- › Severity:変更なし

申請で利用可能な標準規格

- › PMDA Validation Rule V2.0でも変更なし
- › SDTM-IG 3.1.2, 3.1.3, 3.2
- › ADaM-IG 1.0
- › Define-XML 1.0, 2.0

変更点の要約

Rules	SDTM	ADaM	Define-XML
New	115	15	33
Removed	4	2	4
Algorithm change	38	9	
Description/Message	22/7	4/2	10
Rules assignments	+76/-4	+4/-3	
Other	Medical Devices	ADaM OTHER	

ADaM OTHER

- › データセット名が、“AD”で始まる
ADSL,BDS, ADAE以外のデータセット
 - › OCCDSを作成した場合は、IG V1.0ではADaM OTHERとして処理(validate)されます。
 - › 以前はADCMなどのOCCDSデータがBDS判定されていた。
- › ADaMデータに対する共通ルールがADaM OTHERにも適応されています。

新しいチェックの参考

- › Value-Level Metadata in define.xml vs. data
- › TS domains rules
- › New SDTM rules from CDISC
- › Analysis Result Metadata (ARM) rules for Define-XML

バグの修正とアルゴリズムの改善

- › ADaM変数の数値の可変表記について
 - › TRT`xx`P, TR`xx`PG`y`, ANL`zz`FL, etc.
 - › Before: TRT*P – “*”文字もしくはは数値含む値
 - › After: TRT#P – “#”数値のみ
- › “—SEQ”変数の重複チェックについて
 - › 変数“SPDEVID”をサロゲートキーのチェック時に利用
- › 当該症例がDMドメインに存在しない (Reject)
 - › 同一症例(USUBJID)が違う施設(SITEID)で複数回登録されている場合に対応するアルゴリズムへ変更。

Reject Rules

Standard	# of Reject Rules
SDTM	9
ADaM	13 (+1)
Define-XML	14 (+1)

Reject rules (SDTM)

RULE ID	MESSAGE	DESCRIPTION	DOMAINS
CT2001	<Variable Name> value not found in '<Codelist Name>' non-extensible codelist	Variable must be populated with terms from its CDISC controlled terminology codelist. New terms cannot be added into non-extensible codelists.	ALL
CT2004	<Variable Name> value not found in '<Codelist Name>' non-extensible codelist	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.	QS, TS
SD0002	NULL value in variable marked as Required	Required variables (where Core attribute is 'Req') cannot be NULL for any records.	ALL
SD0056	SDTM Required variable not found	Variables described in SDTM IG as Required must be included in the dataset.	ALL
SD0062	Incompatible data source	Domain table must have a valid format (e.g., SAS transport (XPORT) v.5 or text-delimited).	ALL
SD0064	Subject is not present in DM domain	All Subjects (USUBJID) must be present in Demographics (DM) domain.	ALL
SD1020	Missing DM dataset	Demographics (DM) dataset must be included in every submission.	DM
SD1073	Variable prohibited for use in SDTM	Variables described in IG as inappropriate for usage must be not included in the dataset.	ALL
SD1074	Variable which can be used only in SEND	Variables designed only for SEND pre-clinical studies must be not included in the SDTM dataset.	ALL

Reject rules (ADaM)

