

## Appendix 2. Use Cases for the Custom Domain Resource

### Example 1: Mapping micronucleus end-points

A published in vivo mammalian cytogenetics study satisfying the OPPTS 870.5395; OECD 474 guideline was used to model endpoints from an erythrocyte micronucleus assay in mice.

Brief overview of the study (No. 221): Male mice in groups of 6 were administered either test article, vehicle or positive control (cyclophosphamide). Bone marrow was harvested from the hind limb (tibia) 24 and 48 hours after dosing. The following endpoints were assessed:

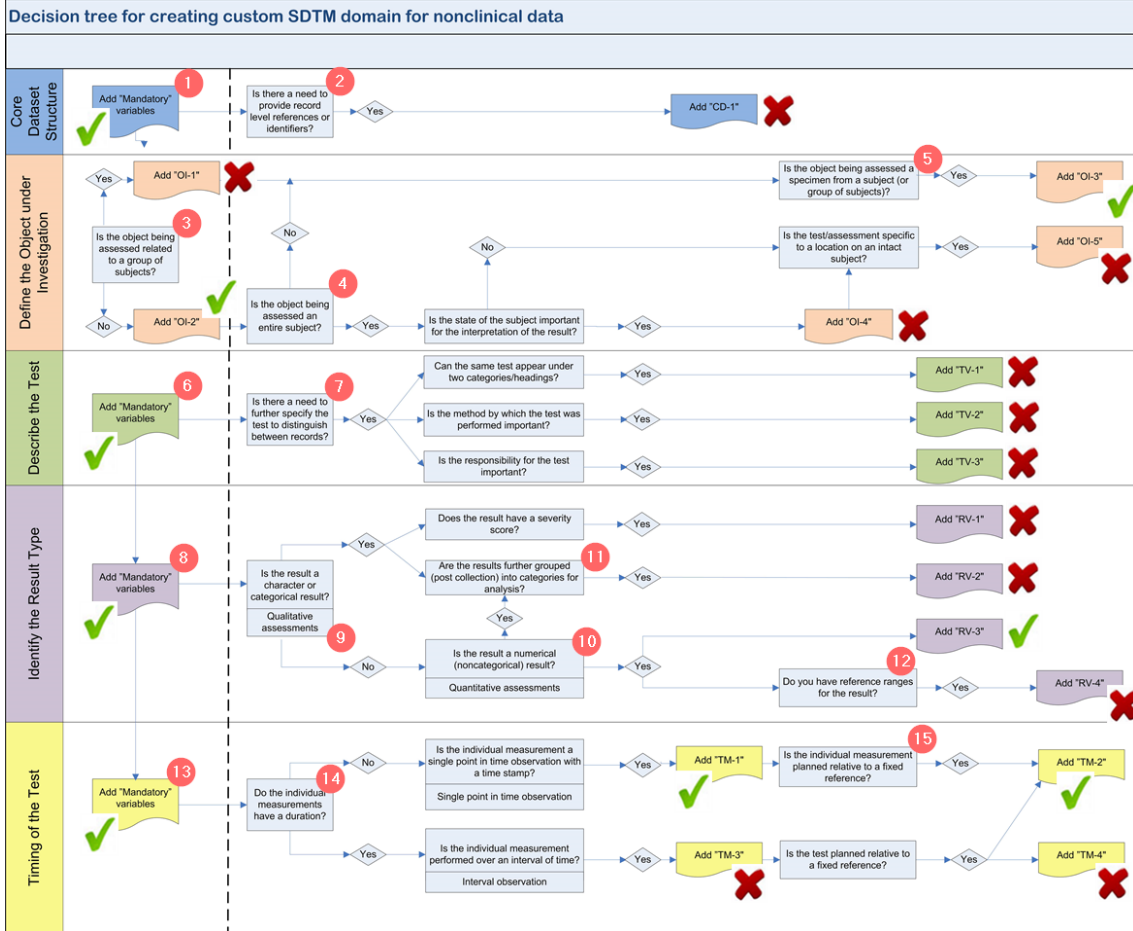
Endpoint	Result type	Unit
<b>Number of micronucleated erythrocytes per 2000 polychromatic erythrocytes (PCE) examined per animal</b>	Number (integer)	/2000 PCEs/animal
<b>Ratio of polychromatic erythrocytes (PCE) to monochromatic erythrocytes (NCE) determined in at least 500 erythrocytes per animal</b>	Number (float)	ratio

