

“Standard Template Programs” の開発

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Development of Standard Template Programs

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要旨:

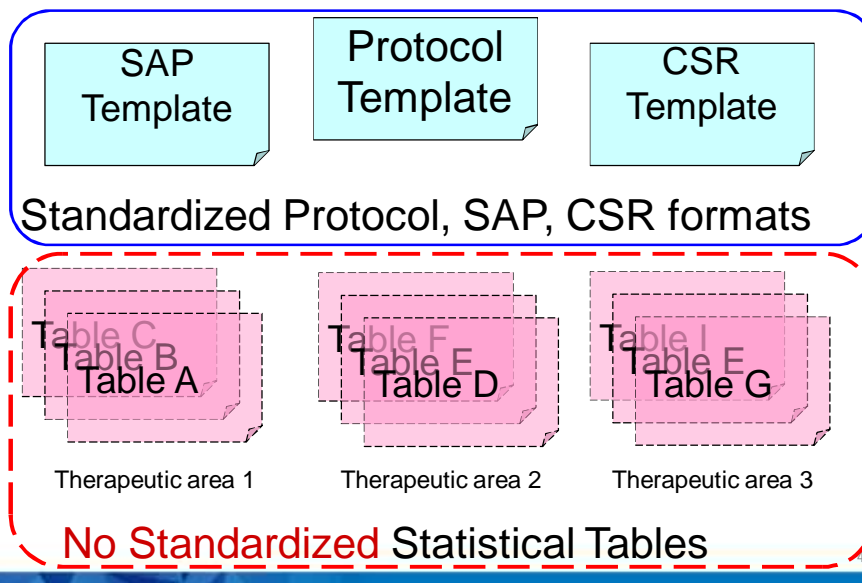
領域を問わず、総括報告書の約65%の帳票を網羅する標準解析出力“Standard Statistical Tables”を日仏米3国間で共同開発。マクロではなくTemplate programというアプローチおよび日本の貢献について報告する。

キーワード: Standard tables, Template program,
Cross region development team

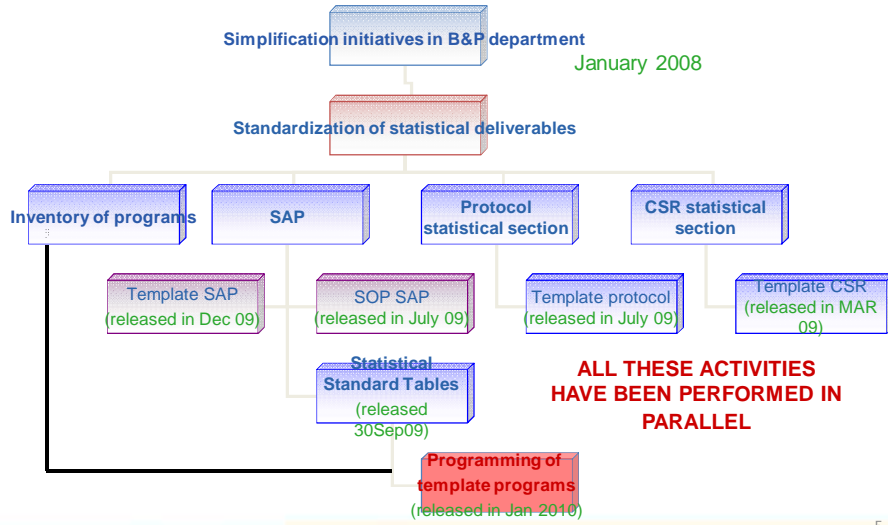
AGENDA

- STANDARD STATISTICAL TABLES
 - Standardization in sanofi-aventis 2008
 - What is Standard Statistical Tables?
- “TEMPLATE” APPROACH
 - Standardization in Statistical Programming
 - “Template” Approach
 - Structure of Template Programs
- CROSS REGION DEVELOPMENT
 - Working Group & Process
 - Harmonization among Standard & Tools
 - Harmonization among Countries
- SUMMARY

STANDARDIZATION in sanofi-aventis 2008



STANDARDIZATION in sanofi-aventis



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WHAT IS STANDARD STATISTICAL TABLES?

Do not cover

Disease characteristics
Study specificities
Efficacy
Specific tables for Clinical and Exploratory
Pharmacology studies

Scope

Patient disposition, Protocol deviations (6)
Demographic data & medication details (8)
Compliance and drug concentration data (2 non-onco + 4 onco)
Adverse events & deaths (35 non-onco + 35 onco)
Clinical laboratory (42 non-onco + 4 onco)
Vital signs & ECG (7)

•Cover **>65% of statistical tables** produced for CSR in all therapeutic areas

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WHAT IS STANDARD STATISTICAL TABLES?

