6 Domain Models Based on the General Observation Classes

6.1 Interventions

Concomitant/Prior Medications (CM)

CM – Description/Overview for the Concomitant/Prior Medication Domain Model

Case report form (CRF) data that captures the concomitant and prior medications/therapies used by the subject. Examples are the concomitant medications/therapies given on an as needed basis and the usual background medications/therapies given for a condition.

CM – Specification for the Concomitant/Prior Medication Domain Model

cm.xpt, Concomitant Medications — Interventions, Version 3.2. One record per recorded intervention occurrence or constant-dosing interval per subject, Tabulation

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	CM	Identifier	Two-character abbreviation for the domain.	Req
USUBJID	Unique Subject Identifier	Char		Identifier	Identifier used to uniquely identify a subject across all studies for all applications or submissions involving the product.	Req
CMSEQ	Sequence Number	Num		Identifier	Sequence Number given to ensure uniqueness of subject records within a domain. May be any valid number.	Req
CMGRPID	Group ID	Char		Identifier	Used to tie together a block of related records in a single domain for a subject.	Perm
CMSPID	Sponsor-Defined Identifier	Char		Identifier	Sponsor-defined reference number. Examples: a number pre-printed on the CRF as an explicit line identifier or record identifier defined in the sponsor's operational database. Example: line number on a concomitant medication page.	Perm
CMTRT	Reported Name of Drug, Med, or Therapy	Char		Topic	Verbatim medication name that is either pre-printed or collected on a CRF.	Req
CMMODIFY	Modified Reported Name	Char		Synonym Qualifier	If CMTRT is modified to facilitate coding, then CMMODIFY will contain the modified text.	Perm

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
CMDECOD	Standardized Medication Name	Char	*	Synonym Qualifier	Standardized or dictionary-derived text description of CMTRT or CMMODIFY. Equivalent to the generic medication name in WHO Drug. The sponsor is expected to provide the dictionary name and version used to map the terms utilizing the define.xml external codelist attributes. If an intervention term does not have a decode value in the dictionary then CMDECOD will be left blank.	Perm
CMCAT	Category for Medication	Char	*	Grouping Qualifier	Used to define a category of medications/treatments. Examples: PRIOR, CONCOMITANT, ANTI-CANCER MEDICATION, or GENERAL CONMED.	Perm
CMSCAT	Subcategory for Medication	Char	*	Grouping Qualifier	A further categorization of medications/ treatment. Examples: CHEMOTHERAPY, HORMONAL THERAPY, ALTERNATIVE THERAPY.	Perm
CMPRESP	CM Pre-Specified	Char	(NY)	Variable Qualifier	Used to indicate whether (Y/null) information about the use of a specific medication was solicited on the CRF.	Perm
CMOCCUR	CM Occurrence	Char	(NY)	Record Qualifier	When the use of specific medications is solicited, CMOCCUR is used to indicate whether or not (Y/N) use of the medication occurred. Values are null for medications not specifically solicited.	Perm
CMSTAT	Completion Status	Char	(ND)	Record Qualifier	Used to indicate that a question about a pre-specified medication was not answered. Should be null or have a value of NOT DONE.	Perm
CMREASND	Reason Medication Not Collected	Char		Record Qualifier	Describes the reason concomitant medication was not collected. Used in conjunction with CMSTAT when value is NOT DONE.	Perm
CMINDC	Indication	Char		Record Qualifier	Denotes why a medication was taken or administered. Examples: NAUSEA, HYPERTENSION.	Perm
CMCLAS	Medication Class	Char	*	Variable Qualifier	Drug class. May be obtained from coding. When coding to a single class, populate with class value. If using a dictionary and coding to multiple classes, then follow ***Section 4: 4.1.2.8.3, Multiple Values For A Non-Result Qualifier Variable*** or omit CMCLAS.	Perm
CMCLASCD	Medication Class Code	Char	*	Variable Qualifier	Class code corresponding to CMCLAS. Drug class. May be obtained from coding. When coding to a single class, populate with class code. If using a dictionary and coding to multiple classes, then follow ***Section 4: 4.1.2.8.3, Multiple Values For A Non-Result Qualifier Variable*** or omit CMCLASCD.	Perm
CMDOSE	Dose per Administration	Num		Record Qualifier	Amount of CMTRT taken. Not populated when CMDOSTXT is populated.	Perm
CMDOSTXT	Dose Description	Char		Record Qualifier	Dosing amounts or a range of dosing information collected in text form. Units may be stored in CMDOSU. Example: 200-400, 15-20. Not populated when CMDOSE is populated.	Perm
CMDOSU	Dose Units	Char	(UNIT)	Variable Qualifier	Units for CMDOSE, CMDOSTOT, and CMDOSTXT. Examples: ng, mg, or mg/kg.	Perm
CMDOSFRM	Dose Form	Char	(FRM)	Variable Qualifier	Dose form for CMTRT. Examples: TABLET, LOTION.	Perm
CMDOSFRQ	Dosing Frequency per Interval	Char	(FREQ)	Variable Qualifier	Usually expressed as the number of repeated administrations of CMDOSE within a specific time period. Examples: BID (twice daily), Q12H (every 12 hours).	Perm

