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薫風の候、先生におかれましては、お元気でお過ごしのことと存じます。

今般、PMDA の主催において CDISC の疾患領域別データ標準に関するシンポジウムが、6 月 1 日に開催される予定です（下記メール及び別添：p3_2016 CDISC Japan Interchange Program-28APRUpdate 参照）。

さて、ご承知のように、橋渡し研究支援、加速ネットワークプログラムにより、AMED 所轄の治験開始案件が 107 件、承認、認証取得が 22 件、先駆け審査案件が 5 件を数え、着々と成果が上がる中で、今後はそれぞれのシーズについてグローバル展開を目指すフェーズに入っております。
FDA、PMDA が、CDISC 標準に基づく電子申請を推奨しており、我が国も本年 9 月より CDISC 標準に基づく e-CTD による申請を受け付けるようになります。
今後新たに開始される治験はすべて CDISC 標準のもとに実施される事となり、また臨床研究においても CDISC 標準に適応することが今後グローバルなデータの統合に際しては必須になると考えております。

つきましては、CDISC 標準において最も医師に直接関係あるプロトコル作成では、各疾患単位に標準化がすでに進んでおり、現時点での既に出版された TAS（Therapeutic Area Standards：疾患領域別標準）をお示しさせていただきます（別添：20160419_TAS 状況）。
これ以外の疾患に関しましても、今後は順次出版の見込みです。

とりわけ、がん領域においては、大腸がんの TAS 作成が既に始まっており、前立腺がんも始まります。乳がんにおいては、乳癌学会の戸井先生、中村先生に連絡して、CDISC 本部からのパブコメ募集に対応いただき、日本の学会からも公式に CDSC 宛提出を行い、CDISC より全世界より寄せられたパブコメに対しての回答がなされております（別添：Public Coomment from Japan_20160128_Final 及び BrCa Consolidated Public Review Comments for SRC）。
パブコメの結果を反映させて今月中にも、正式に乳がんの TAS がリリースされる予定です。

このように日本の学会が積極的に今後 TAS 作成に向かうことは、日本の臨床医学の発展また、グローバルにおけるイニシアチブをとることにおいて不可欠であると同時に、また今回のシンポジウムは絶好の機会でもあります。

ぜひ主旨ご理解の上、本シンポジウムにご参加の上、ご研鑽いただきますよう伏してお願い申し上げます。

平成 28 年 5 月 11 日

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# CDISC Symposium

**WEDNESDAY, 01 June 2016**

**13:00 - 18:00** **Smarter Research through CDISC Standards for Therapeutic Areas**

*Instructors: Dr. Rebecca Kush, CDISC President & CEO*
*Barrie Nelson, CDISC VP, Standards, Terminology & Technical Services*
*Amy Palmer, CDISC Senior Project Manager, Standards Development*

**Location:**

*Tetsumon Memorial Hall, University of Tokyo, 14th Floor of the Faculty of Medicine Experimental Research Building, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033*

日　付：平成 28 年 6 月 1 日（水）
時　刻：13：00～18：00（受付 12：30～）（予定）
場　所：東京大学医学部教育研究棟14階　鉄門記念講堂
（最寄駅：本郷三丁目）
費　用：50米ドル
講　師：Dr. Rebecca Kush, CDISC President & CEO
Barrie Nelson, CDISC VP, Standards, Terminology & Technical Services
Amy Palmer, CDISC Senior Project Manager, Standards Development
※同時通訳あり

参加申込サイトは下記をご参照願います。
https://www.cvent.com/events/cdisc-2016-japan-interchange/registration-8e127e4f32264ffa95cf928971f982b6.aspx
（クレジットカード決裁またはインボイスにより送金）

## SAVE THE DATE!

**CDISC International Interchange 2016**
26-30 September 2016
Bethesda, Maryland

**CDISC Europe Interchange 2017**
Details to be Announced

# 疾患領域別CDISC標準

2016年4月19日現在の状況

TRI企画・広報部

# 疾患別領域CDISC標準(TAS)

- 公開済 ・・・ 18
- 近日公開 ・・・ 1
- パブリックレビュー中 ・・・ 0
- CDISC内部レビュー中 ・・・ 5
- 開発作業進行中 ・・・ 11
- 開発予定 ・・・ 6

# 公開済のTAS

- アルツハイマー病
- 喘息
- 心臓血管病
- 慢性C型肝炎
- COPD
- 糖尿病
- 糖尿病ADaM補足資料
- 脂質異常症
- インフルエンザ
- 多発性硬化症
- 疼痛
- パーキンソン病
- 腎嚢胞症
- QT
- 統合失調症
- 外傷性脳損傷
- 結核
- ウィルス学

# 近日公開のTAS

- 乳がん

# CDISCレビュー中のTAS

- 糖尿病性腎疾患
- リウマチ性関節炎
- 心血管画像
- 腎移植
- ワクチン

# 開発作業進行中のTAS

- 前立腺がん
- 大腸がん
- 大鬱病性障害
- 全般性不安障害
- 双極性障害
- 栄養学
- マラリア
- エボラ
- 中国伝統医学における心臓血管概念
- 冠状動脈性心臓病
- 針治療

