# Guidance for Method Validation in Chemical Analysis

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## ABSTRACT

Guidance for method validation in chemical analysis documentation of Division of Cosmetics and Hazardous Substances was prepared in 1995 when the first chemical test was granted for ISO/IEC Guide 25 accreditation. Current revision of the guidelines documentation i.e. standard operating procedure SOP 06-13-002 (Method Validation for Formulation Analysis), was issued in 2008, which covers and be useful for chemical analysis laboratories within the Division of Cosmetics and Hazardous Substances, especially quantitative analysis of formulated products.

The SOP provides step-by-step single-laboratory validation procedure, together with three worksheets, which are WS 06-13-001 (Method Review and Planning for Method Validation), WS 06-13-002 (Validation Data) and WS 06-13-003 (Report of Method Validation).

The procedures details about validation parameter and statistic techniques. The parameters cover specificity/ selectivity, linearity and working range, percent recovery, precision (repeatability and intermediate precision), limit of detection, limit of quantitation and estimation of measurement uncertainty from validation data. Details in the SOP are based on EURACHEM Guide, 1998, DTI VAM Program : In-house method validation 2004, IUPAC Technical Report 2002, CIPAC 3807 and A Pactical Guide for Single Laboratory Method Validation of Chemical Methods, Department of Medical Sciences 2006. The SOP is intended as a dynamic document and they will expand to cover of more worked examples for various techniques performed in the laboratories.

## INTRODUCTION

The chemical testing laboratory of Division of Cosmetics and Hazardous Substances has been accredited for ISO/IEC Guide 25 accreditation since 1995. The accreditation has been extended in chemical testing for almost 80 tests covering both hazardous substances use in public health products and cosmetic products. Method validation is therefore an essential component of the measures that a laboratory should implement to allow it to produce reliable analytical data. Guidance on the single-laboratory validation of method in chemical analysis documentation was prepared as in-house standard operating procedure in 1995 and the current guideline is SOP 06-13-002 (Method Validation for Formulation Analysis), issued in 2008.

The present SOP being together the essential scientific principles to point the way forward for best practice in single-laboratory method validation for chemical testing laboratories within the Division of Cosmetics and Hazardous Substances. The SOP is applicable for method modified from standard method, method has been published in the scientific literature together with some analytical characteristics or with no characteristic given, validated method but new matrix to be used and method has been developed in-house. The SOP illustrate the require performance criteria for the analytical method applied in the laboratories and provide procedures for method validation in order to estimate the method performance characteristics.

## STUDY OF METHOD PERFORMANCE CHARACTERISTIC

Table 1. Performance parameters required for validation of different type of analysis

| Parameter | Type of analysis | | |
|---|---|---|---|
| | Qualitative | Quantitative | |
| | | Major component | Trace analysis |
| 1. Specificity/selectivity | | ✓ | ✓ |
| 2. Linearity and Working range | ✓ | ✓ | ✓ |
| 3. Percent recovery | | ✓ | ✓ |
| 4. Precision | | ✓ | ✓ |
| 5. Limit of detection | ✓ | | ✓ |
| 6. Limit of quantitation | | | ✓ |

Table 2. Requirement for study of method performance characteristics

| Parameter | Procedure | Acceptable criteria |
|---|---|---|
| 1. Specificity/selectivity | test for interferent that are likely to respond to the test e.g. determination by execution of the procedure on a matrix blank and the same blank spiked with the potential interferent | interferent does not impact the results |

## OBJECTIVE

To provide guidance for chemical analysis laboratory in the Division of Cosmetics and Hazardous Substances in order that test results produce is reliable, credible and traceable.

Table 2 Requirement for study of method performance characteristics (cont.)

| Parameter | Procedure | Acceptable criteria |
|---|---|---|
| 2. Linearity and working range | Construct a calibration curve by fitting with simple linear regression between concentration of six or more (which should be run at least in duplicate) calibration standards and their responses.<br>- Construct a linear regression between added found amount of analyte in spiked sample<br>- Test for general matrix effect by "standard additions" to a test solution derived from a typical test material. The range of addition should encompass the same range as the calibration solutions. | Correlation coefficient (r ) should be close to 1 |
| 3. Percent recovery | Use of spiked sample and analyze by the method under validation both in its original state and after spiking of a known mass of the analyte to the test portion. | Percent recovery should be within acceptable ranges e.g.<br>% w/w Analyte — Acceptable %recovery<br>100 — 95-105<br>10-<100 — 90-110<br>1-<10 — 90-110<br>0.1-<1 — 85-115<br>0.01-<0.1 — 80-120<br>0.001-<0.01 — 75-125<br>0.0001-<0.001 — 70-130 |
| 4. Precision | | |
| 4.1 Repeatability | Minimum of 7 replicates sample determinations under repeatability condition, using method under validation | % relative standard deviation (RSD) should not exceed expected %RSD based on the Horwitz equation e.g.<br>%w/w Analyte — Acceptable % rsd<br>100 — 1.3<br>10-<100 — 1.8<br>1-<10 — 2.6<br>0.1-<1 — 3.7<br>0.01-<0.1 — 5.3<br>0.001-<0.01 — 7.5 |
| 4.2 Intermediate precision | Replicate analyses of the same sample under different measurement conditions e.g. between-day, between-analyst | Analysis of variance (ANOVA), *p*-value ≥ 0.05 |
| 5. Limit of Detection | Analysis of blank and low level spiked sample. Limit of detection could be estimated by various ways. Experiment using spiked sample at estimated concentration should be carried out. | The lowest concentration of analyte in a sample that can be detected under the stated conditions of the test. |
| 6. Limit of Quantitation | Analysis of sample with known lowest concentration of analyte which can be quantified or reported with acceptable precision and accuracy under the stated conditions of the test | %RSD and %recovery should be within acceptable range |

## EVALUATING MEASUREMENT UNCERTAINTY

Knowledge of measurement uncertainty is necessary for the effective comparison of measurements. It is considered to be an essential part of good measurement practice and need to be evaluated as part of method of method validation.

## CONCLUSION

The results from validation experiments and information from other sources needs to be evaluated in order to ensure that the method meets the measurement requirement specification.

When the method is used on a regular basis, periodic measurement of QC samples and the plotting of these data on QC charts is required. Method validation provides information concerning the method's performance capabilities and limitations, when applied under routine circumstances and when it is within statistical control and can be used to set QC limits.

A detailed description of the method and records of the validation study facilitates the consistent application of the method, within the scope and defined performance parameters. Documentation is also required for quality assurance and regulatory purpose.