

# ***Quality Assurance of Chemical Measurements, Metrological or Management Effort***

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## *Confidence in analytical reports*

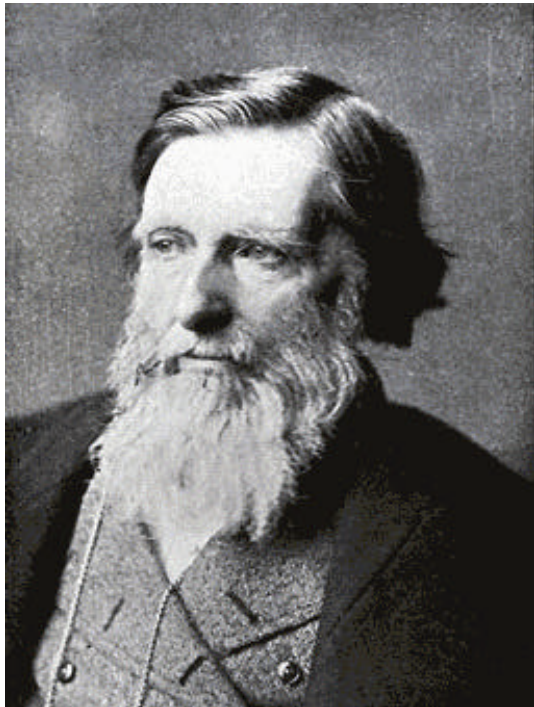
- Results of chemical analysis are very important factors for correct decision-making.
- Users need to be sure about the reported values.
- Analysts have to demonstrate the quality of their work in order to get confidence in community.

## *Analytical measurements*

- Reliable analytical result is not an easy request today.
- But it was not easy also forty or more years ago, when analysts had no sophisticated instruments, computers, and metrological standards. But analytical results were sound and decisions were correct.

**Where was the miracle?**

*John Ruskin (1819-1900)*



Quality is never an accident.  
It is always the result of intelligent  
effort.

There must be the will to produce  
a superior thing.

## *Analytical measurements*

### **The answer is simple.**

- In that time, analyst had to be familiar with analytical management.
- Analytical knowledge was oriented towards understanding and on-line elimination of sample uncertainty and not into formalistic solutions of measurement uncertainty that are so popular today.

## *John Keenan Taylor (1913-1992)*

*“Quality is a subjective term.*

*What is a high quality in one situation may be a low or unacceptable quality in another case.*

*Clearly the tolerable **limits** of error must **be established** for **each** case.*

*Along with this there must be a clear understanding of the measurement process and its capability to provide the results desired.”*