Variable Name	Variable Label	Type	Controlled Terms, Codelist or Format	Role	CDISC Notes	Core
CMDOSTOT	Total Daily Dose	Num		Record Qualifier	Total daily dose of CMTRT using the units in CMDOSU. Used when dosing is collected as Total Daily Dose. Total dose over a period other than day could be recorded in a separate Supplemental Qualifier variable.	Perm
CMDOSRGM	Intended Dose Regimen	Char		Variable Qualifier	Text description of the (intended) schedule or regimen for the Intervention. Examples: TWO WEEKS ON, TWO WEEKS OFF.	Perm
CMROUTE	Route of Administration	Char	(ROUTE)	Variable Qualifier	Route of administration for CMTRT. Examples: ORAL, INTRAVENOUS.	Perm
CMSTDTC	Start Date/Time of Medication	Char	ISO 8601	Timing		Perm
CMENDTC	End Date/Time of Medication	Char	ISO 8601	Timing		Perm
CMSTDY	Study Day of Start of Medication	Num		Timing	Study day of start of medication relative to the sponsor-defined RFSTDTC.	Perm
CMENDY	Study Day of End of Medication	Num		Timing	Study day of end of medication relative to the sponsor-defined RFSTDTC.	Perm
CMDUR	Duration of Medication	Char	ISO 8601	Timing	Collected duration for a treatment episode. Used only if collected on the CRF and not derived from start and end date/times.	Perm
CMSTRF	Start Relative to Reference Period	Char	(STENRF)	Timing	Describes the start of the medication relative to sponsor-defined reference period. The sponsor-defined reference period is a continuous period of time defined by a discrete starting point and a discrete ending point (represented by RFSTDTC and RFENDTC in Demographics). If information such as "PRIOR", ONGOING or "CONTINUING" was collected, this information may be translated into CMSTRF.	Perm
CMENRF	End Relative to Reference Period	Char	(STENRF)	Timing	Describes the end of the medication relative to the sponsor-defined reference period. The sponsor-defined reference period is a continuous period of time defined by a discrete starting point and a discrete ending point (represented by RFSTDTC and RFENDTC in Demographics). If information such as "PRIOR", "ONGOING, or "CONTINUING" was collected, this information may be translated into CMENRF.	Perm
CMSTRTPT	Start Relative to Reference Time Point	Char	(STENRF)	Timing	Identifies the start of the medication as being before or after the reference time point defined by variable CMSTTPT.	Perm
CMSTTPT	Start Reference Time Point	Char		Timing	Description or date/time in ISO 8601 character format of the reference point referred to by CMSTRTPT. Examples: "2003-12-15" or "VISIT 1".	Perm
CMENRTPT	End Relative to Reference Time Point	Char	(STENRF)	Timing	Identifies the end of the medication as being before or after the reference time point defined by variable CMENTPT.	Perm
CMENTPT	End Reference Time Point	Char		Timing	Description or date/time in ISO 8601 character format of the reference point referred to by CMENRTPT. Examples: "2003-12-25" or "VISIT 2".	Perm