# 開発予定のTAS

- 肺がん
- 乾癬
- デュシェンヌ型筋ジストロフィー
- クロストリジウム・ディフィシル関連下痢症
- 閉経後骨粗しょう症
- 皮膚および皮膚組織感染症

# 2016年4月現在の計画表

CFAST　Program Overview – April 2016　CDISC

| Therapeutic Area | Charter Approved | Check of Concepts Completed | 内部レビュー | パブコメ | 公開 |
|---|---|---|---|---|---|
| Breast Cancer v1 | Oct 14 | Oct 14 | Mar 15 | Nov 15 | Q216 |
| Diabetic Kidney Disease v1 | May 15 | Aug 15 | Jan | May | Q216 |
| Rheumatoid Arthritis v1 | Jun 15 | Oct 15 | Jan | Apr | Q216 |
| CV Imaging v1 | May 15 | Jul 15 | Dec 15 | Apr | Q316 |
| Prostate Cancer v1 | Nov 15 | Apr | | | Q316 |
| Major Depressive Disorder v1** | Dec 15 | Feb | May | | Q316 |
| Kidney Transplant v1 | Jan | Apr | Apr | | Q316 |
| Colorectal Cancer v1 | Apr | | | | Q416 |
| Vaccines v1* | Q414 | Oct 15 | Apr | Q216 | Q416 |
| Ebola v1* | Sep 15 | Mar | Mar | Q216 | Q316 |
| Malaria v1* | Oct 15 | May | May | | Q416 |
| Nutritional Standards v1* | Mar 15 | Q116 | Q216 | Q316 | Q416 |
| Coronary Heart Disease – TCM v1* | Q116 | Q216 | | | Q416 |
| Acupuncture – TCM v1* | Q216 | Q316 | | | Q117 |

Key | Stage completed | Stage ongoing | All months reflect when stage is, or is projected to be, completed

*Project duration dependent on volunteer resourcing

## Comments from "The Japanese Breast Cancer Society"

With regards to P9, P13, P14 and P15, these comments are from pathologists. We believe CDISC to understand that it is practically impossible to integrate all of the standardized methods for estimation. Many opinions could be proposed and we recommend that CDISC permit to use additional efficacy estimations as well in the User Guide in order to increase flexibility.

We strongly expect the User Guide to be revised to incorporate other methods for estimation.

P9: Endpoint: We routinely use pCR to estimate the effect of NAC at current practice. For the future, we need to improve the endpoints.

P10: Regions where the patient live, and lived shall be important as information in Asia since Asia is large and has various ethnicities among the regions. The situation is different from North America. Registration of regions in terms of life style and infectious disease is more preferable.

P13: Allred score: We need it for IHC assessment in Japan
Allred is not included (refer to P8 188 "Method of Scoring"). Allred score is necessary in IHC assessment. We see that the scoring system is not determined yet and strongly recommend that all methods used in the current clinical studies be included or CDISC would handle to determine before issuing the User Guide.

P14: RCB score: It has not been penetrated well yet.

P15: We might need to amend the grading method in Japan.

P17: Category of luminal HER2 would be needed. We would like to know why luminal HER2 is not included in as one of the subtypes (Luminal A, Luminal B, HER2 possible, and Basal-like) in the User Guide and recommend that the reason of its exclusion be clarified. We could accept it if it is reasonable not to use HER2.

P23: Risk factors; Viral hepatitis B/C might be important in studies in Asia. Osteoporosis often causes as a side effect and it is a problem for the use of aromatase inhibitors as well.

Germline mutations: PALB2 also might be a candidate for hereditary cancer gene to describe.

P46: Response analysis; Clinical benefit rate having SD>12wks as well as CR/PR might be used particularly for hormonal therapy. We would like the User Guide to permit to use it.

"General points": We comment 1)-3) below since we believe they would be necessary within a couple of years.

1) Circulating tumor cell/ circulating cell-free DNA analysis might be needed (for staging, monitoring).

2) Triple negative breast cancer subgroup; Basal marker details and androgen receptor might need to be added.

3) We may need to consider for therapeutic response to immune therapy such as anti-PD1 antibody and anti-PDL1 antibody for the near future.

