Life

OPTIMIZE PROCEDURES SETUP FOR RDC

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Introduction

- In RDC studies, procedures must be setup on a more precise way, and must also be created faster compared to paper studies

Paper Study	RDC Study
Edit Checks need to be ready to be executed when the first set of CRF is entered	Edit Checks need to be ready when the first Patient is enrolled in the study
An error on one single data point may produce several queries The Data Manager will filter out extra queries and send to the Investigator only what is necessary	One single data error should preferably only generate one query, but all possible errors should still be checked Ideally the number of Edit Checks should be as low as possible…
The default error message may be customized if needed by DM before sending out the DCF	The error message generated should be clear enough to indicate to the Site User what action is required

Accelerate the procedures setup process

Agenda

- Reduce the number of Edit Checks needed
- Optimize setup of Validation Procedures for RDC Studies
- Improve the time spent in creation or modification of Validation Procedures

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Reduce the number of Edit Checks needed

- ✓ Use Univariate and Indicator Discrepancies
- ✓ Use DVGs and Alpha DVGs
- ✓ Adjust Study Definition to the required Edit Checks
- ✓ Self-Evident Corrections for DM

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Use Univariate and Indicator Discrepancies

- One possibility to reduce the number of Validation Procedures is to use Univariate or Indicator checks
  - ✓ Set up Questions as Mandatory

  - ✓ Indicate Ranges for Numeric or Date Questions

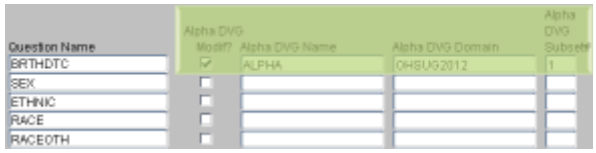
  - ✓ Set up Indicators and create Conditional Blocks in the Graphic Layout

Limitation of Univariate and Indicator Discrepancies

- Some “Univariate” checks are conditional and require the creation of a Validation Procedure
  - ✓ Example: Check for Vital Signs Ranges depends on the Unit entered
- The message of Univariate Discrepancies is not always explicit enough for RDC Studies
  - ✓ Example: A discrepancy may be a protocol deviation for one study and this information is not detailed in the default message
- In such situations, Validation procedures allow a better control on the message and the conditions under which the edit check should fire

Use DVGs to avoid creating Discrepancies

- To avoid Data Types errors, assign Alpha DVGs to numeric and Date fields



- Setup DVGs as "Check Box Groups" in the Global Library to ensure a value out of the DVG cannot be entered…

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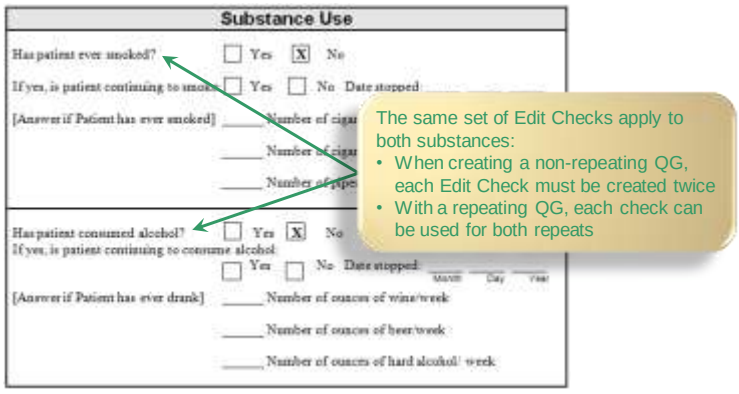
Adjust Study Definition to the required Edit Checks

- If a similar set of Questions is collected several times, the number of Edit Checks will be reduced if using Repeating Question Groups