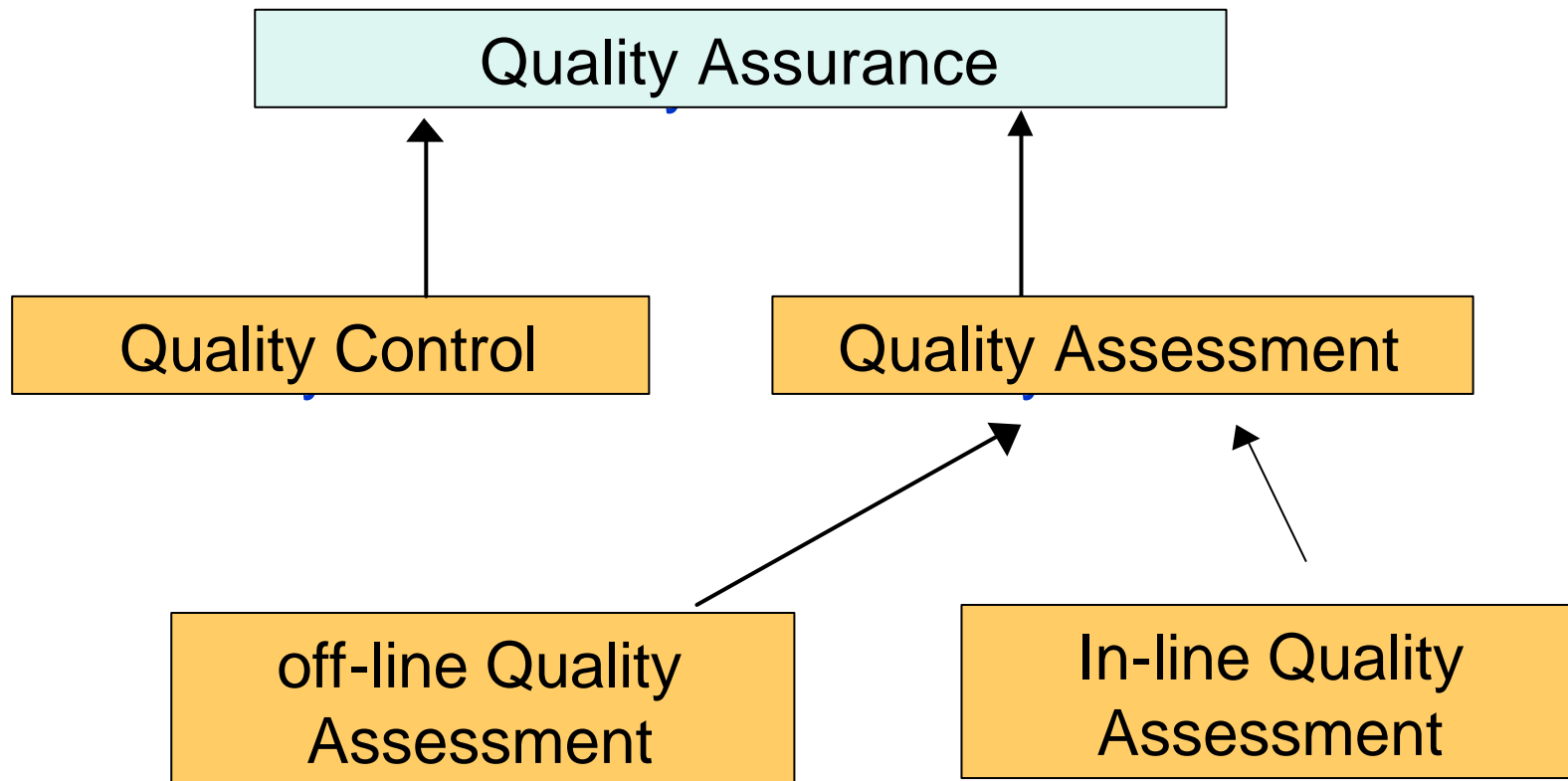


*John Keenan Taylor*

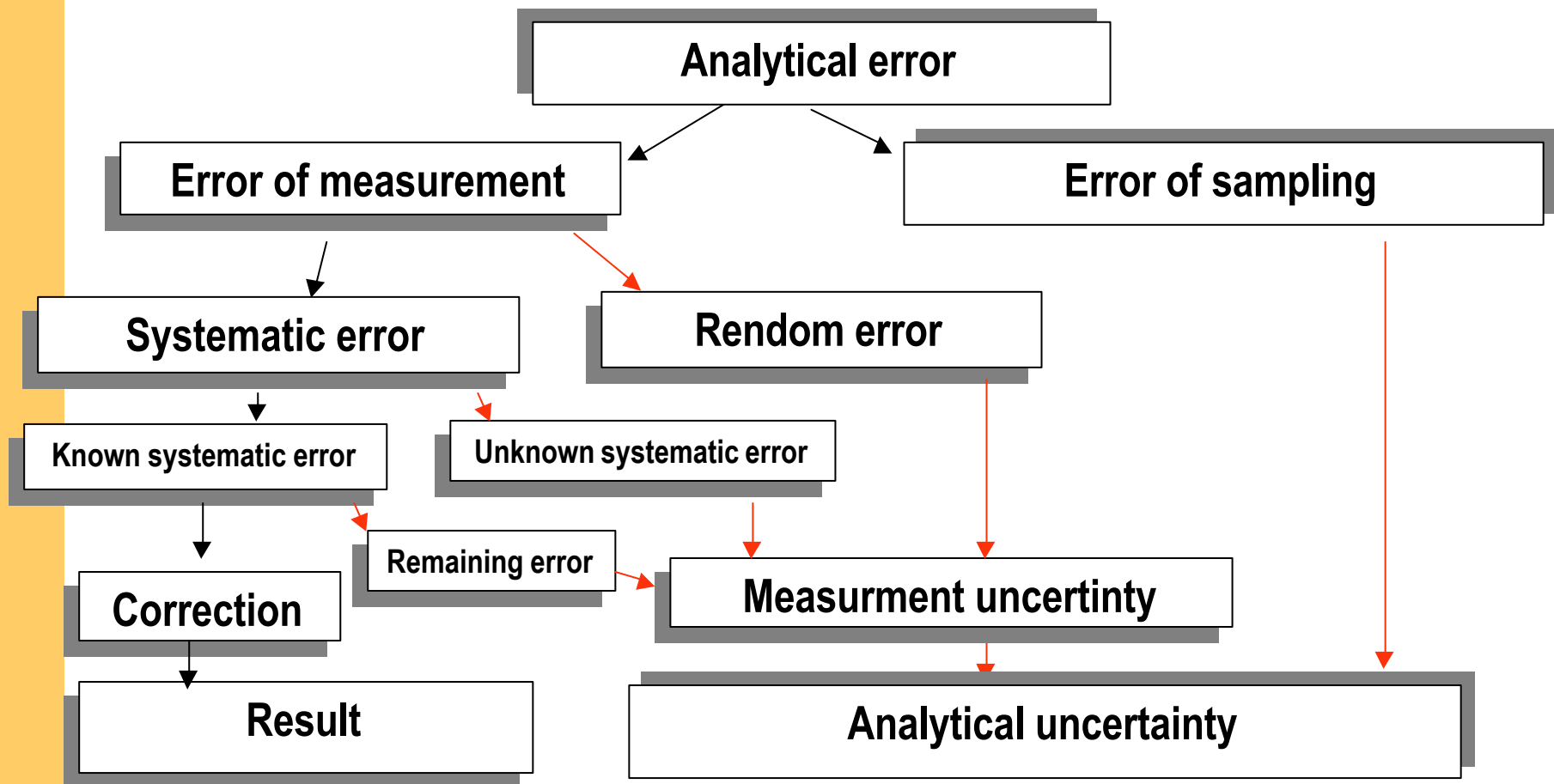
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*“**The objective** of quality assurance programs for analytical measurements is;  
**to reduce** measurements errors to tolerable limits,  
**to provide** a means of ensuring that  
the measurements generated **have a high probability**  
of acceptable quality.”*