| Comment # | Comment | Document Section | Comment Category | Current State | CDISC Comment | CDISC Disposition |
|---|---|---|---|---|---|---|
| 1 | Please add a dot in line 1087, behind "membrane" | Appendix E | Typo | Closed | Updated as requested | Persuasive |
| 2 | Please suggest to add abbreviation "NAC" and its definition (see line 1142) | Appendix C | Minor Issue | Closed | Appendix C updated with NAC | Persuasive |
| 3 | Please list the abbreviations in alphabetical order. "BDS" and "Biomedical Concept" need to be moved | Appendix C | Minor Issue | Closed | BDS and Biomedical Concept moved to be alphabetical.<br>Also other terms checked during final QC | Persuasive |
| 4 | lilne 665, cmap5 :<br>please change text "No Evidence of Diease" to "No Evidence of Disease" | 4.3. Disease Response | Typo | Closed | "No Evidence of Diease" corrected to to "No Evidence of Disease" in concept map 5 | Persuasive |
| 5 | line 559, aCRF for disease response: please change annotation "RSTEST=Non-Target Response" to "RSTEST=Non-target Response" (as it is provided in CDISC Controlled | 4.2.1 Examples for Tumor Identifi | Typo | Closed | Updated as requested | Persuasive |
| 6 | Please add variable PRENDTC in pr.xpt because this variable is mentioned in the explanation (line 513) | 4.1.1 Examples for Treatments | Major Issue | Closed | PRENDTC added to pr.xpt<br>Following dates were added<br>Row 1 - 2011-06-25 - *25 days*<br>Row 2 - 2011-07-15 - *same as start date*<br>Row 3 - 2011-08-21 - *3 days* | Persuasive |
| 7 | Shouldn't be RELID="PRTR" instead of "PRMO"? | 4.1.1 Examples for Treatments | Typo | Closed | Amended the RELID to PRTR for both row 1 and row 2 | Persuasive |
| 8 | line 570:<br>please change "Subject 123-1234" to Subject "ABC123-1234"<br>line 572:<br>please change "Subject 123-2345" to Subject "ABC123-2345" | 4.2.1 Examples for Tumor Identifi | Typo | Closed | Added ABC to the front of the subject numbers for the row captions | Persuasive |
| 9 | lines 368-369:<br>please change "Subject 123-1234" to Subject "ABC123-1234"<br>lines 370-371:<br>please change "Subject 123-2345" to Subject "ABC123-2345"<br>line 391:<br>please change "Subject 123-1234" to Subject "ABC123-1234"<br>line 392:<br>please change "Subject 123-2345" to Subject "ABC123-2345"<br>line 394:<br>please change "Subject 123-2346" to Subject "ABC123-2346" | 3.4.1 Examples for Prior Treatme | Major Issue | Closed | Added ABC to the front of the subject numbers for the row captions | Persuasive |
| 10 | What is the difference between solid and broken line, there is no explanation for this | 2 Overview of Breast Cancer | Select or Blank | Closed | Amended dotted lines to solid lines (Note that this was used just to assist in line cross over but to avoid confusion this was changed to all solid lines) | Persuasive with mod |
| 11 | Please add Non-CR/Non-PD as an option to be used for subjects with only non-target disease at baseline. Per RECIST 1.1, "Non-CR / non-PD is preferred over 'Stable Disease' for non-target disease since SD is increasingly used as an endpoint for assessment of efficacy in some trials. To assign this category when no lesions can be measured is not advised." | Line 559 | Select or Blank | Closed | Refer to TA Specific Usage Rules in CDASH Metadata table: "Non-CR/Non-PD is limited value for patients with non-target disease only; since including this population is protocol-specific, this value has not be included on the CDASH CRF but may be added per Sponsor." There was mixed opinions on whether to include on standard CRF so this statement was the compromise. | Not persuasive |
| 12 | Note that, for non-target response, RECIST 1.1 has both the terms "Stable Disease" and "Non-CR/Non-PD". Recommend removing SD as an option for non-target response. Per RECIST 1.1, "Non-CR / non-PD is preferred over 'Stable Disease' for non-target disease since SD is increasingly used as an endpoint for assessment of efficacy in some trials. To assign this category when no lesions can be measured is not advised." | Line 559 | Select or Blank | Closed | Continuing from comment # 11, refer to TA Specific Usage Rules in CDASH Metadata table: "Patients with Target+Non-target disease have a different allowable set of values than patients with Non-target disease only. Refer to RECIST 1.1 criteria." Sponsors did not create unique codelists for Non-Target response, but rather provided the most exhaustive list allowed per protocol. | Not persuasive |
| 13 | Note that the form does not include an entry indicating that the subject had a new lesion which, when unequivocal progression by RECIST 1.1, leads to an overall response of PD. New lesions are involved in determining overall response, so I believe it should be integrated into the form. | Line 559 – Annotated CRF | Major Issue | Closed | The existence of new lesions is recorded on the Tumor Identification/Results New Lesion CRF (Section 4.2.1) and then mapped appropriately to TU/TR domains | Not persuasive |
| 14 | Regarding the options on the example form for RECIST assessment, the example is only acceptable for subjects with measurable disease. For instance, if a study allowed both measureable and non-measurable (but evaluable) disease on-study, the Disease Response form will not be appropriate. Consider including a "No target lesions at baseline" option for target response. Although cannonical RECIST 1.1 uses the term "Unequivocal PD" for the non-target lesions in the overall response table, I think that the "progressive disease" term is reasonably understood. | Ln 559 – Annotated CRF: Disease | Major Issue | Closed | Refer to responses in comment #11, 12, and 13. All of the tumor CRFs include a lead-in question to confirm the existence of lesion types so that response categories can be cleaned accordingly. Tumor Identification/Results are collected on their own CRFs (mapped appropriately to TU/TR domains). We tried to create a 1:1 relationship between CRF and SDTM target and not introduce many domains in a CRF unless it was exhibited by Sponsor-submitted CRF examples (e.g. TU/TR domains are populated from the lesion CRF). | Not persuasive |
| 15 | Amend the description of PRTYP to Tumor or Lesion Presentation Type<br>Erin to email the ONCO SDS team to inform them of this decision.<br>Discussed at BrCa Team Meeting 01DEC2015 | | Major Issue | Closed | Description amended to Tumor or Lesion Presentation Type in the following sections<br>1) TU NSV Metadata in section 4.2.1 Example 1 and 2<br>2) Appendix D – NSV's<br>3) Section 4.2.1 Annotated CRF's – Non-Target and New Lesions | Persuasive |