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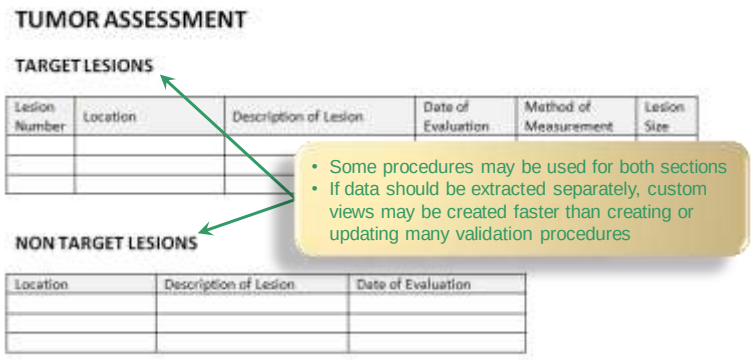
Adjust Study Definition to the required Edit Checks

- Consider creating multiple DCM subsets rather than create multiple DCMs containing the same Question Groups



Process Enhancements

- Other ways to reduce the number of Edit Checks may need some process modification
- For example:
  - ✓ Build Self-Evident Correction rules for Data Management
  - ✓ Adjust Data Standards to EDC Studies in order to facilitate the reusability of Data Collection objects and accelerate the creation of Edit Checks

Optimize setup of Validation Procedures for RDC Studies

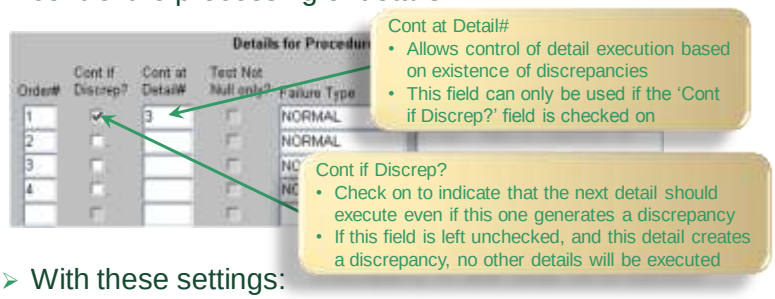
- ✓ Avoid duplicate discrepancies
- ✓ Avoid confusing discrepancies
- ✓ Take advantage of Discrepancies color-coding in RDC

Avoid Duplicate Discrepancies

- Duplicate discrepancies may be produced:
  - ✓ Either if a Univariate or Indicator Check identifies the same error as a Multivariate Check
  - ✓ Or if multiple Multivariate Checks control the same data
- There are ways to control the processing of Procedure Details depending on the existence of other Discrepancies

Avoid Duplicate Discrepancies

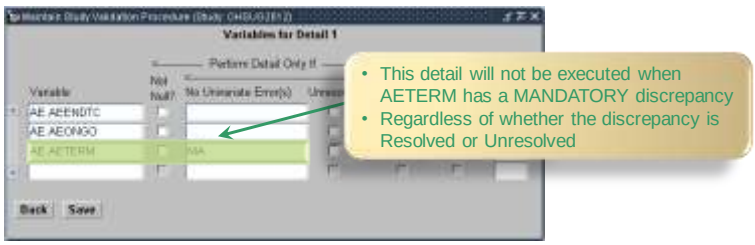
- For procedures having multiple details, it is possible to control the processing of details:



- With these settings:
  - ✓ If detail 1 does not create a discrepancy then detail 2 will execute
  - ✓ If it does then detail 2 will be skipped
  - ✓ For all other details, if a discrepancy is created, no further detail is executed

Avoid Duplicate Discrepancies

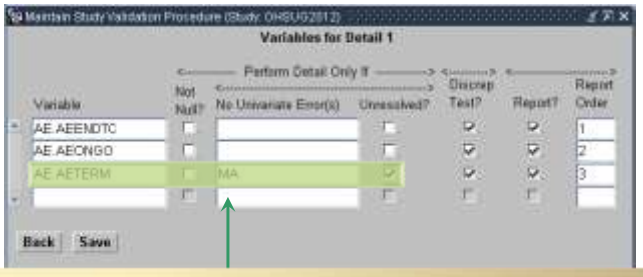
- For each detail within a Validation Procedure the processing can be prevented if a CURRENT univariate discrepancy exists



- The Type of Discrepancies can be selected from a list

Avoid Duplicate Discrepancies

- For each detail within a Validation Procedure the processing can be prevented if an <u>open</u> univariate discrepancy exists



