NCI CDISC Harmonization Working Group

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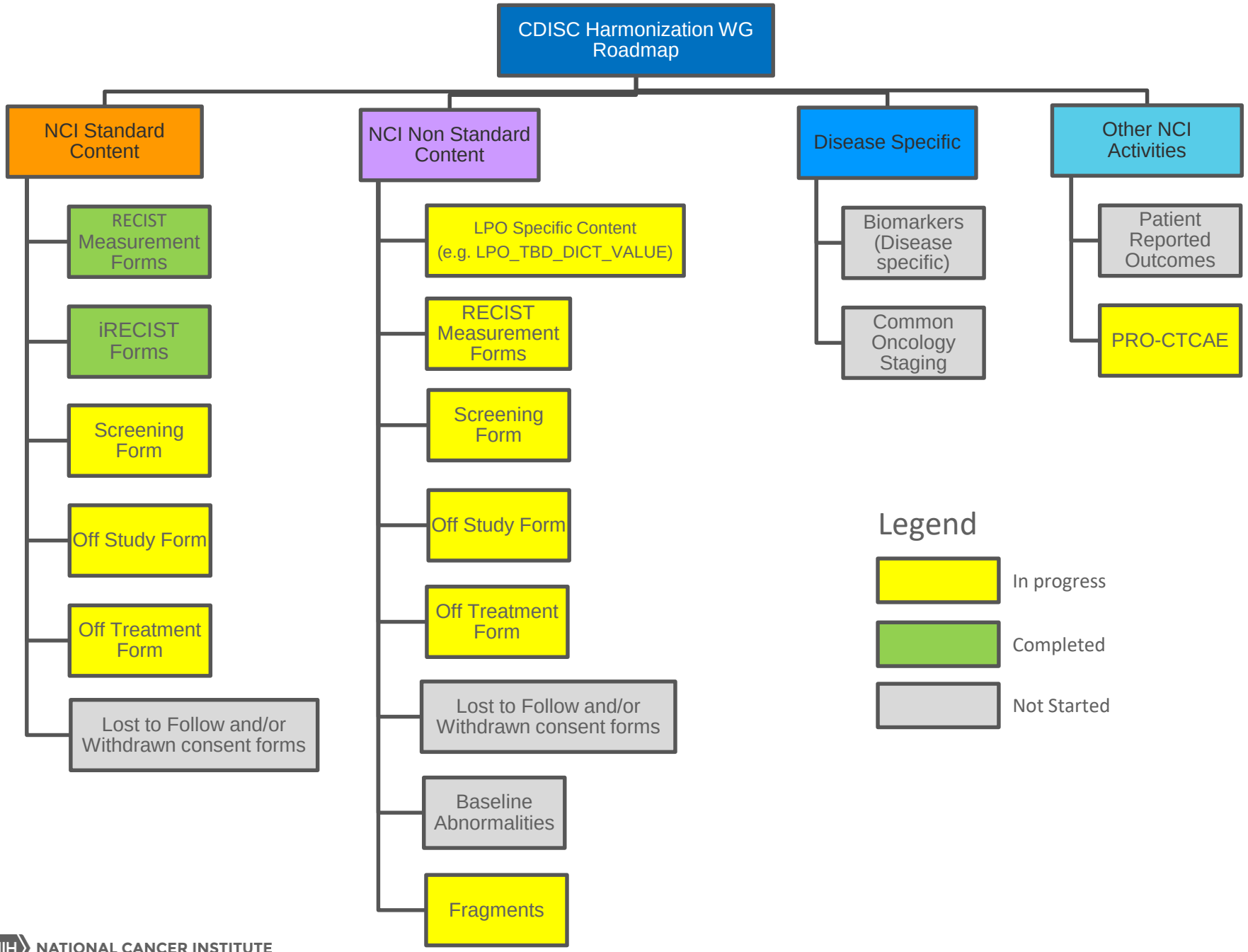
Agenda