| Comment # | Comment | Document Section | Comment Category | Current State | CDISC Comment | CDISC Disposition |
|---|---|---|---|---|---|---|
| 16 | Why is a new contrlled term being intropduced for sym,ptomatic deterioration where there is already an existing term for non-radiologic progress. It is unnecessary changes like this which cause significant problems for sponsors in adopting and keeping current with standards | Disease Response Metadata shee | Major Issue | Closed | From team discussion, the SDS and Controlled Terminology leads realized that Non-Radiographic Progression was a separate concept from Symptomatic Deterioration and that Symptomatic Deterioration was the response concept recognized in RECIST paper. | Not persuasive |
| 17 | I'm assuming in the example that it is assume that a patient does not have disease but this is being assessed in the procedures at screen so the result should also be recorded in RS | section 4.3.1 - line 708 | Suggestion | Closed | IE criteria would probably collect data showing if the patient does not have disease at entry to the study.<br>This was taken to the Metadata Development Forum to confirm if there was a solution using these domains in other TA's where Yes/No diease present at baseline has been modelled.<br>Representing absence of disease is still under discussion and flagged for a future version.<br>To lcarify the examples text better the team updated<br>Line 670<br>"Disease response assessments related to disease recurrence in the adjuvant and neoadjuvant setting are provided below.<br>Examples of response assessment to palliative therapy are provided in section 4.2.1. "<br>This was due to some of the data examples were moved from this section to the section above during internal review. | Persuasive with mod |
| 18 | it would better to include as opposed to referencing TR in the example | section 4.3.1 - line 699 | Suggestion | Closed | Refer to ONCO use cases XL sheet - team felt this should not be duplicated | Not persuasive |
| 19 | the RELREC here should be complete in the example. Is there a definitive link between procedures an the response in this case - surely there is a link between RS and TR | section 4.2.1 - line 646 | Question | Closed | Data is an excerpt from the ONCO use cases hence TR not shown - The user guide should be in conjunction in these examples to show a full data model. | Not persuasive |
| 20 | presentation type should be modelled as new test code in TU not as a supplemental qualifier, it is a finding in itself although related to the identification | section 4.2.1 - line 586 | Suggestion | Closed | Use of a new test code requires further discussion taking into account usage in other TA's - This may be considered for future versions of the TAUG. | Considered for future |
| 21 | The collection of PR observations does not add anything to the collection of method, adding a PR observation is unnecessary duplicating data as the procedure is not of interest outside of the method used for assessing the tumor | section 4.2.1 - line 575 and line 6 | Major Issue | closed | Refer to lines 565-568<br>*"In a findings domain record, --METHOD and --DTC are often enough to identify an imaging procedure. If additional procedure information needs to be captured then the sponsor may choose to create a separate related PR record."*<br>In this example, the sponsor has *chosen* to represent the imaging procedure information using the Procedure (PR) domain." | Not persuasive |
| 22 | If the tumor where the margins are being measure is the one referenced n TU then there should also be a relationship defined between TU and MI | section 3.3.1 - line 358 | Minor Issue | Closed | 1) Added in variable MIREFID = 1001-T01 to the mi.xpt example immeidtely prior to section 3.4 Prior Treatments<br>2) Added the following RELREC fot the relrec table immediatley prior to 4.2.1 Treatment side effetcs<br>Row 3\|ABC\|MI\|\|MIREFID\|\| MANY\|PRMI | Persuasive |
| 23 | Surely the information contained in PTSCL is metadata not data and could/should be easily included in TSTDTL | section 3.3.1 - line 326 | Minor Issue | Closed | Team confirmed that adding the point information is not appropriate for the MITSTDTL variable given its current intended use. By using a non standard variable we are also able to keep control of the terminology for the TSTDTL variable for example without having to create total score terminology for each type of point scale.<br>No update required to the TAUG. | Not persuasive |
| 24 | Examples (and controlled terminology) are needed to support all of the different types of pathology assessments listed in this section for this list to be useful for standardization. | section 3.3 | Suggestion | Closed | Team is aware that development of metadata is required for the pathology section. Due to time limitations this has been tabled for future versions of the TAUG and will also be addressed in the PrCa/CrCa projects. | Considered for future |