- If there is a MANDATORY discrepancy against AETERM which is resolved manually or closed by the System, this detail will be executed
- If there is a MANDATORY discrepancy which is not resolved it will not execute

Avoid Confusing Discrepancies

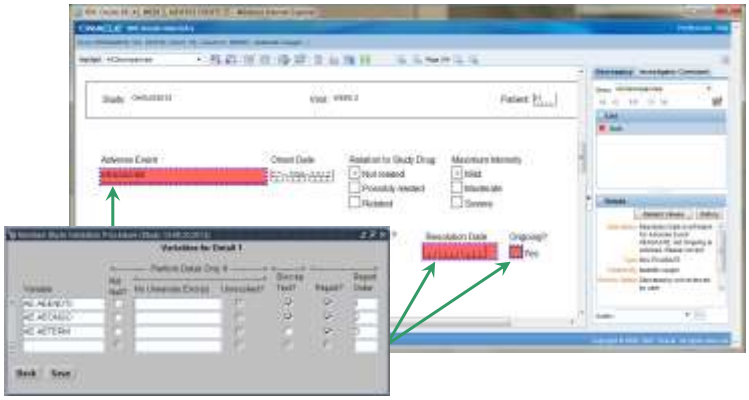
- Some discrepancies may not be clear to site user
- Example:
  - ✓ The Question BIRTHDTC contains the value UNKNOWN
  - ✓ A procedure using the expression ***BIRTHDTC is null*** or ***BIRTHDTC is not null*** will not fire as expected

Regardless of whether an Alpha DVG is attached to the Question

- Solution:
  - ✓ Use also the Exception Value whenever a Data Type error may exist

Take advantage of Discrepancies color-coding in RDC

- When a Multivariate Discrepancy is created, all Detail Variables are highlighted in RDC



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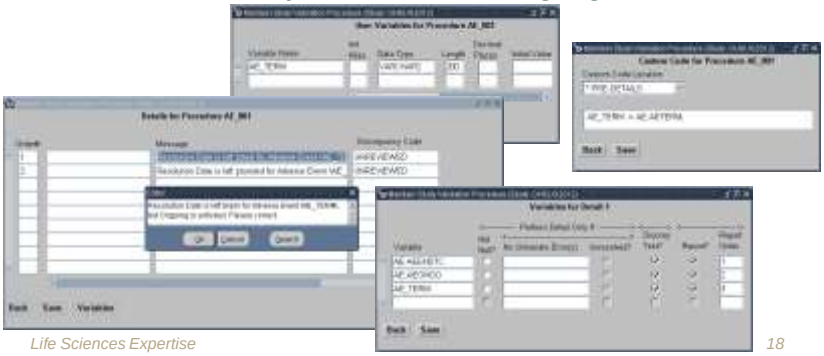
Take advantage of Discrepancies color-coding in RDC

- To facilitate the Resolution of Discrepancies, the number of Responses highlighted should be limited
- Responses that are needed in the Expression or the Message can be replaced with Procedure User Variables if they should not be highlighted



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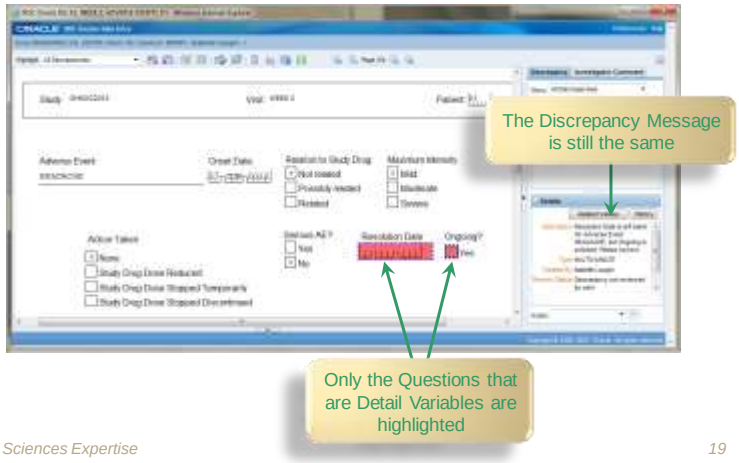
Take advantage of Discrepancies color-coding in RDC

