

Review of Case Report Tabulation (CRT) packages



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ABSTRACT	INTRODUCTION
<p>The FDA requires all new drug applications (NDAs) be submitted electronically. For statistics and programming this involves creating the Case Report Tabulation (CRT). In this poster we describe the process we follow at GSK when carrying out review of CRT packages. Covering both SDTM and ADaM deliverables, we aim to highlight the issues we have encountered with the content of the CRT package itself along with the challenges faced with packages received from a CRO. We will also highlight common issues we have encountered during the review. Finally, we are providing some hints and tips for an effective review based on our experience and give you our proposal for a better CRT experience.</p>	<p>One of our core principles at GSK is to focus on quality culture, governance and compliance. To support this principle we have been performing thorough, in-depth reviews of the CRT packages. This poster aims to give an insight into how we carry out the reviews of both SDTM and ADaM CRT packages at GSK to produce what we consider a quality package.</p>

SDTM	ADaM
<p style="font-size: small;">^ Output from Pinnacle21 is used to complete section 4.2 of SDRG but the output itself is not included in the SDTM CRT package.</p>	<p style="font-size: small;">^ Output from Pinnacle21 is used to complete section 6.2 of ADRG but the output itself is not included in the ADaM CRT package. * Other data sources refers to non-ADaM datasets used as input to ADaM datasets, for example, protocol deviation spreadsheet, AEs of special interest spreadsheet. ~ Analysis Results Metadata which provides traceability from a result used in a statistical display to the data in the analysis datasets.</p>
<p>Step 1: Validation checks</p> <ul style="list-style-type: none"> CRF page Duplicate entry in controlled terminology TYPE for a variable <p>Step 2: Check the Metadata of the package that:</p> <ul style="list-style-type: none"> All variables listed matches xpt datasets All length specified matches xpt dataset Origin or aCRF page should be provided Variables and/or VLM values TYPE is populated, length specified matches xpt dataset Variable and/or VLM length matches xpt dataset 	<p>Check sections 1 to 4 of ADRG for content and accuracy. At GSK we use the PhUSE ADRG template.</p> <p>Review ADRG section 5 Analysis Dataset Descriptions in conjunction with define.xml.</p> <p>Crosscheck the inventory of analysis datasets in ADRG section 5.2 Analysis Datasets with page 1 of define.xml.</p> <p>Review each analysis dataset specification in define.xml along with the corresponding section in ADRG section 5.2 Analysis Datasets.</p> <p style="text-align: center;">Ask yourself 'Could I reproduce this dataset with the information provided in define.xml and ADRG?'</p> <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p style="text-align: center;">SPECIFIC CHECKS FOR ADRG</p> <ul style="list-style-type: none"> Has the source SDTM(s) for the ADaM been specified? Compare the number of observations in the ADaM with the main source SDTM. Are there more, less or the same? An explanation is useful. Check non-ADaM source datasets are described under section 1.4 Source Data Used for Analysis Dataset Creation Check ADaM specific analysis flags are in section 5.2 and those derived consistently are in section 4.4 Variable Conventions Check reasons for deviations from the RAP/SAP are included. Review Pinnacle21 report to ensure issues not resolved have been appropriately listed under section 6.2 Issues Summary of the ADRG. Check all hyperlinks work correctly </div> <div style="width: 45%;"> <p style="text-align: center;">SPECIFIC CHECKS FOR DEFINE XML</p> <ul style="list-style-type: none"> The Keys on page 1 of define.xml should show the unique key for that ADaM. Crosscheck variables with controlled terminology (CT) in define XML with the ADaM dataset. Is it clear how the variables are mapped? Check any VLM has been used appropriately and the information is accurate. Check Computational Methods and confirm that derivation is correct Check that variable derivations are correct and accurate Check all hyperlinks work correctly </div> </div>

COMMON ISSUES	HINTS & TIPS
<ul style="list-style-type: none"> Incorrect or incomplete controlled terminology or derivations in define.xml TYPE for a variable in the define.xml is not defined as: 'Num', 'Char', 'Text', 'Integer', 'Float', 'Date', 'Datetime'. Length specified in define.xml does not match actual data or is missing. For VLM values and dataset variables a 'TYPE' of TEXT, INTEGER or FLOAT, LENGTH not provided. For variables other than RFICFDTC in DM and QVAL in SUPP the Origin or aCRF page not provided. Incorrect use of VLM in define.xml (applying VLM's to PARAM, PARAMCD) Dataset structure on Page 1 of define.xml doesn't match section 5.2 Analysis Datasets in ADRG and incorrect unique key on Page 1 of define.xml 	<ul style="list-style-type: none"> Create and review ADaM specifications prior to ADaM creation at study start and maintain throughout the study. This will reduce the time needed to review define.xml at the end of the study when CRT package is usually created. Mandate QC of the ADaM specifications for pre-programming. Rerun and check the Pinnacle21 report through the course of the study on both SDTM and ADaM datasets Get the CRT package reviewed by an independent programmer. They'll see the study in the same way as the external reviewer. Check the keys on page 1 of the ADaM define.xml are unique by doing a PROC SORT with NODUPKEY. The log should show zero observation were deleted. For variables that use controlled terminology do a quick PROC FREQ on that variable in SAS for crosschecking against define.xml. Make sure you are running the latest version of P21 — it's what the FDA will run. Watch out for special characters in Define XML, e.g. variable names can't have \ / * , ? < > " ' : % # + () { } [] and the comments section can't have " & * ADRG is a living document. Start writing it at any time throughout the study, it doesn't have to be left until the end. Follow the PhUSE template!