| Comment # | Comment | Document Section | Comment Category | Current State | CDISC Comment | CDISC Disposition |
|---|---|---|---|---|---|---|
| 25 | The create of a findings about findings is a over complication of themodel these can already be modeled conveniently as either new findings grouped together or as events or interventions linked via RELREC. Please do not add another layer of complexity that does not provide any benefit and that would significantly hinder adoption at sponsors | 1.6 – line 179 | Major Issue | Closed | Known issue has been deleted from the TAUG since no SDTM examples are provided with this known issue. | Persuasive with mod |
| 26 | Creating a new solution for relatring data in different domain (i.e. adding a new variable) is over complicating the issue. As a fully functional solution already exists it is unnecessary to create more complexity and introduce a change which hinders the adoption of standards | 1.6 – line 164 | Suggestion | Closed | Public Review of any solution would take place where the CDISC community can comment.<br>The known issue text was updated from<br>"A new variable to indicate that interventions are part of a regimen is under discussion"<br>to<br>"A new ***solution*** to indicate that interventions are part of a regimen is under discussion." | Persuasive with mod |
| 27 | Will Tumor grade be captured in QS domain along with TNM? Why not use the CC domain for staging? | Staging | Question | Closed | Discussions to be continued with the CC team about TNM modelling. Also AJCC discussions in progress about copyright permissions. Tumor Grade Modelliing not part of BrCa V1 – Will be addressed in V2 and other ONCO TAUG's (e.g. PrCa, CrCa) | Considered for future |
| 28 | In Example 2 of this section, the Best Outcome of Treatment is mapped to SUPPPR (QNAM=OUTTRT). This is a bit confusing. Why not capture the treatment outcome in TR domain? | 3.4.1 | Suggestion | Closed | This outcome is not associated with tumor results. Per Information for Sponsor's note "Advised for prior treatment or post-treatment collection" | Not persuasive |
| 29 | Would values of (1) Disease progression, and (2) Recurrence be mapped to treatment setting or intent? Also, in the file "Radiation.xlsx", it is mentioned that if the intent is palliative then setting is automatically metastatic. While this is true in most cases, it might not always be the case. Curative therapy may be applied in a metastatic setting.<br>Will there be a controlled terminology for TRTSTT and TRTINT? | 3.4.1 | Question | Closed | We are not capturing PD or Recurrence in these fields. We will soften the wording in the metadata tables and remove "automatically." Sponsors will collect what is relevant for their reporting/analyses. At this time we will not expand example.<br>Team created CT for non-standard variable – revise metadata table to list codelists | Question answered |
| 30 | Example not clear: I see what the total dose is, and understand that in 2 cases it is fractionated, but not how the number of treatments are derived or captured as presented in the listing/table. | Example 2 line 509-518 | Select or Blank | Closed | PRENDTC was added to the example in order to show the number of days of treatment. This was already actioned in comment #6 therefore this comment was closed with no action | Persuasive |
| 31 | While not necessarily relevant feedback on these forms, but probably question in larger context of imaging data—immune-response modified RECIST. While these agents not widely being studied in Breast yet and not yet accepted as a validated endpoint, lots of sponsors are concerned with this and concerns for early discontinuation—unsure if the forms can handle this phenomena, i.e. growth prior to reduction. | | Suggestion | Closed | We have not yet created examples/forms for the immune-response modified RECIST. SDS team is working on initial drafts and we may incorporate in a future version. This will effect Target lesion CRF at minimum. | Considered for future |
| 32 | Linda S – This is very strange. Why is there no "present" option?<br>Also, when a new lesion is "equivocal" (i.e. I see something but I'm not sure if it's a real lesion) that standard guidance is that you don't enter it into forms, but follow it until you're sure, and THEN enter it at the time it's first seen. Putting in an option of "equivocal" is an interesting choice. Again, I would be curious to talk to the designers of this to see how they envision the pieces of data being assembled into the response assessment. | 4.2.1; pg 31 | Major Issue | Closed | This is used to specify non-measurable disease types that cannot be adequately described by anatomical location and other location qualifiers. Tumor State will indicate whether the lesion is present/absent. Some Sponsors/vendors have different rational for capturing new lesions that fall into the "i.e. I see something but I'm not sure if it's a real lesion" bucket. This form allows for various conventions. | Not persuasive |
| 33 | I have never heard of this concept of "tumor presentation type" before. I would be glad to discuss it with someone who knows how this kind of information would be used to come up with the endpoint, and give feedback once I understand the intended application. | Section 4.2.1; pg 30 | Major Issue | Closed | This is used to specify non-measurable disease types that cannot be adequately described by anatomical location and other location qualifiers. These values are specific to the RECIST paper and FDA requests | Not persuasive |
| 34 | The reasons a tumor is inevaluable fall into 4 broad groups:<br>1) poor images: that will include Poor Scan Quality and Insufficient Images/Anatomy<br>2) Changes in the lesion or background that make it hard to measure the lesion: that will include Cavitation, Fibrosis, Necrosis... but other reasons are possible. For example, a lung metastasis may develop pneumonia around it, so the edges are concealed. If it were up to me, I would use a broader term, such as "lesion or background change that prevents evaluation", and use cavitation, necrosis, change in surrounding tissue, etc., as examples. Otherwise, if they won't do this, I would suggest adding "background change that hides lesion" as an option.<br>3) Change in imaging method, such that two timepoints are not fairly comparable. This would include Inconsistent Modality, but would also include things like changes in the use of contrast.<br>4) Focal intervention (focal radiation, ablation, excision, etc.) that makes it no longer fair to evaluate the effects of the trial therapy on the basis of that particular lesion. For example, if you surgically remove a large tumor in a trial where the trial therapy is only systemic, you can nc | Section 4.2.1; pg 29 | Major Issue | Closed | Added some more details about what the values mean in the CDASH metadata tables – CRF values modified<br>· Inserted "Focal intervention" as a value<br>· Removed Cavitation, Fibrosis, Necrosis<br>· Inserted new value of "Lesion or background change that prevents evaluation"<br>Updated metadata table to highlight this is sponsor defined collection as not all sponsors or 3rd party vendors will capture this level of detail. | Persuasive with mod |

