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GUIDELINES FOR THE DEVELOPMENT AND VALIDATION OF SPREADSHEETS

AGIT

November 17, 2010



Outline of the presentation

- Scope and Definitions
 - Regulatory Requirements
 - Development
 - Qualification and Release
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- Different approaches possible, as long as compliant
 - Specials for Spreadsheets only, bases on AGIT Guidelines for the Validation of Computerised Systems



Scope

- Guidance on GLP-compliant development and validation of spreadsheets
- Spreadsheets with data from GLP study
- Data are processed by calculations, transformations, Visual Basic for Applications (VBA) including recorded macros, and add-ins
- spreadsheets may contain electronic raw data



Definitions

- Tabulating spreadsheets
 - Lists: inventory, master schedule
 - Do not contain raw data

Out of
scope

- Processing
 - Raw data generated by computerized system and transferred into spreadsheet for processing
 - Raw data captured in spreadsheet, and further processing

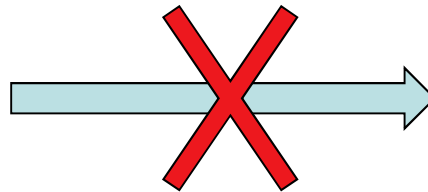
- Single use calculation sheets

Out of
scope



Single use calculation sheets

- Single-use calculation spreadsheets
 - no validation
 - need QC check on completion



Single use
Checked individually

Routine use
Validated
checks according SOP



Regulatory Requirements

- Validation of computerised systems required by OECD Principles of GLP + Swiss Ordinance on GLP
- OECD GLP Consensus Document No. 10 defines requirements for the operation of computerised systems in a GLP regulated environment
- Validation is *the demonstration that a computerised system is suitable for its intended purpose*
- Validation process provides a high degree of assurance that a computerised system meets its pre-determined specifications



Validation Approach

- Validation process (user requirements, risk assessments, specifications, planning, testing, reporting), the assignment of responsibilities, proper validation documentation, and rules for archiving and change management processes
- Simplified, but systematic approach: steps can be summarised
- Extent of the validation depends on risk analysis



User requirements

Practical example: pipette qualification

- **URS-1.** The spreadsheet should be applicable for volumes from 0.01 to 10 mL
- **URS-2.** The spreadsheet should only accept a sample number of 10
- **URS-3.** The spreadsheet should calculate the mean, standard deviation (SD) and relative SD ($RSD = (SD/average) \times 100\%$) of the 10 samples
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User requirements

- **URS-21.** The calculations in the spreadsheet should be protected against unauthorised modifications
- **URS-22.** After completion of the measurement, the spreadsheet should be initialled and dated electronically by the user
- **URS-23.** Making changes to the spreadsheet (modification/deletion) after signing off (initials/date) should not be possible
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Design

Pipette (Inventory Number)	AQ76	Result		Decision criteria	
Nominal Value (ml)	10.00			Max Delta	% 1.0 according to SOP
Measurements Sample		g	ml	RSD	% 1.0 according to SOP
	1	10.0600	10.01	9.983	
	2	9.9999	0.02	0.02	
	3	10.0010	0.2	0.2	Nominal Value ml 10.00 calculated
	4	9.9996	Density @ 23 °C is 0.997538		Max Delta ml 0.10 calculated
	5	10.0000	Accuracy	ok	Temperature deg. C
	6	10.0230	RSD	ok	Density g/ml
	7	9.9919			20 0.998203
	8	10.0002			21 0.997992
	9	9.9999			22 0.99777
10	9.9998			23 0.997538	
Temperature (°C)	23	Date/Time	Operator	24 0.997296	25 0.997044
Enter/Save	Temperature Please enter the temperature as a whole number between 20-25°C				Version 1.00



Design

- Input and output areas separated
- Calculations, constants and parameters cannot be changed by the user (locked cells)
- A blank template is used. Avoid use of “master copies” with typical data
- The template is password-protected (at sheet, workbook and VBA code level)
- Define where the productive template is stored. Adapt file paths for automatic opening or saving of files and security settings



Development testing

- Systematic Testing of URS
- Code review two persons, checking content of cells:
 - formulas and formula locations
 - cell numbers and ranges
 - syntax of additional functionality
 - VBA code
- Formula view, auditing tool view, VBA code
- Documentation

- Release for Qualification



Installation Qualification (IQ)

- Template stored on a server
(controlled environment)
- Use of a document management system
- Automatic access to raw data files
- Use on different hardware/software versions



Operational Qualification (OQ)

- Tests with different and independent data
- Inputs leading to unacceptable/impossible results
- Security aspects

Test relating to URS:	Test	Test result/acceptance criteria
URS-7	Enter "q" as weight in the sample 1 field.	The error message "Please enter a weight in grams!" appears.
URS-7	Enter "q" as temperature in the temperature field.	The error message "Please enter a temperature between 20 and 25°C!" appears.
URS-21	Place the cursor in cell E4 and press "Delete" to erase the content of the cell.	The error message "The cell or chart you are trying to change is protected and therefore read-only" appears.



Performance Qualification (PQ)

- The aim of this final qualification phase is to demonstrate that the spreadsheet meets the initially formulated user requirements, in the user's environment.
- The typical use cases should be run under everyday conditions, by the future user.
- PQ is an internal acceptance test.

Test relating to URS:	Test	Test result/acceptance criteria
URS-3, URS-6	Enter "A1" in the Pipette (Inventory Number) field, "10" for the Nominal Value (ml) and "22" for the Temperature (°C). Enter the following values for samples 1–10: 9.98, 9.98, 9.99, 9.99, 10, 10, 10.01, 10.01, 10.02, 10.02	Results: mean 10 g, SD 0.015, RSD % 0.15, Accuracy ok, RSD ok



Release

- Release by Test Facility Management after
 - Validation Report approved by Validation director
 - Availability of SOPs
 - Documentation of User training



Change Management

- Upon proposed change, perform a risk assessment and determine the amount of testing
 - No risk: change of constants
 - Risk: extension of Temperature range
- After successful testing, formal release
- Archiving, version control, distribution, SOP update and training



Bonus material

- Annex with screenshots
 - Error messages
 - User management
 - VBA code
- Excel file with full functionality will be published on the AGIT web site in www.glp.admin.ch
- Submitted to Quality Assurance Journal



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