OMCL Network of the Council of Europe
QUALITY ASSURANCE DOCUMENT

PA/PH/OMCL (08) 87 2R

VALIDATION OF COMPUTERISED SYSTEMS

ANNEX 1: VALIDATION OF COMPUTERISED CALCULATION SYSTEMS: EXAMPLE OF VALIDATION OF IN-HOUSE SOFTWARE

Full document title and reference	Validation of Computerised Systems Annex 1: Validation of computerised calculation systems: example of validation of in-house software PA/PH/OMCL (08) 87 2R
Document type	Guideline
Legislative basis	-
Date of first adoption	May 2009
Date of original entry into force	July 2009
Date of entry into force of revised document	-
Previous titles/other references	-
Custodian Organisation	The present document was elaborated by the OMCL Network/EDQM of the Council of Europe
Concerned Network	GEON

**ANNEX 1 OF THE OMCL NETWORK GUIDELINE
"VALIDATION OF COMPUTERISED SYSTEMS"**

VALIDATION OF COMPUTERISED CALCULATION SYSTEMS

EXAMPLE OF VALIDATION OF IN-HOUSE SOFTWARE

INTRODUCTION

The present document is the 1st Annex of the core document "Validation of Computerised Systems", and it should be used in combination with it when planning, performing and documenting the validation process of computerised systems.

The core document contains the Introduction, Scope and general requirements for the validation of different types of computerised systems.
This Annex presents an example of Excel$^{®}$ spreadsheet validation, which is to be used in combination with the general recommendations given in the core document.

This document should be considered as a guide to OMCLs for planning, performing and documenting the validation of their computerised systems. It should not be taken as a list of compulsory requirements. It is left to the professional judgement and background experience of each OMCL to decide on the most relevant procedures to be undertaken in order to give evidence that their computerised systems are working properly and are appropriate for their intended use.

1. SOFTWARE PRESENTATION AND GENERAL INFORMATION

This software's aim is to calculate a vaccine titration (Figure 1). From results obtained for a reference product (height measured at 4 concentrations), a calibration curve and its formula are provided. Both of them are needed to calculate the concentrations corresponding to the height measured for the tested vaccine.

In Figure 1, grey cells are filled with numerical data from experimentation and are the only ones that can be changed by the operator. All cells including formula are locked. No more than one cell from the calibration range can be empty; all cells for vaccines must be filled to guarantee proper use.
To access the software, a password is needed to log on the computer.

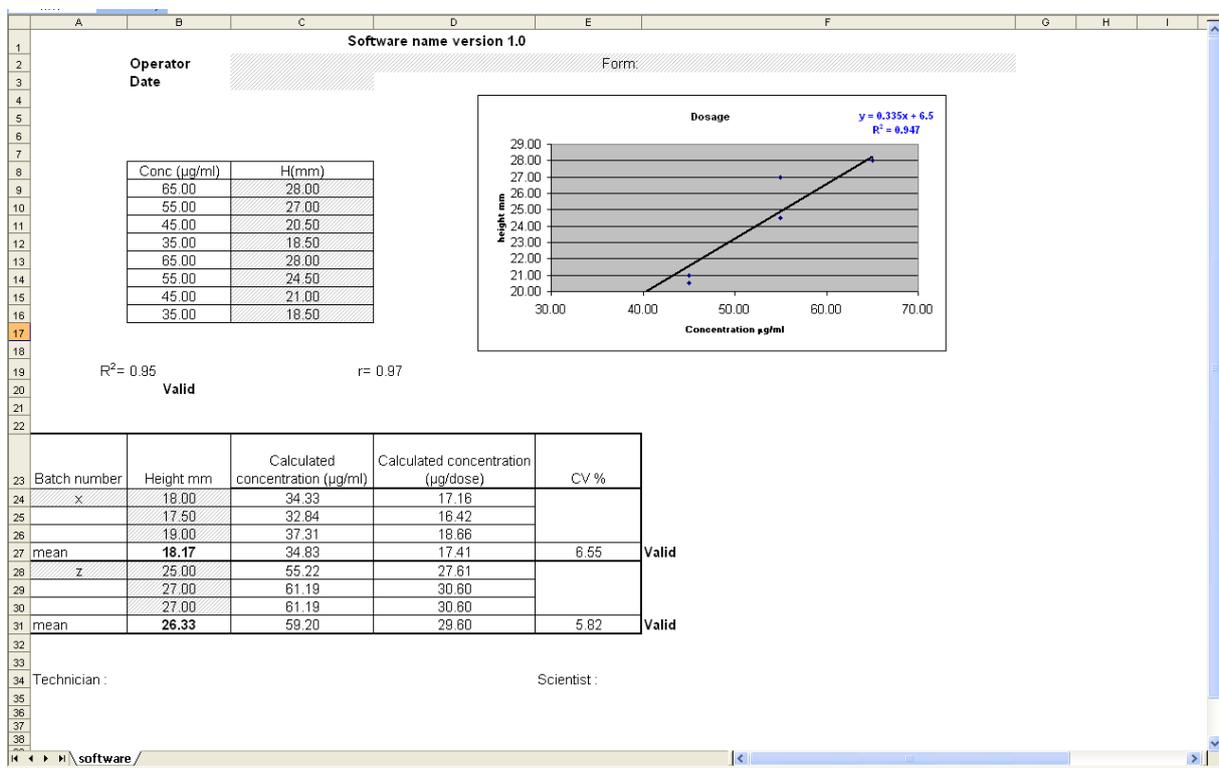Back ups are regularly performed to ensure original files preserving.