| Comment # | Comment | Document Section | Comment Category | Current State | CDISC Comment | CDISC Disposition |
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| 58 | It is not explained how the radiation therapy (internal/external radiation) are coded with Coding Dictionary. | 4.1 | Question | Closed | Due to issues with coding this type of data The Breast Cancer team opted to provide examples where controlled terminology from the PROCEDUR codelist was used on the CRF. It is at the sponsors descretion whether or not to use a coding dictionary. No action required for the TAUG. | Not persuasive |
| 59 | Was it considered to use the PRDECOD for the CT used for the radiation types, and then use PRTRT for the other specify as an option. Avoids the use of SUPPQ.<br><br>Also, would allow coding if a sponsor decided to code, then sponsor could just use PRTRT and then use the DECOD from the dictionary without needing the SUPPQ. | Line 385 | Suggestion | Closed | Cannot leave the topic variable blank so this solution isn't an ideal, also using —DECOD in this way is a bit of a stretch from its intended purpose. How to handle combination therapies/radiation will be addressed in the 2016 Winter IntraChange and we will explore best practices with —DECOD as one. Currently the commonly used coding dictionaries do not offer satisfactory values to illustrate clinical concepts. Therefore we created the codelist PROCEDUR for this unmet need. | Not persuasive |
| 60 | SUPPQ.<br><br>This seem to introduce the concept that CDASH includes the domain name in SUPPQ, but then when mapped to SDTM the domain letters are removed. PROUTTRT, and several other SUPPQ. . Is this convention being followed in all places. I do not think this was implemented in CDASH model 2.0.<br><br>Also, we neeed to be careful. This item has question text what is the best response? when others may use this as what was the outcome of treatment. We have to be able to create generic question text and prompts or else we should assign a new SUPP name to the item. THe same situation with the definitons. This is very specific to radiation when the name implies a more generic defintion is needed. What is the outcome of the ttreatment? | Line 385 | Select or Blank | Closed | SDS team gave direction about dropping the domain letter from SUPPQUAL in the event the non-standard variable becomes adopted as a general Observation Class variable and that it needed to be 6 characters or less. Maybe once there is definitive direction we can revise NSVs and CDASH variables (as this TAUG was created with the direction available at the time)? For the Best Outcome, PROUTTRT variable was somewhat dictated to be as aligned as possible with the HepC variable. However Hep C is strictly for prior response and several of the BrCa volunteers with Data Management experience, myself included, have collected treatment Outcome in follow-up periods (as well as prior treatment) so we cannot adopt the Hep C label. All Sponsor submitted forms indicated "Best". The team decided to change to NSV to TRTBOR – The concepts in BrCa are different to HEP C hence the need for a different NSV. BOR is a common abbreviation for Best Overall Response. | Question answered |
| 61 | DS.DSSTDTC when PARAMCD = 'DISPOSIT' Can you explain-why we have a DISPOSIT for TREAT on this record<br>ABC-123-001 Seq4<br><br>I would expect that randomization is in DS, but why is the start date of the randomized treatment in DS as a different record. This does not look like a protocol milestone or a actual dispostion event -which is the actual treatment for the PD in Seq 13. Is this the DECOD value used in DS SDTM. Is this confusing because the TREAT seems to have 2 different meanings. the start date of randomized treatment , versus a failure reason/protocol violation.<br><br>It is not clear that this record for the start date of the randomized treatment is needed in this dataset. | 5.3.2.1 Use of a Provisional Varia | Select or Blank | Closed | [SSAWANT 2016FEB03] In many studies, date of randomization is not same as date of first study treatment. The example has been provided to cover various cases as per multiple study designs. This is just a reference example for the readers. No Action Required. | Considered-no action required |
| 62 | Why do the xpt not include the variables SRCDOM,SRCVAR when the SRCSEQ is included. All three are needed. Also, the example should explain that only a few variables were shown and not all the variables in the meta table. | 1024 | Question | Closed | [PSLAGLE 2016JAN13] The examples provided are for reference and are not complete examples per the SDTM-IG. The intent is to provide an explanation of the concept but not to train on ADaM-IG. The reader is expected to understand ADaM prior to this document. No Action Required. | Considered-no action required |
| 63 | Set to 'RS' when PARAMCD = 'ASSESS' The sponsor may elect to use the date from the plannned schedule to handle missing assessment. What seq in the RS domain should be referenced. This RS could have an assessment of Unk, but this is the date being used for calculation of duration. Hence, the PD and the actual date used- may not be from the same assessment record.<br><br>ALso, the TU/TR domain may contain the dates of all the scans. The investigator date of response may not reflect the date the sponosr uses in the calculation. The investigator uses the last scan, the sponsor uses the date of the scan which showed the progression etc. The central review may use a different date. These dates may not be reflected in RS that is in SDTM. It not clear how you trace this detail. These rules can become very complex.<br><br>ALso, when you look at the example, the dates for Progression are different by 1 day. This looks like the date the assessment was recorded and not the date of the actual event. | 1015 | Major Issue | Closed | [SSAWANT 2016FEB03] The desciption provided in this example are not the standard rules for the derivation. Sponsor may decide to use different dates for analysis. This is just an example for the readers. No Action Required. | Considered-no action required |
| 64 | I would prefer that the title of the table is Time to Event and not Analysis of Survival. With the sub heading as listed. | Line 949 | Suggestion | Closed | [SSAWANT 2016JAN22] Title updated to "Analysis of Radiological Progression". | Persuasive with mod |

| Comment # | Comment | Document Section | Comment Category | Current State | CDISC Comment | CDISC Disposition |
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| 65 | I think that it would be better to refer to the two types of analysis as Time to event and response rate.<br><br>The sentence One consideration with both survival analysis and duration of response analysis is that both types of analysis will involve events that are censored. Rather than 763 repeating the concept of censoring for all of the types of analysis, the concept of censoring is covered within progression-free survival and then referenced in the 764 other types of analysis.<br><br>These are both the same type of analysis -time to event. This can be confusing to readers. | Line Number 757 | Suggestion | Closed | [SSAWANT 2016JAN22] The headers for the section 5.1.1 and 5.1.2 would be changed to "Time to Event" and "Response Rate" respectively.<br>Change Line 763 to "The primary consideration with time to event analysis is that it will involve the events that are censored." | Persuasive |
| 66 | Please check for this typo in the metadata table. If ADTTE is created directly from SDTOM domains, then SRCSEQ is equal to the --SEQ of the corresponding row in the SRCDOM where the data is captured. This should be the SDTM domains, and not SDTOM. | 1022-1023 | Typo | Closed | Variable SRCSEQ - SDTOM replaced with SDTM | Persuasive |
| 67 | Symptomatic Deterioration: This annotation does not show the ORRES for this test. Is the result the no yes, or the actual date of the deterioration.<br><br>This could be the result of No yes-but is this really a date of collection date- using DTC rather than as a result. | Line 560 | Major Issue | Closed | Add annotation to include NY codelist as ORRES and STRESC. | Persuasive |
| 68 | PARAMCD = 'OS' : ADVENT.ASTDY when ADEVENT .ANL01FL = 'Y' and ADVENT.PARAMCD = 'EVENT' and ADVENT.AVALC = 'DEATH' or when ADEVENT.ANL01FL = 'Y' and ADVENT.PARAMCD = 'ASSESS' and maximum ADEVENT.ASTDY.<br><br>It needs to be clear that these are example-derivations. The last date of contact for OS surival would likely not be recorded in the RS domain. Subjects are typically, not be followed for lesions after PD. THe SS domain would most likely contain the last date of contact. Hence, using the PARMCD="ASSESS' which seems to be linked to the RS domain is maybe incomplete.<br><br>Agreed that all derivation can not be provided-but its confusing to imply that the last date of contact would be in the RS domain itself. | Line 1022 | Suggestion | Closed | Variable AVAL - ADEVENT.PARAMCD="ASSESS" updated to ADEVENT.PARAMCD="DISPOSIT" | Persuasive |
| 69 | With regards to P9, P13, P14 and P15, these comments are from pathologists. We believe CDISC to understand that it is practically impossible to integrate all of the standardized methods for estimation. Many opinions could be proposed and we recommend that CDISC permit to use additional efficacy estimations as well in the User Guide in order to increase flexibility.<br>We strongly expect the User Guide to be revised to incorporate other methods for estimation. | | | Closed - JAPAN | The team agreed we should make it clear that these pathologic assessments are not the only ones that may be used.<br>Short introductory text was added before all pathology tables ending with the following note<br>*Please note that the following table is not an exhaustive list but details the more common types.* | Persuasive |
| 70 | P9: Endpoint: We routinely use pCR to estimate the effect of NAC at current practice. For the future, we need to improve the endpoints | | | Closed - JAPAN | No additional action required to the TAUG. This is only an example and not a complete guide. | Not persuasive |
| 71 | P10: Regions where the patient live, and lived shall be important as information in Asia since Asia is large and has various ethnicities among the regions. The situation is different from North America. Registration of regions in terms of life style and infectious disease is more preferable | | | Closed - JAPAN | The following text was added to the introduction to section 3<br>"Individual sponsors/protocols may collect other relevant information (e.g. more granular ethnicity) as needed." | Persuasive with mod |