RULE ID	MESSAGE	DESCRIPTION	DOMAINS
AD0001	Missing ADSL dataset	ADaM Subject level (ADSL) dataset should be included in every submission.	ADSL
AD0005	*FL value is not Y, N or null	A variable with a suffix of FL must have value that is Y, N or null (exception 1: RFL, PFL , ABLFL, ANLzzFL. Exception 2: Population flags COMPLFL,FASFL,ITTFL,PPROTFL,SAFFL,RANDFL,ENRFL cannot be null and at least 1 must be included in ADSL).	ALL
AD0006	*FN value is not 0, 1 or null	A variable with a suffix of FN has a value that is not 0, 1 or null (exception: RFN, PFN, ABLFN, ANLzzFN and population flags Numeric COMPLFN,FASFN,ITTFN,PPROTFN,SAFFN,RANDFN,ENRFLFN cannot be null and at least 1 must be included in ADSL).	ALL
AD0033	*RFL value is not Y or null	A variable with a suffix of RFL must have a value that is Y or null (R = record level flag variable).	BDS, ADAMOTHER
AD0034	*PFL value is not Y or null	A variable with a suffix of PFL must have a value that is Y or null (P = parameter level flag variable).	BDS, ADAMOTHER
AD0035	*RFN value is not 1 or null	A variable with a suffix of RFN must have a value that is 1 or null (R = record level flag variable).	BDS, ADAMOTHER
AD0036	*PFN value is not 1 or null	A variable with a suffix of PFN must have a value that is 1 or null (P = parameter level flag variable).	BDS, ADAMOTHER
AD0176	ABLFL value is not Y or null	ABLFL (Analysis Baseline Flag character) must be Y or null. For parameter-level and record-level character population flag variables: Y = yes (included). Null values are allowed (ADaM IG v1.0 p.13).	BDS
AD0178	ANLzzFL value is not Y or null	A variable of form ANLzzFL (analysis record flag) must be Y or null. Also mentioned in ADAE IG v1.0 p.16.	BDS, ADAE, ADAMOTHER
AD0211	ABLFN value is not 1 or null	ABLFN (Analysis Baseline Flag Numeric) must be 1 or null. For parameter-level and record-level numeric population flag variables: 1 = yes (included). Null values are allowed (ADaM IG v1.0 p.13).	BDS
AD0212	ANLzzFN value is not 1 or null	ANLzzFN (Analyzed Record Flag zz Numeric) must be 1 or null. For parameter-level and record-level numeric population flag variables: 1 = yes (included). Null values are allowed.	BDS, ADAE, ADAMOTHER
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.	ALL
SD0062	Incompatible data source	Domain table must have a valid format (e.g., SAS transport (XPORT) v.5 or text-delimited).	ALL

Reject rules (Define-XML)

RULE ID	MESSAGE	DESCRIPTION
DD0001	XML schema validation issue within Define.xml	There is an XML schema validation issue with either Define.xml structure or content that is not covered by one of the other rules. It is most likely an issue with element declarations.
DD0002	Missing or invalid <namespace> namespace reference	Define.xml must reference the following namespaces: 1) CDISC ODM xmlns="http://www.cdisc.org/ns/odm/v1.3" for Define-XML v2.0 or xmlns="http://www.cdisc.org/ns/odm/v1.2" for Define-XML v1.0; 2) CDISC Define xmlns:def="http://www.cdisc.org/ns/def/v2.0" for Define-XML v2.0 or xmlns:def="http://www.cdisc.org/ns/def/v1.0" for Define-XML v1.0; 3) XML Schema Instance xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"; and 4) XLink xmlns:xlink="http://www.w3.org/1999/xlink". The XML Schema Instance namespace is only required when a local schema is provided, while the XLink namespace is only required when external documents are provided.
DD0003	Missing required <attribute> value for <object>	Required attributes must be included in Define.xml and cannot be empty.
DD0006	Missing required <element> value	Required elements must be included in Define.xml and cannot be empty.
DD0020	Invalid def:DefineVersion	The def:DefineVersion should have a value of '1.0.0' for Define-XML v1.0 and '2.0.0' for Define-XML v2.0.
DD0021	Invalid Standard Name value <value>	Allowable values of Standard Name are: 'SDTM-IG', 'SEND-IG', or 'ADaM-IG' for Define-XML v2.0 or 'CDISC SDTM', 'CDISC SEND' or 'CDISC ADaM' for Define-XML v1.0. Values must conform to this list of values. Define-XML specification represents Standard Name as def:StandardName attribute on MetaDataVersion element. Note: Refer to the data standards catalog by the relevant Regulatory Agency for acceptance of standards and their versions.
DD0022	Invalid Standard Version value <value> for <standard>	Standard Version must have a valid value for the given Standard Name. Allowed values are '3.1.2', '3.1.3', or '3.2' for SDTM-IG, '3.0' or '3.1' for SEND-IG, and '1.0' or '1.1' for ADaM-IG. Define-XML specification represents Standard Version as def:StandardVersion attribute on MetaDataVersion element. Note: Refer to the data standards catalog by the relevant Regulatory Agency for acceptance of standards and their versions.
DD0025	Invalid MedDRA Version <version>	MedDRA version must be set to decimal value ending with 0 or 1, for example '9.0' or '14.1'. Define-XML specification represents MedDRA version as Version attribute on ExternalCodeList element within CodeList element.
DD0101	Missing define.xml file	Guidance provided by regulatory agencies (FDA and PMDA) states that eCTD submissions must include a define.xml file for each study in Module 4 (nonclinical) and Module 5 (clinical). Note: Refer to the data standards catalog by the relevant Regulatory Agency for acceptance of standards and their versions.
OD0001	XML is not well-formed	Define.xml must contain well-formed XML.
OD0010	Missing XML declaration	Define.xml must start with an XML declaration.
OD0012	Invalid root element	Define.xml must contain a root element called ODM.
OD0022	Duplicate Study OID	The OID attribute for Study element must be unique within a related series of ODM documents.
OD0027	Duplicate MetaDataVersion OID	The OID attribute for MetaDataVersion element must be unique within a single study.