** Indicates variable may be subject to controlled terminology, (Parenthesis indicates CDISC/NCI codelist code value)*

CM – Assumptions for the Concomitant/Prior Medication Domain Model

1. CM Definition and Structure
   a. CRF data that captures the Concomitant and Prior Medications/Therapies used by the subject. Examples are the Concomitant Medications/Therapies given on an as-needed basis and the usual and background medications/therapies given for a condition.
   b. The structure of the CM domain is one record per medication intervention episode, constant-dosing interval, or pre-specified medication assessment per subject. It is the sponsor's responsibility to define an intervention episode. This definition may vary based on the sponsor's requirements for review and analysis. The submission dataset structure may differ from the structure used for collection. One common approach is to submit a new record when there is a change in the dosing regimen. Another approach is to collapse all records for a medication to a summary level with either a dose range or the highest dose level. Other approaches may also be reasonable as long as they meet the sponsor's evaluation requirements.

2. Concomitant Medications Description and Coding
   a. CMTRT captures the name of the Concomitant Medications/Therapy and it is the topic variable. It is a required variable and must have a value. CMTRT should only include the medication/therapy name and should not include dosage, formulation, or other qualifying information. For example, “ASPIRIN 100MG TABLET” is not a valid value for CMTRT. This example should be expressed as CMTRT= “ASPIRIN”, CMDOSE= “100”, CMDOSU= “MG”, and CMDOSFRM= “TABLET”.
   b. CMMODIFY should be included if the sponsor’s procedure permits modification of a verbatim term for coding.
   c. CMDECOD is the standardized medication/therapy term derived by the sponsor from the coding dictionary. It is expected that the reported term (CMTRT) or the modified term (CMMODIFY) will be coded using a standard dictionary. The sponsor is expected to provide the dictionary name and version used to map the terms utilizing the define.xml external codelist attributes.

3. Pre-specified Terms; Presence or Absence of Concomitant Medications
   a. Information on concomitant medications is generally collected in two different ways, either by recording free text or using a pre-specified list of terms. Since the solicitation of information on specific concomitant medications may affect the frequency at which they are reported, the fact that a specific medication was solicited may be of interest to reviewers. CMPRESP and CMOCCUR are used together to indicate whether the intervention in CMTRT was pre-specified and whether it occurred, respectively.
   b. CMOCCUR is used to indicate whether a pre-specified medication was used. A value of Y indicates that the medication was used and N indicates that it was not.
   c. If a medication was not pre-specified the value of CMOCCUR should be null. CMPRESP and CMOCCUR is a permissible fields and may be omitted from the dataset if all medications were collected as free text. Values of CMOCCUR may also be null for pre-specified medications if no Y/N response was collected; in this case, CMSTAT = NOT DONE, and CMREASND could be used to describe the reason the answer was missing.

4. Additional Timing Variables
   a. CMSTRTPT, CMSTTPT, CMENRTPT and CMENTPT may be populated as necessary to indicate when a medication was used relative to specified time points. For example, assume a subject uses birth control medication. The subject has used the same medication for many years and continues to do so. The date the subject began using the medication (or at least a partial date) would be stored in CMSTDTC. CMENDTC is null since the end date is unknown (it hasn’t happened yet). This fact can be recorded by setting CMENTPT=”2007-04-30” (the date the assessment was made) and CMENRTPT=”ONGOING”.

5. Additional Permissible Interventions Qualifiers
   a. Any additional Qualifiers from the Interventions Class may be added to this domain.

CM – Examples for the Concomitant/Prior Medication Domain Model

***Example 1*: Spontaneous concomitant medications with dosing information**

Sponsors collect the timing of concomitant medication use with varying specificity, depending on the pattern of use; the type, purpose, and importance of the medication; and the needs of the study. It is often unnecessary to record every unique instance of medication use, since the same information can be conveyed with start and end dates and frequency of use. If appropriate, medications taken as needed (intermittently or sporadically over a time period) may be reported with a start and end date and a frequency of "PRN".