Standard statistical tables document specifies:

The image shows a standard statistical table with the following components highlighted by callouts:

- Title:** DIS STD populations
- Contents:** Patient disposition, Analysis populations
- Header:** Tri A, Tri B, All
- Status (Mandatory or Optional):** This table is a mandatory in-text table
- Footnote:** *Note: The safety population patients are tabulated according to treatment actually received (as treated)/as randomized. For the other populations patients are tabulated according to their randomized treatment.
- Location in CSR (Intext vs Appendix only):** This table is a mandatory in-text table

	Tri A	Tri B	All
Randomized/Eligible populations	xxx (100%)	xxx (100%)	xxx (100%)
Efficacy populations			
Inten-tio to Treat (ITT) /Modified Inten-tio to Treat (mITT)	xxx (xx.x %)	xxx (xx.x %)	xxx (xx.x %)
Safety popu-	xxx	xxx	xxx

Notes: *

*Note: The safety population patients are tabulated according to treatment actually received (as treated)/as randomized. For the other populations patients are tabulated according to their randomized treatment.

Notes: *

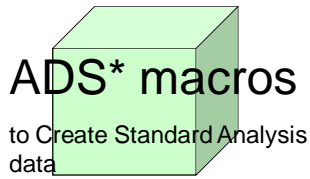
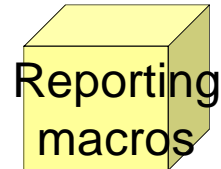
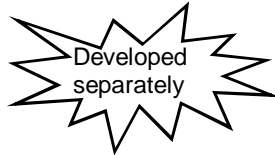
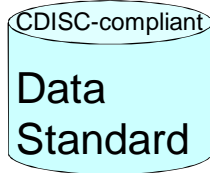
This table is a mandatory in-text table

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STANDARDIZATION in STATISTICAL PROGRAMMING

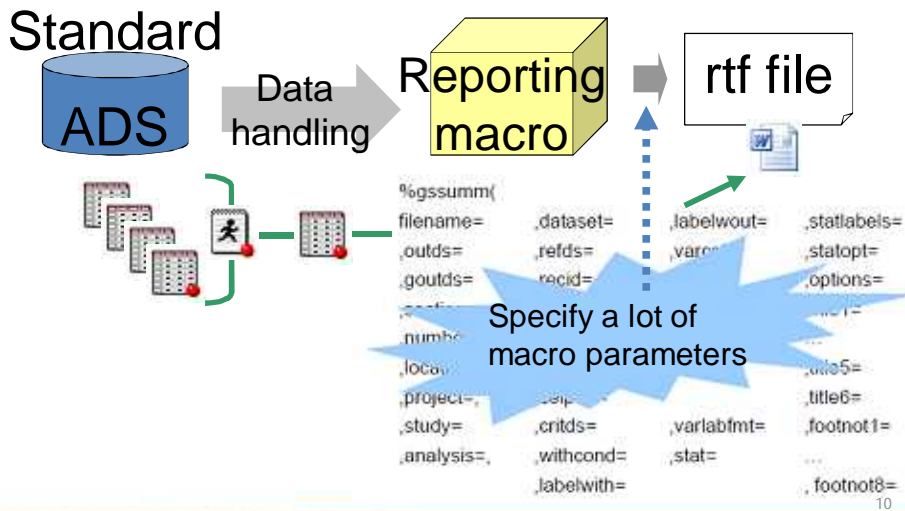
[No Standardized Statistical Tables]



*Analysis Dataset

- Cover various analysis, very flexible,...
- But
- Need experience to use (User manual is over 140 pages)
- Can create non-standard tables

PROGRAMMING PROCESS BEFORE TEMPLATE PROGRAMS



“TEMPLATE” APPROACH

Template

- Template program is unified SAS programs using reporting macro to create standard statistical tables.
- 1 program to 1 output table



New Macro

VS

Why “Template”?