| Comment # | Comment | Document Section | Comment Category | Current State | CDISC Comment | CDISC Disposition |
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| 72 | P13: Allred score: We need it for IHC assessment in Japan<br>Allred is not included (refer to P8 188 "Method of Scoring"). Allred score is necessary in IHC assessment. We see that the scoring system is not determined yet and strongly recommend that all methods used in the current clinical studies be included or CDISC would handle to determine before issuing the User Guide. | | | Closed – JAPAN | Terminology for both the Allred and H-Score scoring systems has been developed and will be published with P25 in March 2016. The receptor name (ER or PR) goes into MITEST and the following new terminology for MITSTDTL (which corresponds with the Allred scoring system) has been developed: ALLRED PROPORTION POSITIVE SCORE; ALLRED STAINING INTENSITY SCORE; ALLRED TOTAL SCORE.<br>It is anticipated that examples of these will be included in the next version of the TAUG. | Considered for future |
| 73 | P14: RCB score: It has not been penetrated well yet. | | | Closed – JAPAN | RCB (Residual Cancer Burden) was not in scope for the first version of the TAUG and will be considered for future releases. | Considered for future |
| 74 | P15: We might need to amend the grading method in Japan. | | | Closed – JAPAN | The following text was added after Table 3.3.3 Primary Tumor Grade Assessments<br><br>*"The table above show examples of some of the most common grading scales. There are other grading scales that might be used depending upon sponsor/protocol requirements."* | Persuasive with mod |
| 75 | P17: Category of luminal HER2 would be needed. We would like to know why luminal HER2 is not included in as one of the subtypes (Luminal A, Luminal B, HER2 possible, and Basal-like) in the User Guide and recommend that the reason of its exclusion be clarified. We could accept it if it is reasonable not to use HER2. | | | Closed – JAPAN | Referring to luminal B/HER2- or luminal B/HER2+ breast cancer. These are combinations of findings. The luminal B/HER2- breast cancer has a higher risk of mortality for all stages of the disease, as compared to luminal B/HER2+ breast ca. It is recommended to post-coordinate luminal B type breast cancer with HER2- or HER2+.<br>The team felt that it is enough that the list contains the HER2-enriched type and the Luminal B types of Breast cancer listed separately and these do not need to be pre-coordinated into a single concept. | Not persuasive |
| 76 | P23: Risk factors; Viral hepatitis B/C might be important in studies in Asia. Osteoporosis often causes as a side effect and it is a problem for the use of aromatase inhibitors as well. | | | Closed – JAPAN | *Hepatitis B*<br>*Hepatitis C*<br>*Osteoporosis*<br>Were added to the list of Major comorbid conditions under section 3.5 | Persuasive |
| 77 | Germline mutations: PALB2 also might be a candidate for hereditary cancer gene to describe. | | | Closed – JAPAN | PALB2 is a relatively new 'biomarker' in breast cancer (2014). While it is certainly relevant for breast cancer the team felt it might be too new for the TAUG to be absolutely required to write something up about it. The team felt that addition of this could 'date' the TAUG if it becomes less important over time, unlike BRCA whose importance has stood the test of time. The team agreed that this would be re-reviewed for the next version | Considered for future |
| 78 | P46: Response analysis; Clinical benefit rate having SD>12wks as well as CR/PR might be used particularly for hormonal therapy. We would like the User Guide to permit to use it. | | | Closed – JAPAN | The TAUG only contains examples and does not consitute definitive guidance. Other endpoints can be used as required by the protocol. No action required for the TAUG.<br>Also reference the second to last paragraph in section 1.1 – Purpose) | Not persuasive |
| 79 | "General points": We comment 1)-3) below since we believe they would be necessary within a couple of years.<br>1) Circulating tumor cell/ circulating cell-free DNA analysis might be needed (for staging, monitoring).<br>2) Triple negative breast cancer subgroup; Basal marker details and androgen receptor might need to be added.<br>3) We may need to consider for therapeutic response to immune therapy such as anti-PD1 antibody and anti-PDL1 antibody for the near future. | | | Closed – JAPAN | CDISC understand that new research will always be present and increase need for tracking or reporting. The TAUG should be considered as a guide for implementation should be used as a template for new concepts that are emerging. These new concepts may be considered for inclusion into future versions of the TAUG. | Considered for future |
| 80 | CDASH annotation TUDAT is missing from Target, Non Target and New Lesion CRF pages | | | Closed | CDASH annotation TUDAT is missing from Target, Non Target and New Lesion CRF pages in section 4.2.1 | Persuasive |