Figure 1. Software presentation

2. VALIDATION STAGES

The different stages of the validation are:
2.1   Printing of formulas
2.2   Validation of the calculations
2.3   Validation certificate
2.4   Software installation and documentation

2.1 Printing of formulas

In order to validate the Excel® spreadsheet, formulas are printed, and the print is kept in the software validation file (Figures 2.1 and 2.2).

Figure 2.1. Printed formulas of the software

Figure 2.2. Printed formulas of the software (Cont.)

2.2 Validation of the calculations

All calculations are verified with a system completely independent from the self developed software. One part of the recalculation is performed by validation versus a commercial software, the other part with a pocket calculator.

2.2.1 Validation of the calculations versus commercial software

Then, a dataset as close to real values as possible is chosen (Figure 1). Excel® calculations are compared to the results given by commercial software, since it is considered as validated (Figure 3). The commercial software provides the coefficient of correlation, R^2 and the coefficients of the calibration curve. As no discrepancy occurs, the validation of this part of calculation is considered as fulfilled.

```
Regression Analysis - Linear model: Y = a + b*X
---------------------------------------------------------------------------
Dependent variable: H
Independent variable: Conc
---------------------------------------------------------------------------
                                    Standard           T
Parameter          Estimate          Error        Statistic        P-Value
---------------------------------------------------------------------------
Intercept             6.5           1.6569         3.92299          0.0078
Slope                0.335        0.0323393        10.3589          0.0000
---------------------------------------------------------------------------


                          Analysis of Variance
---------------------------------------------------------------------------
Source            Sum of Squares   Df  Mean Square   F-Ratio       P-Value
---------------------------------------------------------------------------
Model                 112.225       1    112.225     107.31        0.0000
Residual                6.275       6    1.04583
---------------------------------------------------------------------------
Total (Corr.)         118.5         7

Correlation Coefficient = 0.973163
R-squared = 94.7046 percent
Standard Error of Est. = 1.02266


The StatAdvisor
---------------
   The output shows the results of fitting a linear model to describe
the relationship between H and Conc.  The equation of the fitted model
is

   H = 6.5 + 0.335*Conc

Since the P-value in the ANOVA table is less than 0.01, there is a
statistically significant relationship between H and Conc at the 99%
confidence level.

   The R-Squared statistic indicates that the model as fitted explains
94.7046% of the variability in H.  The correlation coefficient equals
0.973163, indicating a relatively strong relationship between the
variables.  The standard error of the estimate shows the standard
deviation of the residuals to be 1.02266.  This value can be used to
construct prediction limits for new observations by selecting the
Forecasts option from the text menu.
```

Figure 3. Commercial software results

2.2.2 Validation of the calculations with a pocket calculator (Manual calculations)

Concerning the other calculations, from printed formula from the spreadsheet, concentrations are calculated using a pocket calculator (Figure 4) and then compared to the results of Figure 1. As no discrepancy occurs, the validation of this part of calculation is considered as fulfilled.