- The same discrepancies are created

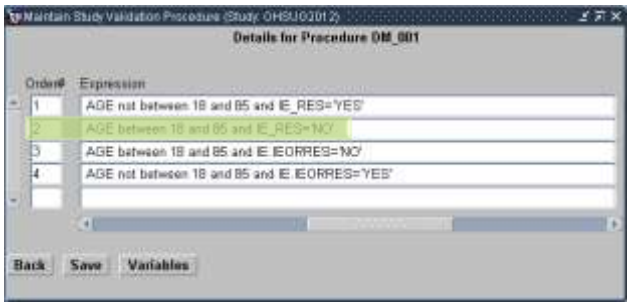


Take advantage of Discrepancies color-coding in RDC

- For Discrepancies produced by Procedures including multiple DCIs:
  - ✓ The CRF containing the Primary Reference is displayed in Red or Yellow
  - ✓ CRFs containing the other Procedure DCMs are white
  - ✓ The Discrepancy is displayed only on CRFs containing Questions included as Detail Variables

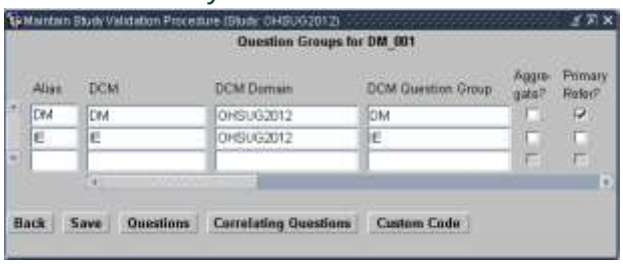
Take advantage of Discrepancies color-coding in RDC

- Example:
  - ✓ The following procedure checks the consistency between the Date of Birth and the Response to the Inclusion Criteria “IS AGE 18-85”



Take advantage of Discrepancies color-coding in RDC

- DM is the Primary Reference



- If a Discrepancy is created
  - ✓ The Demography CRF will turn to red
  - ✓ The Eligibility CRF will stay white

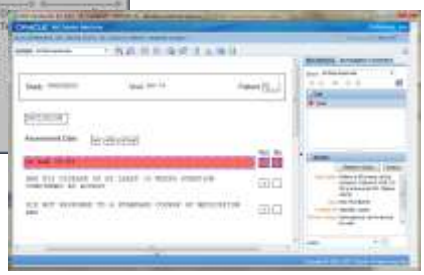
Take advantage of Discrepancies color-coding in RDC

- BRTHDTC is the only DCM Question declared as Detail Variable (the others are User Variables)

- This means that the Discrepancy will only be visible on the Demography CRF, not on Eligibility

Take advantage of Discrepancies color-coding in RDC

- However, with the following Detail Variables



- The DCM Questions defined as Detail Variables are in IE
- The Discrepancy will be visible only on the CRF Eligibility but not Demography

- Which may be confusing for the Site User

The white CRF contains a Discrepancy

The red one does not…

Improve the time spent in creation or modification of Validation Procedures

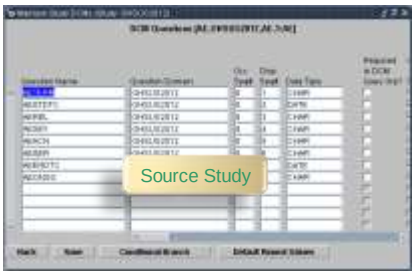
- ✓ Copy Procedures when DCM and Question Groups are not identical
- ✓ Use Custom Code to facilitate update of copied standard procedures
- ✓ Use the most appropriate procedure features to create Edit checks