Reject Rules (例外1)

- CT2001は以下の変数とコードリストのペアについては、逸脱するとRejectになります。それ以外がErrorです。

Variable	Codelist
AGEU	AGEU
COUNTRY	COUNTRY
IECAT	IECAT
RELTYPE	RELTYPE
SEX	SEX
--BLFL	NY
--DRVFL	NY
--FAST	NY

Variable	Codelist
--OCCUR	NY
--PRESP	NY
AESER	NY
AESCONG	NY
AESDISAB	NY
AESDTH	NY
AESHOSP	NY
AESLIFE	NY

Variable	Codelist
AECONTR	NY
AESCAN	NY
AESMIE	NY
AESOD	NY
IEORRES	NY
IESTRESC	NY
--STAT	ND

Reject Rules (例外2)

- ルール”CT2004”に関して以下の3つのレコードとコードリストのペアから逸脱する場合、Rejectに該当します。これ以外は、Errorに該当します。

Variable	Codelist
TSVAL when TSPARMCD value is SEXPOP	SEXPOP
TSVAL when TSPARMCD value is ADDON	NY
TSVAL when TSPARMCD value is RANDOM	NY

Reject Rules (例外3)

- › ”SD0002“に関する逸脱はRejectになります。ただしDMドメインの以下の変数は、欠損でもErrorになります。

Variable
ARMCD
ARM
ACTARMCD
ACTARM

New Reject rules

› ADaM

- › SD0062: *xport* ファイルが壊れている場合です。
- › “ADaM OTHER”に関して以下のルールが適応されています。
 - › AD0005: このルールがADSLのみからBDS ADAM OTHERも対象になります。
 - › AD0033: 接尾語が”RFL”に該当する変数の値が”Y” Null以外の場合、Rejectになりますが、BDSに加えてADaM OTHERも対象です。
 - › ENRFL (*Enrolment Flag*) –症例レベルの採否フラグで接尾語がRFLだと“N”が値として入るので命名規則で予約語とされている接頭語・接尾語に気をつけてください。

› Define-XML

- › DD0101: 同一フォルダ内にメタデータがないとReject

New Error Rules

› SDTM – 47

- › SD1233: Device is not present in DI domain
- › SD1254: AE.AEOUT = 'FATAL' の場合、変数”DTHFL” の値が“Y”でない。
- › SD1273:変数名の接尾語が--TRT場合、値が'OTHER'である。

› ADaM – 12

- › AD0253:症例単位でSDTMのAEレコードが全てADAEに引き継がれている。
- › AD0011: $--FL \wedge = N$ and $--FN \wedge = 0$

› Define-XML – 19

- › DD0012: MedDRAが定義されていない
- › DD0008: “define.xml”で要素の順番が間違っている。
- › DD0092: ParameterOIDが存在しない。

”Engine”の選び方

- › 申請日に従ってENGINEを選ぶこと
 - › 2020-04-01より前
 - › Rules v1.0
 - › Community V2.1.3 or Enterprise V3.0.5
 - › (Engine 1511.6)
 - › 2020-04-01以降
 - › Rules v2.0, Engine 1810.3
 - › オプション : Rules v1.0, Engine 1511.6

Community Validation

- › Version 3.x以上の利用を推奨
- › MedDRAの初期設定
- › Validationの間は、ユーザIDでログインした状態でインターネットへのアクセスがある方が良いでしょう。（更新がある。）
- › ADaMのデータをValidationするときにSDTM(AE、DM、EX)を同梱することを忘れない。

まとめとして

- › Ruleが変更になってない場合もアルゴリズムが更新されている場合があります。
- › PMDAのEngine 1810.3は、PMDA Validation Rule V2.0に対応しています申請時期が未定のものなど、相談前の場合はこちらを推奨します。
- › ソフトウェアの利用方法に従って必ずxportファイル、define.xmlその内部から参照した文書をバリデーションしてください。

Questions

Chikaaki NAKAO
cnakao@pinnacle21.com