#### Data from the study:

Study day	Animal Number	# MN PCEs /2000 PCEs /animal	Ratio PCE:NCE
<b>24</b>	2602	1	0.47
<b>24</b>	2606	0	0.78
<b>48</b>	2632	2	0.56

The endpoints in the table above are sent through the decision tree, starting from the top left side. Ideally each of the two endpoints above should be processed through the decision tree separately; however the outcome through the decision will be the same for both, so only one run through the decision tree is described below.

The figure below illustrates the steps that this particular data will go through and the categories of variables selected by answering the questions.



#### Decision steps:

1. The Core Dataset Structure mandatory variables (STUDYID, DOMAIN, --SEQ) are added
2. There is no need to provide record level references or identifiers, so CD-1 variables are omitted.
3. The object assessed is not a group of subjects, so the answer to 3 is no.
4. The object assessed is not an entire subject, so the answer to 4 is no.
5. The object assessed is a specimen from a subject (i.e. bone marrow from the hind limb), so the answer to 5 is yes. Therefore OI-2 (USUBJID), and OI-3 (--REFID, --SPEC, --ANTREG, --SPCCND, --LAT, --DIR, --PORTOT) variables are added. Note: The answer to either 3, 4 or 5 must be yes, in this case it was no. 5.
6. The Test mandatory variables (--TESTCD, --TEST) are added.
7. There is no need to further specify the test to distinguish between records, so all other test variables (TV-1, TV-2 and TV-3) are omitted. The need to further specify a test could be if the same test was measured using two different methods (i.e. dipstick and mass spectrometry) or the same test performed by two different labs.
8. The Result mandatory variables (--ORRES, --STRESC, --STAT, --REASND, --EXCLFL, --REASEX) are added.
9. The results are not character or categorical data, so the answer to 9 is no.
10. The results are numeric (i.e. integer and float), so the answer to 10 is yes. The RV-3 variables (--ORRESU, --STRESN, --STRESU, --BLFL) are added.
11. The results are not categorized for further analysis, so the answer to 11 is no and RV-2 variables are omitted.
12. There are no references ranges provided for the results, so the answer to 12 is no and RV-4 variables are omitted.
13. The Timing mandatory variable (VISITDY) is added.
14. The test does not have a duration, so the answer to 14 is no. The test is performed at a single point in time, TM-1 variables (--DTC, --DY) are added.
15. The test is performed relative to a fixed reference (i.e. 24 and 48 hours post dose), so the answer to 15 is yes and TM-2 variables (--TPT, --TPTNUM, --ELTM, --TPTREF, --RFTDTC) are added.

The resulting domain structure is given below with all omitted variables removed.