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STRUCTURE OF TEMPLATE PROGRAMS

- Header
- Body
 - Data handling
 - Reporting macro call



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HEADER : Pay attention before use

- The following information is provided in standard program header:
 - Template program name
 - Description
 - Input mandatory variables (ADS)
 - Mandatory formats
 - Input optional variables (ADS)
 - Optional formats
 - Precaution for use

HEADER : Pay attention before use

- Input mandatory/optional variables
 - All the variables and ADS needed for the Template program are listed.
- Precaution for use



User can optimize ADS creation process

BODY: Indication by three kinds of tags

- **<ACTION>**
 - Users must modify code
- **<CAUTION>**
 - Users must verify if code correctly applies to study and modify if needed
- **<NOTE>**
 - Comments on standard specificities but no modification of the program line is needed

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Example: <ACTION> tag

```
*** <ACTION> Add / delete varlin parameter as appropriate to adapt to the study ***;
```

```
,varlin = %str(age [label='Age(years)' decimal=0]
           agegrp# [fmt=agegrp. label='Age Group (years) [n (%)]'
                 noshow=. totalrow=first]
           sexn# [fmt=sexn. label='Sex [n (%)]' noshow=. totalrow=first]
           racen# [fmt=racen. label='Race [n (%)]' noshow=. totalrow=first]
```

DELETE

```
weightbl[label='Weight (kg)' decimal=1 ]
wtgrp# [fmt=wtgrp. label='Weight (kg) [n (%)]'
       noshow=.....
       .....
```

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Example: <CAUTION> tag

*** <CAUTION> If no imputation (example <20 will be imputed to 20) is required for any standardized result value and ADLB dataset doesn't have the imputed result variable LBSTRENI, use LBSTRESN instead. ***;

```
data lb_01;
  length lbtestcd $10;
  set adsd.adlb(keep=USUBJID LBTEST: LBPCSA: LBBL: LBTRTEFL LBSTRESN ;
```

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Example: <NOTE> tag

*** <NOTE> Sort template dataset for reporting***;

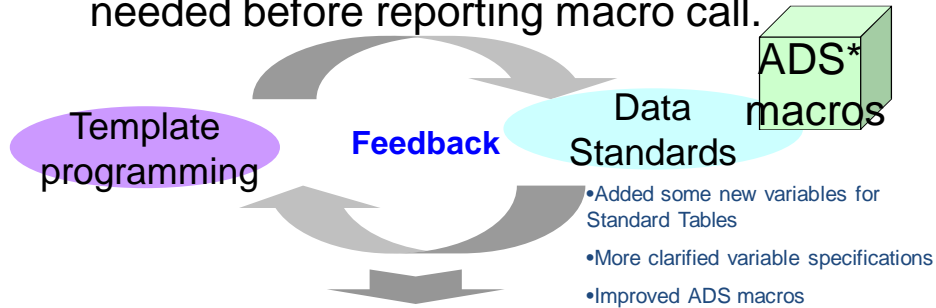
```
proc sort data=pcsa_lb01 out=lb_templateds (keep=lborder _lbtestcd
      lbtest _pcsanrep _pcsairep
      rename=( _lbtestcd=lbtestcd
      _pcsanrep=p_pcsanrep _pcsairep=p_pcsairep));
  by lborder lbtestcd descending _pcsafl _pcsan;
run;
```

Read and understand the reason why the sort is executed here.

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BODY: Data handling

- “One-procedure-away” is ideal.
- But usually some data handling steps was needed before reporting macro call.




Minimization of data handling steps

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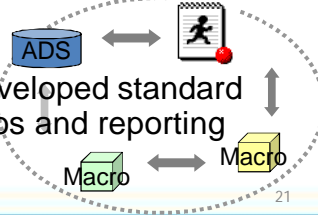
BODY: reporting macro call

- Pre-specify reporting macro parameters in Template programs.
- Users can change the parameters according to <ACTION> and <CAUTION> tags, even if they don't know all the parameters well.

No need to go back to reporting macro manual 

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“TEMPLATE” APPROACH : Summary

- **Flexible**
 - More concise and easier adaptation for study specificities than straight macro coding.
- **User friendly**
 - No manuals for Template programs!  
 - All the information needed for programming is in the Template program.
- **Total Packaging**
 - Harmonization among separately developed standard and tools: ADS standard, ADS macros and reporting macros 

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Standard Statistical Tables & Template programs achieve...

- **Improve performance**
 - In Biostatistics & Programming
 - Template programs can be used in all projects
 - No point “reinventing the wheel”
 - No need to re-program from projects to projects
 - Flexible
 - Minimum adaptation for study specificities
 - In other functions
 - Facilitate review of mock tables
 - No time to spend on these standard tables
- **Improve quality**
 - Validated templates programs
 - Full consistency with clinical templates (protocol template, SAP, CSR)
 - Standard tables reviewed by main functions representatives
- More time to focus on project specificities, efficacy and other ‘new’ challenges (Data surveillance, interactive data exploration, preparation/submission of SDTM to FDA ..)