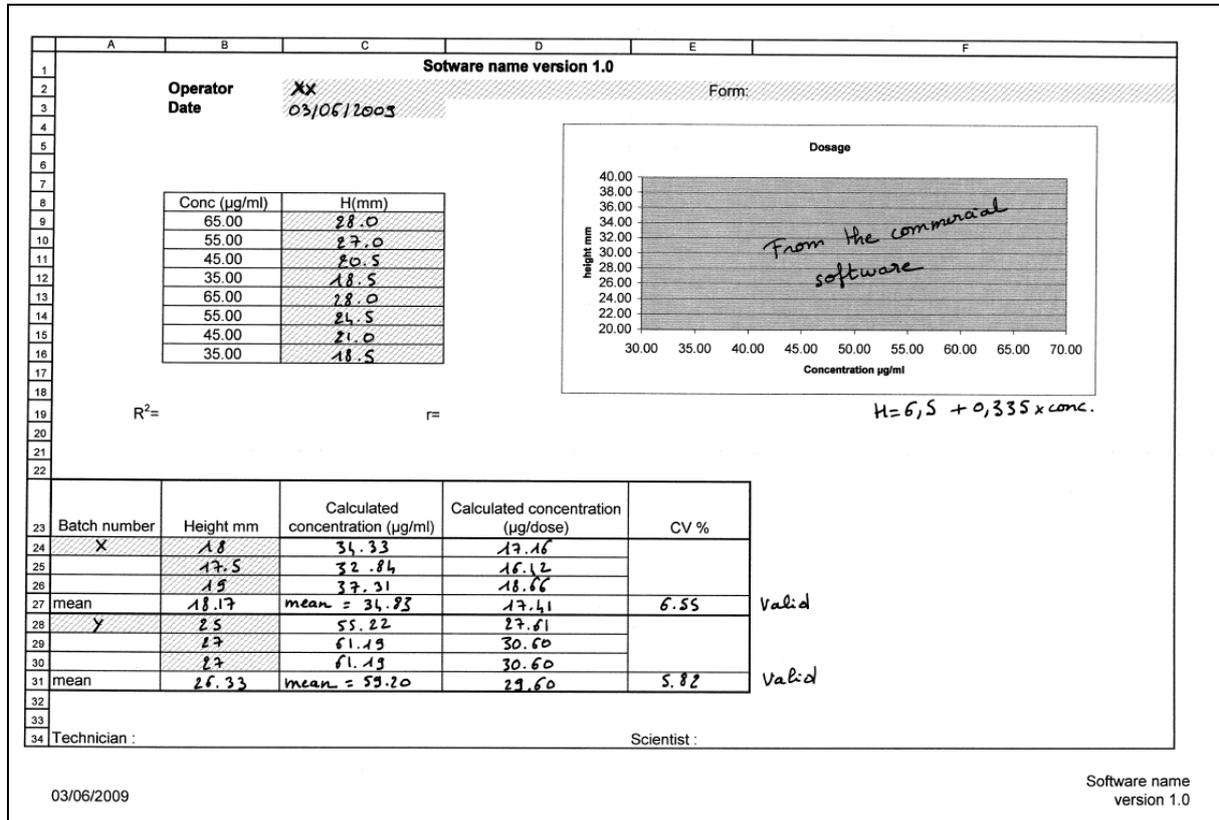**Figure 4. Manual validation**

Moreover, calculations in paragraph 2.2.1 and 2.2.2 are re-performed with other datasets including exceptional situations, as for example: OOS-results, missing data, or nonsense-data. Calculations are also validated under these conditions (data not shown).

At this stage, the software is considered as validated.
To ensure traceability of validation a certificate is emitted.

2.3 Validation certificate

As the software is validated, a certificate of validation is provided. It includes the name and the version of the software, the date of validation, the person responsible for the validation, the person responsible for the release for use of the software and their signatures. This document (Figure 5) is kept in the software documentation.

Name of the control laboratory

| Certificate of software validation |

Name of the software:

Validated version:

Date of validation:

Person responsible for the validation:

Person responsible for the release for use of the software:

Conclusion of validation:

Date and signature of person responsible for the validation

Date and signature of person responsible for the release for use of the software

Figure 5. Certificate of software validation

Comment: This certificate is an example of the formalisation of the validation. Alternatively, a Quality Assurance form could be used**.**
Moreover, the person responsible for the validation can be the same as the one responsible for the release for use of the software.

2.4   Software installation and documentation

The concrete installation is completed after validation of the software. The operator signs the life form to attest its proper installation. This form, which actually is a QA document, includes the name of the software, unique identification, localisation, and person responsible for the software. It includes also verification and other specification as updates or any problem encountered (Figure 6). Verification is completed after installation and reported in the life form.

Life Form		Name of the software		Form number
Unique identification:			Manufacturer:	
			Localization:	
			Person responsible for the software:	

Date	Encountered problem	Intervention	Comment Next intervention	Operator	Signature of the person responsible for the software
30/04/2009		Installation		XC	✕
30/04/2009		Verification	Next verification 30/10/2009	XC	✕

AQ number : ELYO/XXX Version Y 30/01/2007

Validated by ZZZ

QA Manager registration

Figure 6. Life Form

Comment:
Another way to secure this Excel spreadsheet would have been to install the software on a network-drive with restricted access. Only authorised staff would be able to write on this drive. The user would have no right to save data or spreadsheets and would have only the right to fill the (permitted) cells and to print the data.