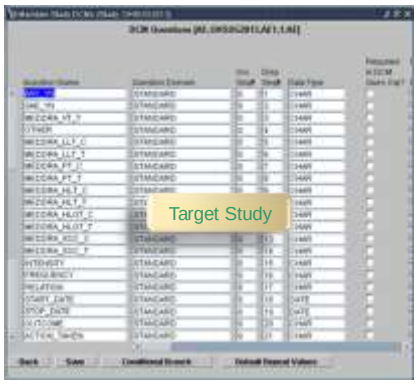
Copy Procedures

- To improve the time spent in developing Edit Checks, the immediate idea is:
  - ✓ Use standard DCMs and standard Procedures
  - ✓ Create Copy Groups
  - ✓ Take advantage of the reusability features of OC
- Unfortunately in real life:
  - ✓ Standard DCMs and standard Procedures do not cover all needs: new objects must be created, and copied objects must be updated
  - ✓ DCMs are usually modified before Procedures are created or copied

Copy Procedures

- It seems evident that if we have two studies having each an AE DCM containing following questions:





- OC won't be able to copy a procedure from one study to the other
- But how much differences can OC handle?

Copy Procedures

- Example:
  - ✓ Source Study has a CONMED DCM with a repeating Question Group containing many questions including CMTRT, CMSTDTC and CMENDTC
  - ✓ Target Study has a CONMED DCM with a non-repeating Question Group containing only the questions CMTRT, CMSTDTC and CMENDTC
  - ✓ We want to copy a procedure from the Source Study to the Target Study that includes the 3 common questions but that applies in the Source Study only to visit "DAY -14" which does not exist in the Target Study…

Copy Procedures

- If we try, OC will provide several Messages:


- And finally:

- The procedure is (really) copied in the Target Study, and we know that:
  - ✓ There is a reference to a Visit that must be changed
  - ✓ Any potential reference to a Repeat must be removed

Copy Procedures

- Another example:
  - ✓ All procedures for Concomitant Medications have been created for a new Study
  - ✓ We want to copy them for Prior Meds or AE because it is faster than recreate everything from scratch
- Solution:
  - ✓ Activate the DCM (not the DCI or views)
  - ✓ Activate the procedures to be copied
  - ✓ Perform the copy
  - ✓ Delete the DCM QG Questions, update the DCM Name and QG, and insert the new Questions
  - ✓ Update the Question names where needed

Custom Code and User variables

- If many User Variables need to be created, it is also possible to define these via the Custom Code rather than use the User Vars screen

- This method is faster as several User Variables may be copied via copy/paste in one single step
- Such variables can be used as usually

Custom Code and User variables

- However Variables created on that way cannot be used in the Discrepancy Message:

- But they can be used in the Expression field:

Custom Code and User variables

- Even if a standard procedure is copied, it is frequently necessary to refine some details
  - ✓ Detail Expression or Discrepancy Message
  - ✓ Question Group attributes (e.g. Qualifying Expression or Where Clause)
  - ✓ Initial Value of User Variables
  - ✓ Custom Code
- In order to facilitate the study adjustments of a copied procedure, it may be helpful to perform all potential changes in one single place
  - ✓ For example the Custom Code

Custom Code and User variables

- Example – Date Fields:
  - ✓ Each date collected on a CRF is usually checked against a date that should be prior and a date that should be after
  - ✓ However the best comparison dates to choose may vary for each study, even though the basic check is standard
- Let's consider the following example:
  - ✓ Informed Consent Date must be prior to Screening Visit Date
  - ✓ Informed Consent Date must be after patient's Date of Birth

Custom Code and User variables

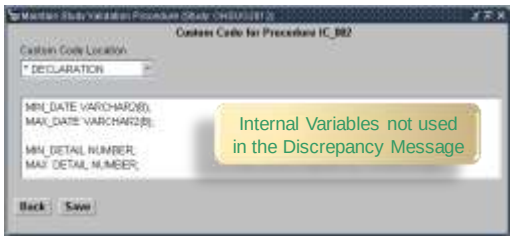
- Such an Edit Check can be created on the following way:

Expression	Message
IC.DSSTDTC > VISIT_DATE	Informed Consent Date \DATE_ST\IC.DSSTD\
IC.DSSTDTC < BIRTH_DATE	Informed Consent Date \DATE_ST\IC.DSSTD\