| Comment # | Comment | Document Section | Comment Category | Current State | CDISC Comment | CDISC Disposition |
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| 81 | The following NSV's do not have corresponding variables in the SDTM example<br>1. **TRTINT** Treatment Itnent *(included in the accompanying SDTM example0*<br>2. **TRTSTT** (Treatment) Setting *(used in other examples, so extrapolation to radiation therapy data is straight forward.)*<br>3. **TRTDTL** Modality Type (kind of radiation, e.g., Alpha, Electron, Neutron, Proton, Photon, Mixed)<br>4. **TRTLOC** Radiation Relative Location Category (e.g., local, regional, distant)<br>5. **CMLDOS** Cumulative Dose<br>6. **RTTFR** Total Fractions Count<br>7. **OUTTRT** Best Outcome of Treatment | | | Closed | Line 388 states This sponsor narrowed Radiation CRF collection to therapy type, treatment setting, start and end date.<br>The team acknowledges that showing further examples of the use of these variables would be beneficial however given the timelines for publication this would be tabled for a future version | Considered for future |
| 82 | **TRTDTL** – This non-standard variable is described in a s a non-standard variable I haven't seen before. It's not clear to me whether the kind of radiation shouldn't be part of the name of the radiation in **PRTRT**, instead of in a non-standard variable.<br>Get an opinion from Erin about whether the type of radiation should be part of TRT or in a separate variable. The terms used in the SDTM example refer to a different aspect of treatment, brachytherapy vs. external beam radiotherapy. If this can't be resolved quickly, add a known issue about terminology for PRTRT not being developed | | | Closed | Team confirmed that the TRT variable and the TRTDTL are needed in order to be able to capture different granularities of information. It is acknowledged that for future versions of the TAUG it would be beneficial to show examples of on study and off study radiation therapy. | Considered for future |
| 83 | **TRTLOC** – is described in the Known Issue "Radiation Location Category" but is not used in any SDTM example. The name of the known issue doesn't match the prompt in the CRF. TRTLOC is a poor name for this variable, since it doesn't really differentiate it from the standard variable LOC. (This is an interventions domain where LOC can be assumed to be location of treatment).<br>Make the association between the known issue "Radiation Location Category" and the CRF clearer; consider changing the NSV name. | | | Closed | Team agreed to amend the variable name to RRLTLC – Radiation Relative Location<br>John Owen to amend in the TAUG<br>– Annotated CRF – Radiation Therapy section 3.4.1 example 2 – amend SDTM and CDASH variable name<br>– Appendix D – amend variable name<br>– Know issues reference to this variable<br>CDASH metadata tables were also updated | Persuasive |
| 84 | **CMLDOS** – depends on STDTC and ENDTC being present (per the information in Appendix D). This would be a problem if dates are not available for a prior treatment – something that is fairly likely<br>Decide whether change the descriptions of CMLDS and RTTFR. I think these would really only apply to complete courses of radiotherapy. | | | Closed | There are many use cases where Start and End dates are not fully captured for previous radiotherapy however the Cumulative Dose and Total Fraction Count are still provided.<br>The closer the treament to the start of the study the more likely sponsors are to ensure that this informaton is collected.<br>Team agreed to amend the description to<br>"For treatments with a cumulative effect, the total dose administered over a ~~the~~ time period (maybe defined by – STDTC and – ENDTC). Used instead of --DOSE." | Persuasive |
| 85 | **RTTFR** – is something that is used (I think) only when discussing a planned or completed course of radiation. I don't think it would be used to describe a part of a course.<br>Decide whether change the descriptions of CMLDS and RTTFR. I think these would really only apply to complete courses of radiotherapy. | | | Closed | There are many use cases where Start and End dates are not fully captured for previous radiotherapy however the Cumulative Dose and Total Fraction Count are still provided.<br>The closer the treament to the start of the study the more likely sponsors are to ensure that this informaton is collected<br>Description was amended to<br>"A qualifier of CMLDOS describing the number of fractions the total dose was administered in." | Persuasive |

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| 86 | OUTTRT – has been used in other user guides. I don't think it's always been described as "best" outcome of treatment. In Hep C, I'm pretty sure that the outcome of treatment was not the best outcome. For instance, someone who had a early response followed by a breakthrough while on treatment would not be described by referring only to their early response. I think we may need a slightly different name.<br>Consider whether "best outcome of trt" needs to be a separate NSV from "outcome of trt" | | | Closed | The team discussed that this may best be represented in the FA domain, however, due to timelines of public release a known issue will be written stating that the modelling of this may change as a result of discussions (these are planned for the WInter IntraChange along with the Regimen discussion)<br>Team amended the NSV name to ***TRTBOR – Best Overall Response***<br>The initial intent was to align with HEP C however these are two different concepts and require different NSV's<br>TAUG amended as below<br>– Annotated CRF – Raditation Therapy section 3.4.1 example 2<br>– amend SDTM and CDASH variable name and CRF label<br>– Appendix D – amend variable name and description<br>known issue added<br>· Best Overall Response: There are planned discussions on the modeling of this variable. The user is cautioned that this therefore may be subject to change.<br>CDASH metadata tables updated.<br>No impact on the Analysis section | Persuasive |