- Recap
- Form Structure
- LPO Questions


CDISC Harmonization WG Roadmap
NCI Standard Content
RECIST Measurement Forms
iRECIST Forms
Screening Form
Off Study Form
Off Treatment Form
Lost to Follow and/or Withdrawn consent forms
NCI Non Standard Content
LPO Specific Content (e.g. LPO_TBD_DICT_VALUE)
RECIST Measurement Forms
Screening Form
Off Study Form
Off Treatment Form
Lost to Follow and/or Withdrawn consent forms
Baseline Abnormalities
Fragments
Disease Specific
Biomarkers (Disease specific)
Common Oncology Staging
Other NCI Activities
Patient Reported Outcomes
PRO-CTCAE
Legend
In progress
Completed
Not Started

LPO Q & A

Question 1

- ***Question 1 (Alliance): Having trouble figuring out the correct domains for the following questions:***
  - Was there residual disease?
  - Does the patient have unresectable diseases

- ***Can we review your form(s) to see these questions in context?***
- ***What are these questions used for?***
  - ***Form navigation (i.e., to collect additional details)?***

Question 1 Response

- ***From Discussion on Harmonization WG meeting:***
  - ***It sounds like these are TR records***
  - ***Would need to extend the TRTEST/TRTESTCD terminology to create indicator questions for these***

C-code (Concept Code)	Tumor or Lesion Properties Test Code (TRTESTCD) (codelist code = C96779)	Tumor or Lesion Properties Test Name (TRTEST) (codelist code = C96778)
C126056	CALCFIND	Calcification Indicator
C126056	CALCFIND	Calcification Indicator
C126056	CALCFIND	Calcification Indicator
C119551	LESFLIND	Lesion Failure Indicator
C119551	LESFLIND	Lesion Failure Indicator
C119551	LESFLIND	Lesion Failure Indicator
C119552	LESRVIND	Lesion Revascularization Indicator
C119552	LESRVIND	Lesion Revascularization Indicator
C119552	LESRVIND	Lesion Revascularization Indicator
C119553	LESSCIND	Lesion Success Indicator
C119553	LESSCIND	Lesion Success Indicator
C119553	LESSCIND	Lesion Success Indicator
C119554	LMBFLIND	Limb Failure Indicator
C119554	LMBFLIND	Limb Failure Indicator
C119554	LMBFLIND	Limb Failure Indicator
C119555	LRISCIND	Lesion Revas Ischemia Indicator
C119555	LRISCIND	Lesion Revas Ischemia Indicator
C119555	LRISCIND	Lesion Revas Ischemia Indicator
C119556	LRVCLIND	Lesion Revas Clinical Indicator
C119556	LRVCLIND	Lesion Revas Clinical Indicator
C119556	LRVCLIND	Lesion Revas Clinical Indicator
C132490	NBNL2IND	Two or More New Bone Lesions Indicator
C132490	NBNL2IND	Two or More New Bone Lesions Indicator
C132490	NBNL2IND	Two or More New Bone Lesions Indicator
C119557	VSLFLIND	Vessel Failure Indicator
C119557	VSLFLIND	Vessel Failure Indicator
C119557	VSLFLIND	Vessel Failure Indicator
C119558	VSLPIND	Vessel Patency Indicator
C119558	VSLPIND	Vessel Patency Indicator
C119558	VSLPIND	Vessel Patency Indicator
C119559	VSLRVIND	Vessel Revascularization Indicator
C119559	VSLRVIND	Vessel Revascularization Indicator
C119559	VSLRVIND	Vessel Revascularization Indicator

Question 2

- **The NCI Off Treatment module that is used for CDUS reporting collects an Off Treatment date. I am not sure which domain this off treatment date would fall under. Can you please provide some guidance? (NRG)**

Question 2 Response

- An assessment of the *status* of a person coming off treatment would be a **Disposition Event (DS)**

Completed
Adverse Event
Death
Lost to Follow-Up
Physician Decision
Withdrawal by Subject

Disposition (DS) domain
Status = DSDECOD (DSTERM)
Date of disposition status = DSSTDAT

Question 3

- We are working to implement RAVE and are starting to build forms in the system for our project, AMC . The Rave system has a feature that will integrate the ‘specify’ field with a codelist. The “other”, specify field will not need to be built out separately. Is the feature offered by Rave CDISC compliant and acceptable for use? I have included a screenshot of what it will look like below. (EMMES)

Instead of this:

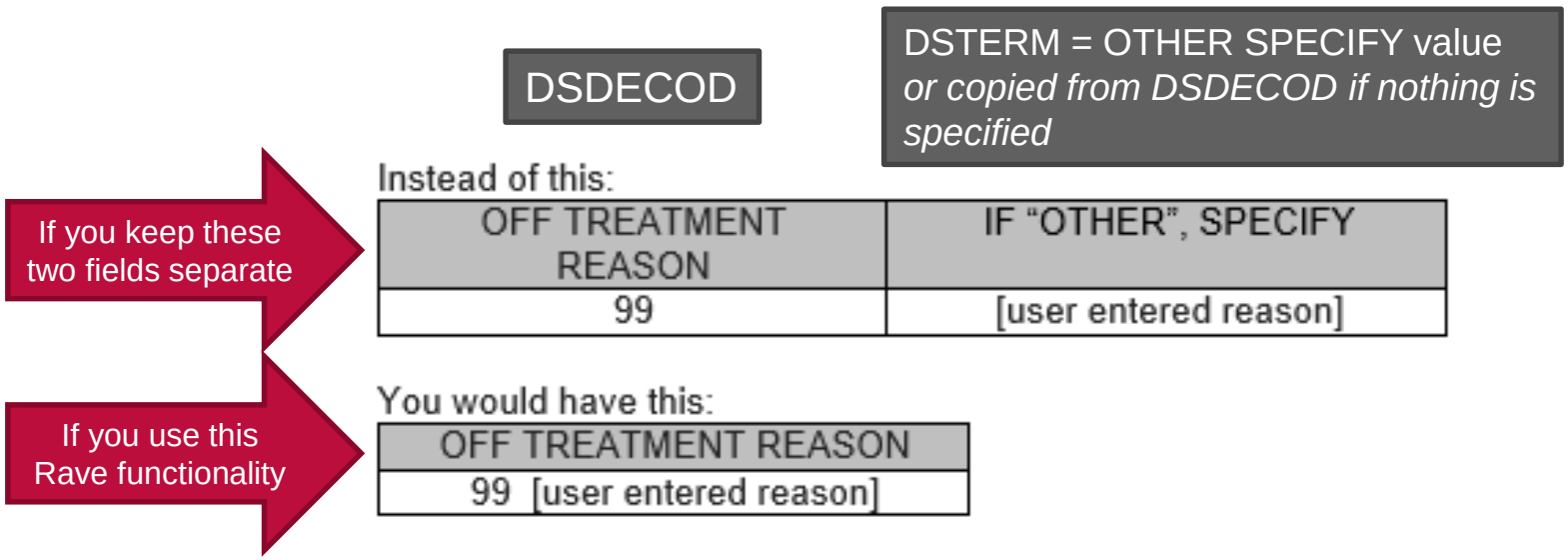
OFF TREATMENT REASON	IF “OTHER”, SPECIFY
99	[user entered reason]

You would have this:

OFF TREATMENT REASON
99 [user entered reason]

Question 3 Response

This is not a CDASH conformance issue, because CDASH gives us the flexibility to use DSTERM or DSDECOD (or both),
but it might help to understand the impact to SDTM programming.



DSTERM could be used to collect whatever is entered - the codelist value or the specified value.
Then the SDTM programmer would have to populate DSDECOD from the NCOMPLT for every record)

Question 4

- While reviewing our concomitant medication form it was determined that two of the options on our codelist for units of medications were not listed in the current codelist : units and drops. (Emmes)
- Would it be recommended to add to the current CT by CDE curation?
- Or should we just use the current options available in the NCI preferred terms for con med?

Question 4 Response

- Per CDASH, ok to add values that are needed to an extensible codelist.
- For Units
  - Add new values from the UNIT codelist (if the values are available)
    - DROP (C69441)
  - If the value you need is not already there, you can extend the codelist by adding it
    - Ensure the value you are adding is not already there (by definition)
    - UNIT is not already in the list (reference UNIT codelist C71620 for more specific values that include the word “unit”)
- Also need to follow curation process required by NCI if you are adding to an existing codelist with a PID

Question 5

- We are developing a Pharmacodynamics result form. Is there a domain you would recommend for this data? I see in older documents it was mentioned in PF, however other papers suggest a custom domain, such as PD. (Theradex)