Decision based adding of variables			Custom SDTM dataset specification – Micronucleus data					
Decision steps	Variable category	Variable group	Core (within variable group)	Variable Name	Variable Label	Type	Controlled Terms, Codelist, or Format	Role
Step 1	Core Dataset structure	Mandatory	Req	STUDYID	Study Identifier	Char		Identifier
Step 1	Core Dataset structure	Mandatory	Req	DOMAIN	Domain Abbreviation	Char	XX	Identifier
Step 5	Object Identifier	OI-2	Req	USUBJID	Unique Subject Identifier	Char		Identifier
Step 1	Core Dataset structure	Mandatory	Req	--SEQ	Sequence Number	Num		Identifier
Step 5	Object Identifier	OI-3	Perm	--REFID	Reference Identifier	Char		Identifier
Step 6	Test Variables	Mandatory	Req	--TESTCD	Measurement, Test or Examination Short Name	Char	Controlled terminology is expected	Topic
Step 6	Test Variables	Mandatory	Req	--TEST	Measurement, Test or Examination Name	Char	Controlled terminology is expected	Synonym Qualifier
Step 8	Result Variables	Mandatory	Exp	--ORRES	Result or Finding as Collected	Char		Result Qualifier
Step 10	Results Variables	RV-3	Exp	--ORRESU	Unit of the Original Result	Char	(UNIT)	Variable Qualifier
Step 8	Results Variables	Mandatory	Exp	--STRESC	Standardized Result in Character Format	Char	Controlled terminology is expected	Result Qualifier
Step 10	Results Variables	RV-3	Exp	--STRESN	Standardized Result in Numeric Format	Num		Result Qualifier
Step 10	Results Variables	RV-3	Exp	--STRESU	Unit of the Standardized Result	Char	(UNIT)	Variable Qualifier
Step 8	Result Variables	Mandatory	Perm	--STAT	Completion Status	Char	(ND)	Record Qualifier
Step 8	Result Variables	Mandatory	Perm	--REASND	Reason Not Done	Char		Record Qualifier
Step 5	Object Identifier	OI-3	Exp	--SPEC	Specimen Material Type	Char	(SPEC)	Record Qualifier
Step 5	Object Identifier	OI-3	Exp	--ANTREG	Anatomical Region of Specimen	Char		Variable Qualifier

Decision based adding of variables			Custom SDTM dataset specification – Micronucleus data					
Decision steps	Variable category	Variable group	Core (within variable group)	Variable Name	Variable Label	Type	Controlled Terms, Codelist, or Format	Role
Step 5	Object Identifier	OI-3	Perm	--SPCCND	Specimen Condition	Char		Variable Qualifier
Step 5	Object Identifier	OI-3	Perm	--SPCUFL	Specimen Usability for the Test	Char	(NY)	Variable Qualifier
Step 5	Object Identifier	OI-3	Perm	--LAT	Specimen Laterality within Subject	Char	(LAT)	Variable Qualifier
Step 5	Object Identifier	OI-3	Perm	--DIR	Specimen Directionality within Subject	Char	(DIR)	Variable Qualifier
Step 5	Object Identifier	OI-3	Perm	--PORTOT	Portion or Totality	Char	(PORTOT)	Variable Qualifier
Step 10	Result Variables	RV-3	Exp	--BLFL	Baseline Flag	Char	(NY)	Record Qualifier
Step 8	Results Variables	Mandatory	Perm	--EXCLFL	Exclusion Flag	Char	(NY)	Record Qualifier
Step 8	Results Variable	Mandatory	Perm	--REASEX	Reason for Exclusion	Char		Record Qualifier
Step 13	Timing Variables	Mandatory	Exp	VISITDY	Planned Study Day	Num		Timing
Step 14	Timing Variables	TM-1	Exp	--DTC	Date/Time of Test	Char	ISO 8601	Timing
Step 14	Timing Variables	TM-1	Exp	--DY	Study Day of Test	Num		Timing
Step 15	Timing Variables	TM-2	Exp	--TPT	Planned Time Point Name	Char		Timing
Step 15	Timing Variables	TM-2	Exp	--TPTNUM	Planned Time Point Number	Num		Timing
Step 15	Timing Variables	TM-2	Exp	--ELTM	Planned Elapsed Time from Time Point Ref	Char	ISO 8601	Timing
Step 15	Timing Variables	TM-2	Exp	--TPTREF	Time Point Reference	Char		Timing
Step 15	Timing Variables	TM-2	Exp	--RFTDTC	Date/Time of Reference Time Point	Char	ISO 8601	Timing

The dataset outline based on the domain structure above including example data is shown below. I have decided to name it "MN" (for Micronucleus), which is populated in the DOMAIN variable and also used as prefix for all variables with -- in their name in the domain structure.