Full benefice for quality in clinical projects

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Continued Evolution

STANDARD/SPECIFIC tags

- **To evaluate use of standard template programs in projects after release**

- Line “USAGE” in study program header
 - **STANDARD** tag: should be used if template program is used without any modification other than ACTION & CAUTION
 - **SPECIFIC** tag: should be used if user modified some programming lines (other than ACTION & CAUTION) to adapt template program to study specificities

```
* Date completed      : DDMMYYYY
* Modified by        : Date + user name + modifications des
*
* Template program used: STD AP HCT serious.sas (V1.0)
* Usage              : STANDARD/SPECIFIC
*
```

Keep appropriate tag


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AGENDA

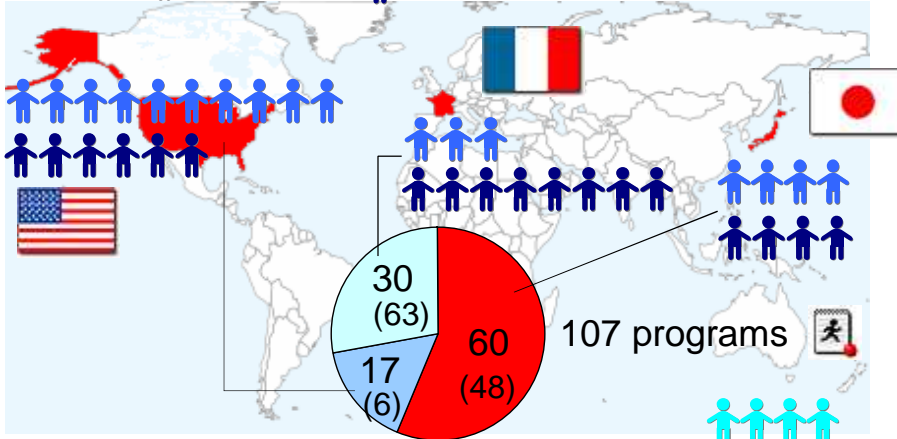
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CROSS REGION DEVELOPMENT TEAM

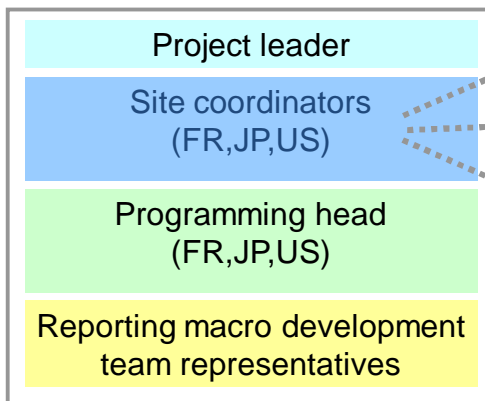
Developer 

Validator 



Reviewers from reporting macro development team

PROGRAMMING of TEMPLATE PROGRAMS WORKING GROUP

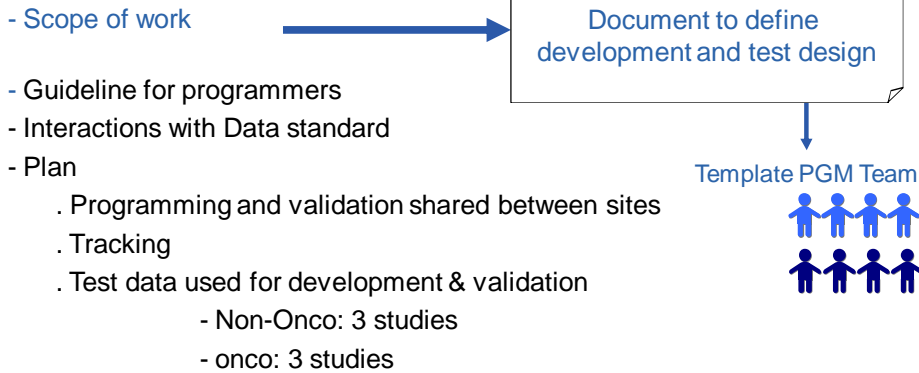


•Site coordinators to organize regular meetings with programmers for information and discuss any issue