- But can only be re-used in another study if all parameter match
- Alternative solution:
  - ✓ Create user variables for the MIN_DATE and MAX_DATE
  - ✓ Create user variables for the Detail Expression and the Message
  - ✓ This will minimize the update effort

Custom Code and User variables

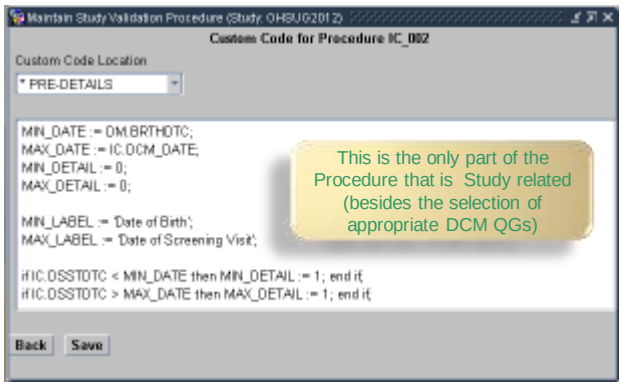
- Create the following User Variables



  - ✓ AND

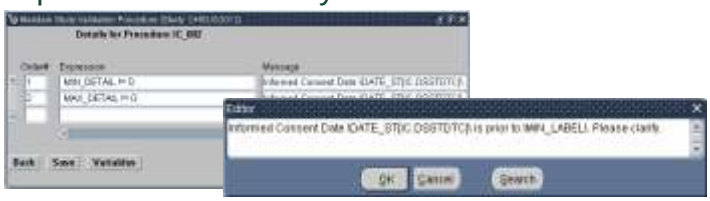
Custom Code and User variables

- Set all needed values in the Custom Code



Custom Code and User variables

- Define the Detail lines on a way they won't need any further modification in case the procedure is copied to another study



- Detail Variables should not need any modification neither

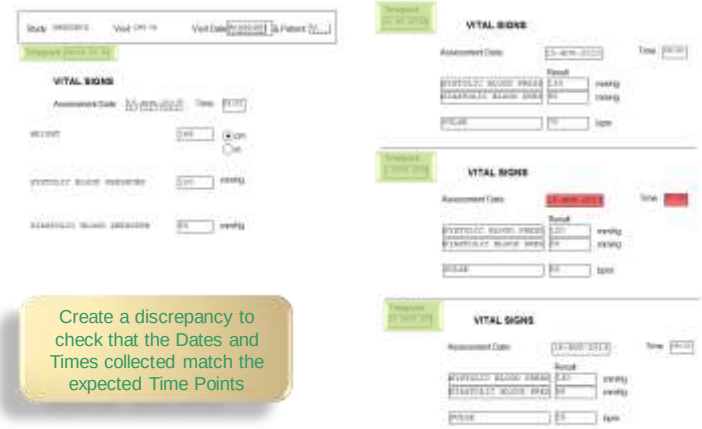
Use all Procedure Features

- Some features available when creating Procedures are “traditionally” not used, even though very useful because they are under certain circumstances “scary” or “unreliable”… but work fine in other circumstances!

- Example:
  - ✓ The Vital Signs are collected several times at each visit for different Time Points
  - ✓ The Time Points are collected as Qualifying Values associated to the DCM VS collected several times within the DCI VS

Use all Procedure Features

- The following Data is collected:



Use all Procedure Features

- As Time Points cannot be sorted by name:

Sequence	Time Point
1	PRIOR TO DOSING
2	30 MN AFTER DOSING
3	1 HOUR AFTER DOSING
4	24 HOURS AFTER DOSING

- It is not possible to set the Sort Order – Extension field to “RDCM.QUALIFYING_VALUE DESC…”
- A “safe” solution might be :
  - ✓ Add 4 times the DCM Question Group VS
  - ✓ For each occurrence set the Where Clause to the appropriate value of “RDCM.QUALIFYING_VALUE”