Question 5 Response

- The term *pharmacodynamics* (PD) refers to the study of
  - The relationship between the concentration of the drug in the body and the biological and physiological effects of the drug on the body or on other organisms (bacteria, parasites, and so forth) on or in the body.
- …the distinction between PK and PD (can be remembered) by the following simple description:
  - **Pharmacokinetics** is the study of what the *body* does to the *drug.*
  - **Pharmacodynamics** is the study of what the *drug* does to the *body.*

- Physiological
- Morphological

*https://www.dummies.com/education/science/biology/pharmacokinetics-and-pharmacodynamics-pkpd-studies/

Question 5 Response

- We already have a lot of standard SDTMIG/CDASHIG domains that hold physiological / morphological findings
- So, the answer to *where "PD" data goes in SDTM is*
  - *Where it belongs* in standard domains e.g.,
  - If it is a lab test result/ value, it goes in LB
  - If it is a vital signs measurement, it goes in VS
  - If it is tumor uptake assessment, it goes in TR (reference TRTEST codelist C96778)
    - Etc.
  - *If there is no existing domain defined for the data you are collecting, you could create a custom PD domain for the physiological/morphological findings*
- ADaM provides the flexibility to create a PD dataset (ADPD) with the relevant SDTM datasets as the source

Question 6

- Can we get a background on the MI vs PF Domain. (Alliance)
- I also find that if the group really wants to tie the entire domain together…if they have a procedure (biopsy) the first through is to record the “outcome” or “results” in the PR Domain but not sure if that is the best place, can you provide guidance on how to go about this?

Question 6 Response

- Generally speaking, you would only use the Procedures (PR) domain if the Procedure is the record of interest, and you are collecting details of interest about the procedure (e.g., Start Date/Time and End Date/Time) that would required the PR record structure
- If the procedure is a method for obtaining a result, it would be more typical to represent the procedure information as --METHOD in the results record:

STUDYID	DOMAIN	USUBJID	MISEQ	MITESTCD	MITEST	MITSTDTL	MIORRES	MISTRESC	MIRESCAT	MISPEC	MILOC	MIMETHOD	VISIT	MIDTC
ABC	MI	ABC-1001	1	HER2	Human Epidermal Growth Factor Receptor 2	Reaction Score	0	0	NEGATIVE	TISSUE	BREAST	IHC	SCREENING	2001-06-15
ABC	MI	ABC-2002	1	HER2	Human Epidermal Growth Factor Receptor 2	Reaction Score	2+	2+	POSITIVE	TISSUE	BREAST	IHC	SCREENING	2001-06-15

Question 6 Response

- Microscopic Findings (MI)
  - Standard domain in SDTMIG V3.3
  - A findings domain that contains histopathology findings and evaluations resulting from the *microscopic examination of tissue samples*. These examinations are performed on a specimen, usually one that has been prepared with some type of stain. Biomarkers assessed by histologic or histopathological examination (by employing cytochemical / immunocytochemical stains) will be stored in the MI domain.

MI Examples

STUDYID	DOMAIN	USUBJID	MISEQ	MITESTCD	MITEST	MITSTDTL	MIORRES	MISTRESC	MIRESCAT	MISPEC	MILOC	MIMETHOD	VISIT	MIDTC
ABC	MI	ABC-1001	1	HER2	Human Epidermal Growth Factor Receptor 2	Reaction Score	0	0	NEGATIVE	TISSUE	BREAST	IHC	SCREENING	2001-06-15
ABC	MI	ABC-2002	1	HER2	Human Epidermal Growth Factor Receptor 2	Reaction Score	2+	2+	POSITIVE	TISSUE	BREAST	IHC	SCREENING	2001-06-15

STUDYID	DOMAIN	USUBJID	MISEQ	MIGRPID	MITESTCD	MITEST	MITSTDTL	MIORRES	MISTRESC	MISTRESN	MISPEC	MILOC	MIMETHOD	MIDRVFL	VISIT	MIDTC
ABC	MI	ABC-1001	1	1	BRCA1	Breast Cancer Susceptibility Gene 1	Reaction Score	2	2	2	TISSUE	BREAST	IHC		SCREENING	2001-06-15
ABC	MI	ABC-1001	2	1	BRCA1	Breast Cancer Susceptibility Gene 1	Stain Intensity Score	STRONG	3	3	TISSUE	BREAST	IHC		SCREENING	2001-06-15
ABC	MI	ABC-1001	3	1	BRCA1	Breast Cancer Susceptibility Gene 1	Composite Score		6	6	TISSUE	BREAST	IHC	Y	SCREENING	2001-06-15