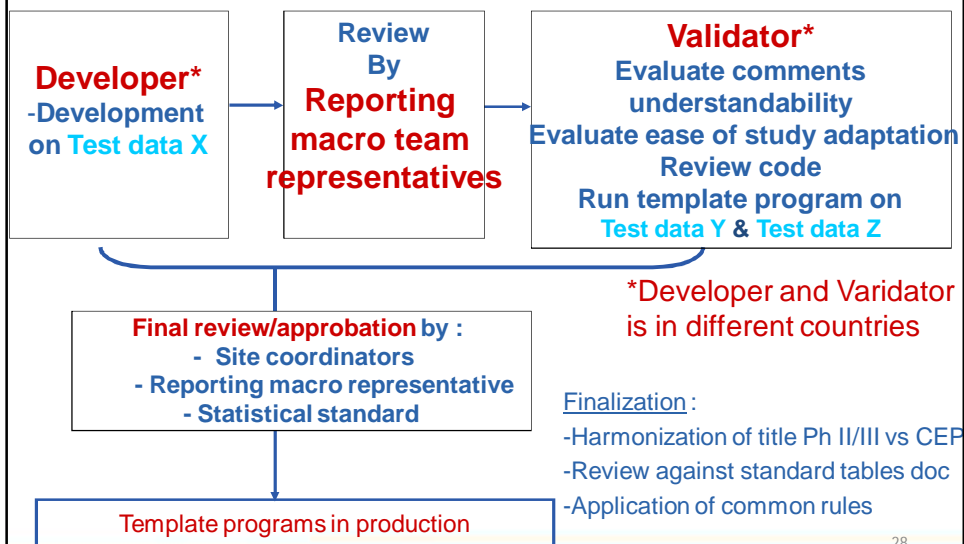


•Site coordinators to conduct regular meetings to ensure homogeneity across countries

Programming of Template Programs Working Group: ORGANIZATION




DEVELOPMENT OF TEMPLATE PROGRAMS



HARMONIZATION AMONG STANDARDS & TOOLS



Interaction with other standards and tools

- Review by Reporting macro development team representatives 
- Data standard and ADS macros were updated in relation to Standard Statistical Tables and Template programs

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HARMONIZATION AMONG COUNTRIES

Developed in 1 site, Validated in another site.

- Programmers had chance to see the variability of programs among site:

Coding Style

The extent to which the use of tools (Reporting macro and ADS macro)

Communication among countries

Interaction with other standards and tools



Coding Rule

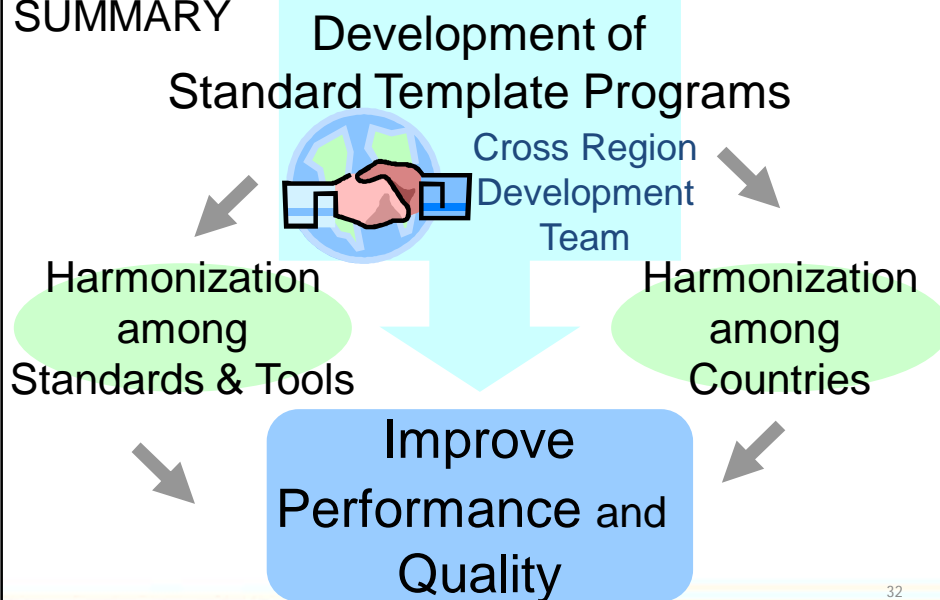
Appropriate use of tools

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CROSS REGION DEVELOPMENT

- Frequent communication for difficult problems were needed.
- ↓
- Improve communication skill and mindset of Japanese members
 - Awareness of cultural difference
 - Communication style
 - Point of focus differs among country
 - Confidence to take initiative in global standard activity

SUMMARY



Acknowledgement

- Many thanks to...
 - Laurence Le Lann - Project leader
 - Yvane Boudraa - Programming Head in FR
 - Mei Wu - Programming Head in US
 - Patrice Sevestre - Site coordinator in FR
 - James Wu - Site coordinator in US
 - Eric Sun – GStars (Reporting macro) representative
 - Many programmers, statisticians, GStars members
and SuSADs (ADS macro) members in FR,US and JP