The example below shows three subjects who took the same medication on the same day.

Rows 1-6: For the first subject (USUBJID=ABC-0001, each instance is recorded separately, and frequency (CMDOSFRQ) is ONCE.
Rows 7-9: For the second subject (USUBJID=ABC-0002, the second record (CMSEQ=2) shows that aspirin was taken twice on January 7th, so the frequency is BID. The frequency is also included for the other daily records to avoid confusion.
Row 10: Records for the third subject are collapsed (this is shown as an example only, not as a recommendation) into a single entry that spans the relevant time period, with a frequency of PRN. This approach assumes that knowing exactly when aspirin was used is not important for evaluating safety and efficacy in this study.

Row	STUDYID	DOMAIN	USUBJID	CMSEQ	CMTRT	CMDOSE	CMDOSU	CMDOSFRQ	CMSTDTC	CMENDTC
1	ABC	CM	ABC-0001	1	ASPIRIN	100	MG	ONCE	2004-01-01	2004-01-01
2	ABC	CM	ABC-0001	2	ASPIRIN	100	MG	ONCE	2004-01-02	2004-01-02
3	ABC	CM	ABC-0001	3	ASPIRIN	100	MG	ONCE	2004-01-03	2004-01-03
4	ABC	CM	ABC-0001	4	ASPIRIN	100	MG	ONCE	2004-01-07	2004-01-07
5	ABC	CM	ABC-0001	5	ASPIRIN	100	MG	ONCE	2004-01-07	2004-01-07
6	ABC	CM	ABC-0001	6	ASPIRIN	100	MG	ONCE	2004-01-09	2004-01-09
7	ABC	CM	ABC-0002	1	ASPIRIN	100	MG	Q24H	2004-01-01	2004-01-03
8	ABC	CM	ABC-0002	2	ASPIRIN	100	MG	BID	2004-01-07	2004-01-07
9	ABC	CM	ABC-0002	3	ASPIRIN	100	MG	Q24H	2004-01-09	2004-01-09
10	ABC	CM	ABC-0003	1	ASPIRIN	100	MG	PRN	2004-01-01	2004-01-09

***Example 2*: Spontaneous concomitant medications without dosing information**

The example below is for a study that has a particular interest in whether subjects use any anticonvulsant medications. The medication history, dosing, etc. is not of interest; the study only asks for the anticonvulsants to which subjects are being exposed.

Row	STUDYID	DOMAIN	USUBJID	CMSEQ	CMTRT	CMCAT
1	ABC123	CM	1	1	LITHIUM	ANTI-CONVULSANT
2	ABC123	CM	2	1	VPA	ANTI-CONVULSANT

***Example 3*: Pre-specified concomitant medications using CMPRESP, CMOCCUR, CMSTAT, and CMREASND**

Sponsors often are interested in whether subjects are exposed to specific concomitant medications, and collect this information using a checklist. The example below is for a study that has a particular interest in the antidepressant medications that subjects use. For the study's purposes, the absence is just as important as the presence of a medication. This can be clearly shown by using CMOCCUR.

In this example, CMPRESP shows that the subjects were specifically asked if they use any of three antidepressants (Zoloft, Prozac, or Paxil). The value of CMOCCUR indicates the response to the pre-specified medication question. CMSTAT indicates whether the response was missing for a pre-specified medication, and CMREASND shows the reason for missing response. The medication details (e.g., dose, frequency) were not of interest in this study.

Row 1: Medication was solicited on CRF and was taken.
Row 2: Medication use solicited in CRF and was not taken.
Row 3: Medication use solicited in CRF but data was not collected.

Row	STUDYID	DOMAIN	USUBJID	CMSEQ	CMTRT	CMPRESP	CMOCCUR	CMSTAT	CMREASND
1	ABC123	CM	1	1	ZOLOFT	Y	Y		
2	ABC123	CM	1	2	PROZAC	Y	N		
3	ABC123	CM	1	3	PAXIL	Y		NOT DONE	Didn't ask due to interruption