Use all Procedure Features

- This method works fine, but the procedure must be changed for each study, and the appropriate Qualifying Values must be entered manually…
  - ✓ Which costs time and produces a risk regarding Quality
- OC provides two features that could resolve the issue easily:
  - ✓ The Extension Sort Order field may contain any column of the Received_DCMs table (e.g. the Sequence Number of DCI Modules)
  - ✓ The Lag feature allows to retrieve easily the “previous” value

Use all Procedure Features

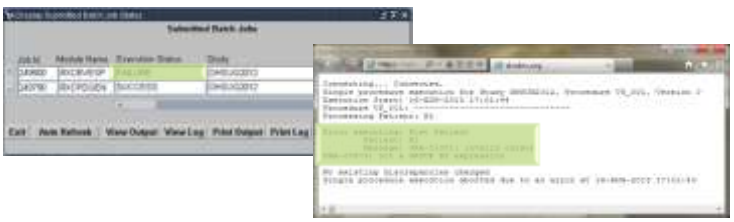
- Implementation:
  - ✓Set the sort order

  - ✓Use Lags to retrieve the previous value

Use all Procedure Features

- The Detail Expression is simple:

- However, even though the code is successfully generated, the procedure fails at Execution…

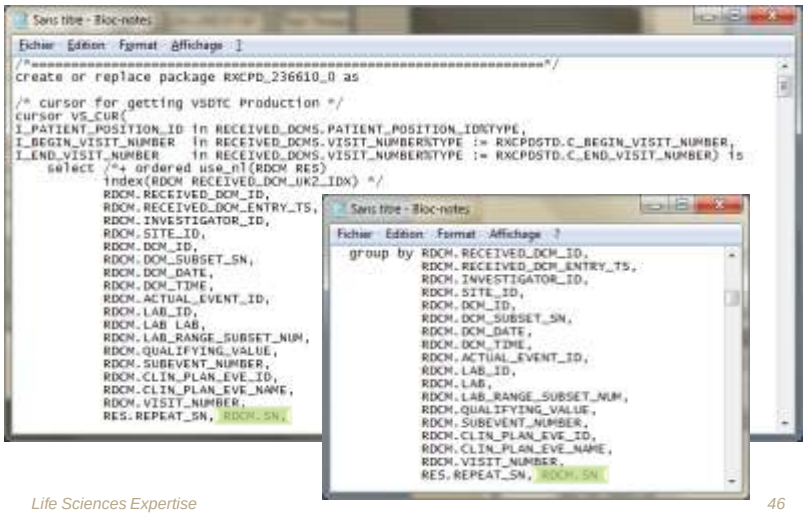


Use all Procedure Features

- Cause of this error:
  - ✓ The code generated does not take into account the variable RDCM.SN included in the sort order
- Solution: update the generated code!
  - ✓ In this case:
    - ✦ There is no risk as the procedure fails at execution, there is no way to forget making the fix
  - ✓ The fix is easy:
    - ✦ Add “RDCM.SN” in the SELECT command and in the GROUP BY clause for Production and Test cursors

Use all Procedure Features

- Once the generated code is updated:

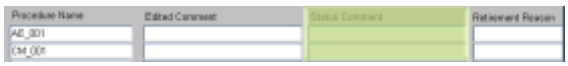


Use all Procedure Features

- It executes as expected and can easily be re-used in any other study:

Conclusion

- All tips provided in this presentation are not always applicable to all possible studies, and are even not always compliant with each other…
  - ✓ But all may help to improve the validation of EDC data!
- Ideally the process of creating RDC Edit Checks should be:
  - ✓ Different from Paper study process
  - ✓ Reconsidered regularly based on lesson learned
- One last tip: the status Comment field, usually left blank, may be used to comment any procedure particularity



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Questions?

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Biography

- Isabelle Laugel has a background of mathematician and software developer specialized in security of computer systems and optimization
- She is working in the pharmaceutical industry since 15 years and provides training, validation, consulting and support services for Life Sciences applications and business processes to pharmaceutical companies, medical devices companies and CROs of any size worldwide
- She founded Life Sciences Expertise in 2011 in order to share her experience in Data Management and Drug Safety