The permissibility (Core within each variable group) is included. Once the data has been successfully mapped into the dataset structure and you make sure that you have been able to map all information about each result, then a last exercise to remove any non-used permissible variables (highlighted in blue) should be performed.

Note that as part of this final step we are removing four mandatory Result Variables because they are permissible and were not used in the dataset. The expected but unused variables are still kept in the dataset structure.

The actual date/time information about the results is likely available for data collected in today's data capture systems, but in this example that information cannot be populated because of the legacy nature of the used data.

	<i>Req</i>	<i>Req</i>	<i>Req</i>	<i>Req</i>	<i>Perm</i>	<i>Req</i>	<i>Req</i>	<i>Exp</i>	<i>Exp</i>	<i>Exp</i>	<i>Exp</i>	<i>Exp</i>
<i>Row no.</i>	STUD YID	DOM AIN	USUB JID	MNS EQ	MNRE FID	MNTES TCD	MNTEST	MNOR RES	MNOR RESU	MNST RESC	MNST RESN	MNST RESU
1	221	MN	221-2602	1		MN_P CE	Micronucleated Polychromatic Erythrocyte	1	/2000 PCEs /animal	1	1	/2000 PCEs /animal
2	221	MN	221-2602	2		PCE/NCE	Polychromatic Monochromatic Ratio	0.47	Ratio	0.47	0.47	Ratio
3	221	MN	221-2606	1		MN_P CE	Micronucleated Polychromatic Erythrocyte	0	/2000 PCEs /animal	0	0	/2000 PCEs /animal
4	221	MN	221-2606	2		PCE/NCE	Polychromatic Monochromatic Ratio	0.78	Ratio	0.78	0.78	Ratio
5	221	MN	221-2632	1		MN_P CE	Micronucleated Polychromatic Erythrocyte	2	/2000 PCEs /animal	2	2	/2000 PCEs /animal
6	221	MN	221-2632	2		PCE/NCE	Polychromatic Monochromatic Ratio	0.56	Ratio	0.56	0.56	Ratio

<i>(Cont.)</i>	<i>Perm</i>	<i>Perm</i>	<i>Exp</i>	<i>Exp</i>	<i>Perm</i>	<i>Perm</i>	<i>Perm</i>	<i>Perm</i>	<i>Perm</i>	<i>Exp</i>	<i>Perm</i>	<i>Perm</i>
<i>Row no.</i>	MNST AT	MNRE ASND	MNSP EC	MNANT REG	MNSP CND	MNSP CUFL	MNL AT	MND IR	MNPOR TOT	MNB LFL	MNEX CLFL	MNREA SEX
1			BONE MAR ROW									

2		BONE MAR ROW								
3		BONE MAR ROW								
4		BONE MAR ROW								
5		BONE MAR ROW								
6		BONE MAR ROW								

(Cont.)	Exp	Exp	Exp	Exp	Exp	Exp	Exp	Exp
<i>Row no.</i>	<b>VISITDY</b>	<b>MNDTC</b>	<b>MNDY</b>	<b>MNTPT</b>	<b>MNTPTNUM</b>	<b>MNELTM</b>	<b>MNTPTRF</b>	<b>MNRFTDT C</b>
1	2		2	24 hours after dose	1	P24H	Day 1 dose	
2	2		2	24 hours after dose	1	P24H	Day 1 dose	
3	2		2	24 hours after dose	1	P24H	Day 1 dose	
4	2		2	24 hours after dose	1	P24H	Day 1 dose	
5	3		3	48 hours after dose	2	P48H	Day 1 dose	
6	3		3	48 hours after dose	2	P48H	Day 1 dose	

Reference: [http://www.epa.gov/opp00001/chem\\_search/cleared\\_reviews/csr\\_PC-072506\\_27-Jul-05\\_a.pdf](http://www.epa.gov/opp00001/chem_search/cleared_reviews/csr_PC-072506_27-Jul-05_a.pdf)