3. REGULAR VERIFICATION OF THE SOFTWARE

Regularly (for example, every 6 months) or after every change performed in the soft- or hardware configuration, the software is checked to be sure that results have not changed. A known dataset is used and the results are compared to the standard one (Figure 1).

In order to help the operator, verification instructions with required information have been written (Figure 7).
Results from the verification are printed, dated, signed and kept with the life form.
Each verification is registered in the life form (Figure 6) with the following information: Date of operation, intervention (i.e. verification), comments, and operator's signature.

Comments:
In case of an installation on a network drive with restricted access (cf. comment in chapter 2.5), the regular verification would be optional.
The check could have included the verification if the save date of the software is still the same as after original installation.

Verification instructions

This document provides instructions for the periodic review of the software described below.

Localisation of the original file: C:\Name of the software\name.xls

Verification: All grey cells must be completed and compared to the template below.

- **Information**: Name of the operator, form number and date of verification.

- **Reference product data**: Heights.

- **Vaccine data**: Batch number and heights for the two batches.

Results: Print, date, sign and keep the results in the software file.

Life form: Register your verification in the software life form.
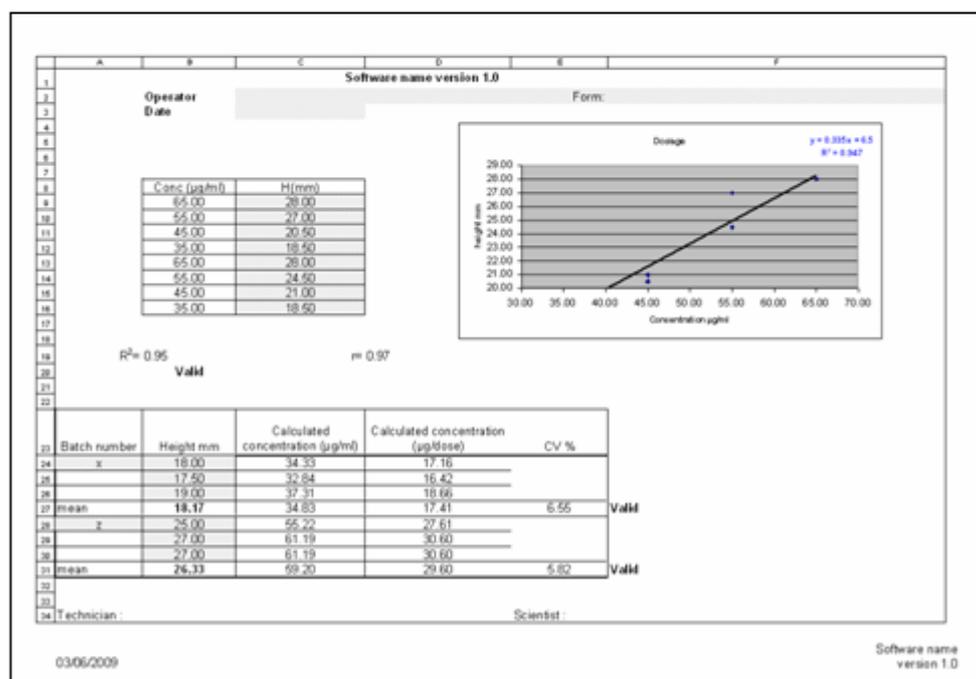

Figure 7. Verification instructions

4. SPECIFIC DOCUMENTATION

According to the guideline, in-house software should be completed with the following specific documentation. The correspondence between the guideline table and each information/documentation of the validation of this Excel® software (Specific documents and Figures) is indicated below:

Information/documentation that should be available	In-house	Specific documents	Figures
Name, version and unique identification of the software	X	Life form and printings	Figure 6
Original files (CD-ROM…) or storage location to install the software and software to manage the computer environment	X	Backup of the software on the network	
Date at which the software was put into operation	X	Life form	Figure 6
Current physical location, where appropriate	X	Life form	Figure 6
Responsible person in charge of the software	X	Life form	Figure 6
Conditions under which the software runs, where applicable (hardware, operating system,…)	X	Not applicable	
Name of the person who developed and validated the software, and the date of validation	X	Validation certificate	Figure 5
Source code (if available)	X	Printing of formulas	Figures 2.1 and 2.2
Operating rules, where appropriate	X	Not appropriate	
Documentation on software regular verification	X	Life form Verification instructions	Figures 6 and 7
Documentation on software validation	X	Software validation file	Figures 1, 2.1, 2.2, 3, 4 and 5
Follow-up of encountered failures, maintenance of the process, updated versions and, where appropriate, configuration management	X	Life form	Figure 6