Reference: Microscopic Findings Test - Terminology
MI Test Code - C132263, MI Test Name - C132262, MI Test Details - C125922

Question 6 Response

- Pharmacogenomics Findings (PF)
  - Provisional domain in SDTMIG-PGx V1.0 (Provisional)
  - The Pharmacogenomics/Genetics Findings (PF) domain is a findings domain for gene expression and genetic variation assessments
  - **Major revision is underway; likely to be replaced by Genetic Findings (GF) defined as:**

➢ *(DRAFT) The GF domain captures results data related to the structure, function, evolution, mapping and editing of subject and non-host organism genomes through the assessment of material of interest. This domain includes, but is not limited to, assessments and results for genetic variation, gene expression, and summary measures derived from these assessments. This domain is used for findings from characteristics assessed from nucleic acids and may include subsequent inferences and/or predictions about related proteins/amino acids. However, direct assessments of proteins (e.g., assessments of amino acids) are out of scope for this domain.*

PF Examples

STUDYID	DOMAIN	USUBJID	PFSEQ	PFREFID	PFTESTCD	PFTEST	PFGENRI	PFCAT	PFORRES	PFSTRESC	PFALLELC	PFNAM	PFSPEC	PFMETHOD
ABC-123	PF	022-3467	1	33-405-1509B	ALE	Allele	HLA-A	GENETIC VARIATION	*33:01	*33:01	1	Papa Scripps	DNA	Sanger Sequencing
ABC-123	PF	022-3467	2	33-405-1509B	ALE	Allele	HLA-A	GENETIC VARIATION	*68:01	*68:01	2	Papa Scripps	DNA	Sanger Sequencing
ABC-123	PF	022-3467	3	33-405-1509B	ALE	Allele	HLA-B	GENETIC VARIATION	*14:02:05	*14:02:05	1	Papa Scripps	DNA	Sanger Sequencing
ABC-123	PF	022-3467	4	33-405-1509B	ALE	Allele	HLA-B	GENETIC VARIATION	*53:01:01:03	*53:01:01:03	2	Papa Scripps	DNA	Sanger Sequencing
ABC-123	PF	022-3467	5	33-405-1509B	ALE	Allele	HLA-C	GENETIC VARIATION	*04:01	*04:01	1	Papa Scripps	DNA	Sanger Sequencing
ABC-123	PF	022-3467	6	33-405-1509B	ALE	Allele	HLA-C	GENETIC VARIATION	*07:02	*07:02	2	Papa Scripps	DNA	Sanger Sequencing
ABC-123	PF	022-3467	7	33-405-1509B	ALE	Allele	HLA-DRB1	GENETIC VARIATION	*11:01	*11:01	1	Papa Scripps	DNA	Sanger Sequencing
ABC-123	PF	022-3467	8	33-405-1509B	ALE	Allele	HLA-DRB1	GENETIC VARIATION	*15:01	*15:01	2	Papa Scripps	DNA	Sanger Sequencing
ABC-123	PF	022-3467	9	33-405-1509B	ALE	Allele	HLA-DQA1	GENETIC VARIATION	*01:05	*01:05	1	Papa Scripps	DNA	Sanger Sequencing
ABC-123	PF	022-3467	10	33-405-1509B	ALE	Allele	HLA-DQA1	GENETIC VARIATION	*02:01	*02:01	2	Papa Scripps	DNA	Sanger Sequencing
ABC-123	PF	022-3467	11	33-405-1509B	ALE	Allele	HLA-DQB1	GENETIC VARIATION	*02:02	*02:02	1	Papa Scripps	DNA	Sanger Sequencing
ABC-123	PF	022-3467	12	33-405-1509B	ALE	Allele	HLA-DQB1	GENETIC VARIATION	*05:01	*05:01	2	Papa Scripps	DNA	Sanger Sequencing

Reference: Pharmacogenomics Findings Test - Terminology
PF Test Code - C116106, PF Test Name - C116105

PF Examples

PFTESTCD	PFTEST	PFGENRI	PFGENTYP	PFCAT	PFSCAT	PFORRES	PFSTRESC	PFSTRESN	PFXFN	PFNAM	PFSPEC	PFMETHOD
NINT1VAL	Normalized Intensity 1 Value	EGFR	GENE	GENE EXPRESSION	Pre-Analytic	1.16279	1.16279	1.16279	2.16.090.1.135764.3.4:7280912	Deluxe Central Labs	RNA	TWO-COLOR MICROARRAY
NINT2VAL	Normalized Intensity 2 Value	EGFR	GENE	GENE EXPRESSION	Pre-Analytic	0.96469	0.96469	0.96469	2.16.090.1.135764.3.4:7280912	Deluxe Central Labs	RNA	TWO-COLOR MICROARRAY
PVAL	P Value	EGFR	GENE	GENE EXPRESSION	Analytic	0.05391	0.05391	0.05391	2.16.090.1.135764.3.4:7280912	Deluxe Central Labs	RNA	TWO-COLOR MICROARRAY
FOLDCHG	Fold Change	EGFR	GENE	GENE EXPRESSION	Analytic	1.8	1.8	1.8	2.16.090.1.135764.3.4:7280912	Deluxe Central Labs	RNA	TWO-COLOR MICROARRAY
NTASMN	Net Assessment	EGFR	GENE	GENE EXPRESSION	Interpretation	Over-expressed	Over-expressed		2.16.090.1.135764.3.4:7280912	Deluxe Central Labs	RNA	TWO-COLOR MICROARRAY

Reference: Pharmacogenomics Findings Test - Terminology
PF Test Code - C116106, PF Test Name - C116105

PF Examples

PFTESTCD	PFTEST	PFGENRI	PFREFSEQ	PFCAT	PFORRES	PFORREF	PFGENLOC	PFSTRESC	PFRSNUM	PFALLELC	PFXNAM	PFNAM	PFSPEC	PFMETHOD
NUC	Nucleotide	HBB	NM_000518.4	GENETIC VARIATION	A	A	20	c.=		A	10081.30297/1011x1lala-hbb.xml	Lab D	DNA	NUCLEIC ACID SEQUENCINC
NUC	Nucleotide	HBB	NM_000518.4	GENETIC VARIATION	A	A	20	c.=		B	10081.30297/1011x1lala-hbb.xml	Lab D	DNA	NUCLEIC ACID SEQUENCINC
NUC	Nucleotide	HBB	NM_000518.4	GENETIC VARIATION	T	A	20	c.20A>T	rs334	A	10081.30297/3011x1lala-hbb.xml	Lab D	DNA	NUCLEIC ACID SEQUENCINC
NUC	Nucleotide	HBB	NM_000518.4	GENETIC VARIATION	T	A	20	c.20A>T	rs334	B	10081.30297/3011x1lala-hbb.xml	Lab D	DNA	NUCLEIC ACID SEQUENCINC
NUC	Nucleotide	HBB	NM_000518.4	GENETIC VARIATION	A	A	20	c.=		A	10081.30297/2012x1lala-hbb.xml	Lab D	DNA	NUCLEIC ACID SEQUENCINC
NUC	Nucleotide	HBB	NM_000518.4	GENETIC VARIATION	T	A	20	c.20A>T	rs334	B	10081.30297/2012x1lala-hbb.xml	Lab D	DNA	NUCLEIC ACID SEQUENCINC
NUC	Nucleotide	HBB	NM_000518.4	GENETIC VARIATION	C	A	20	c.20A>C	rs334	A	10081.30297/3022x4lala-hbb.xml	Lab D	DNA	NUCLEIC ACID SEQUENCINC
NUC	Nucleotide	HBB	NM_000518.4	GENETIC VARIATION	del	A	20	c.20delA	rs63749819	B	10081.30297/3022x4lala-hbb.xml	Lab D	DNA	NUCLEIC ACID SEQUENCINC

Reference: Pharmacogenomics Findings Test - Terminology
PF Test Code - C116106, PF Test Name - C116105

Next Steps

- **CDISC Project Team Activities**
  - Package up completed content to send to CDISC for proposed standards
  - Begin tracking active studies that are harmonized with CDISC
  - Update roadmap as needed
  - Continue to track LPO Use Cases

LPO Management of Supplemental Questions Workflow