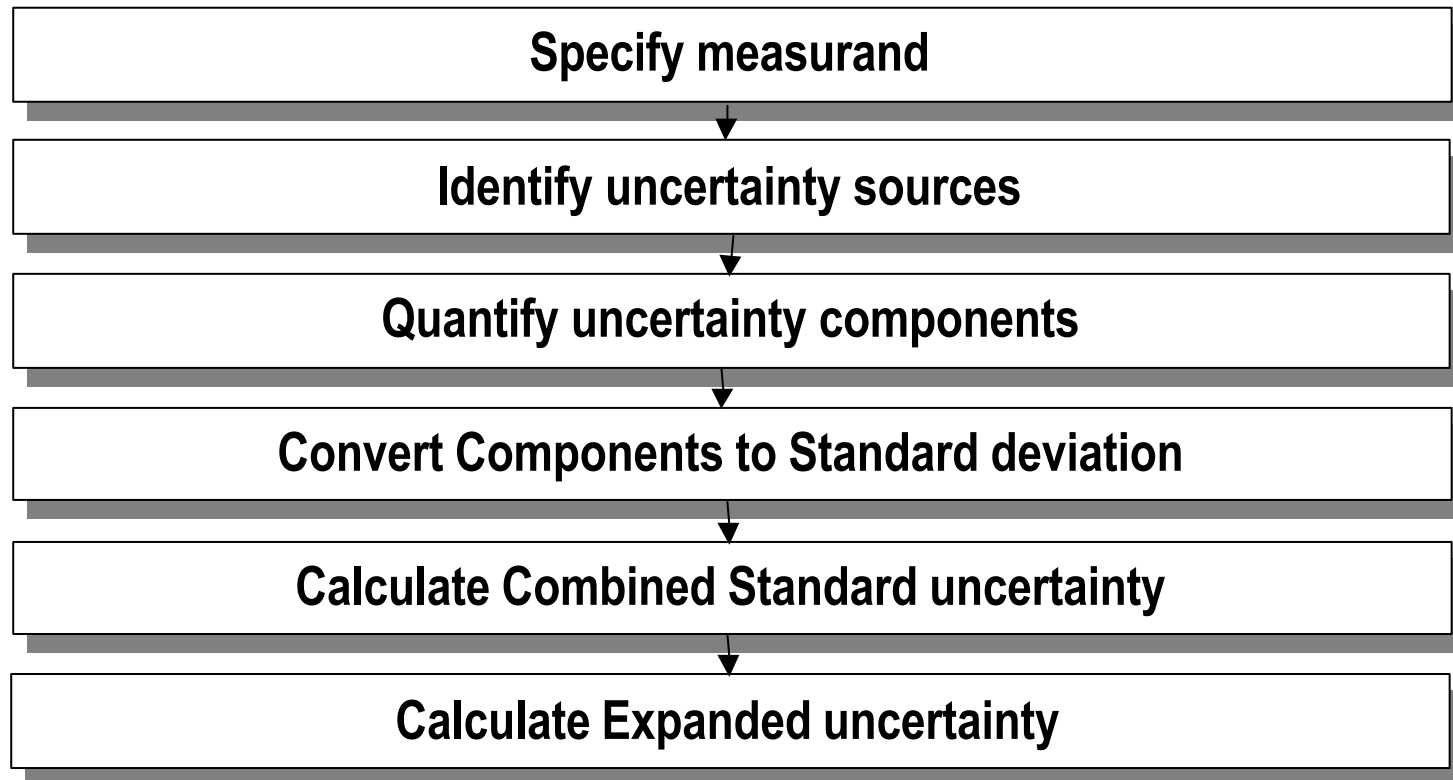
# Quality Assurance



# Analytical uncertainty



## *Uncertainty estimation process*



## *Quality Assurance in practice*

- From the “chemical approach” which based on the idea that a quality assurance in an analytical laboratory was a product of two closely related tasks - **the quality control** and **the quality assessment**
- We have now arrived to the “physical approach” which base on metrological parameters such as **traceability** and **measuring uncertainty**.

## *Quality Assurance in Practice*

The more precisely the measurement is determined, the less precisely the sample concentration is known.

$$s_A^2 = s_M^2 + s_S^2$$

$$\Delta s_M \Delta s_S \geq f_{(\text{sample})}$$

Obviously the analytical uncertainty has a minimum, which is a function of a sample.

This minimum can be achieved only with adequate analytical management.

## Heisenberg, uncertainty paper, 1927

The more precisely the position is determined, the less precisely the momentum is known in this instant, and vice

versa

$$\Delta p \Delta q \geq h / 4\pi$$

$$\Delta E \Delta t \geq h / 4\pi$$

canonically conjugate variables

## *Quality Assurance in Practice*

- Metrology and standardization create a solid base for reliable measurements,
- This is not sufficient for reliable chemical analysis.
- Only validated analytical procedures promise reliable results.
- Analytical management minimize analytical uncertainty.
- The will “to do”, improves the quality in analytical chemistry.

## *Evaluation of analytical uncertainty with an experiment*

In order to show that  
**quality assurance** in chemical analytical laboratory  
**primarily depends** on correct **scientific-based**  
**analytical management** and only on the **second level** it  
depends on **metrological parameters**

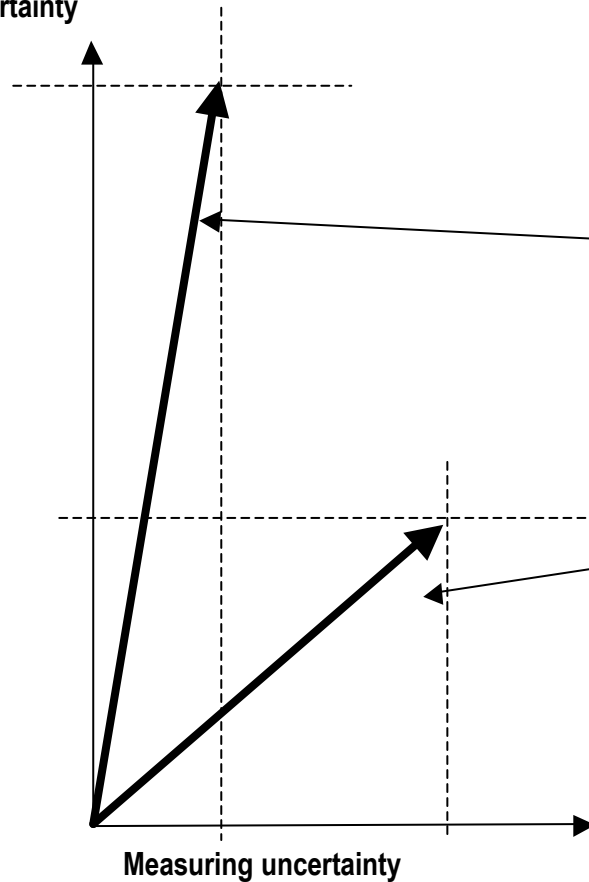
we carried out some new experiments  
based on more and more popular cleaning validations.

## *Sample uncertainty*

- Prepared experiments and calculations show how important is analytical management for reliable results.
- Selection of measurement uncertainty has second priority.
- Method with measurement uncertainty of 10% (expressed as RSD) is normally rejected;
- Meanwhile the sample uncertainty of 50% or more is normally tolerated or worse not recognised.

# Analytical uncertainty

Sample uncertainty



## Analytical uncertainty

$$s_0^2 = s_M^2 + s_S^2$$

### HPLC

Measuring uncertainty = 2.00 %

Sample uncertainty = 16.00 %

Analytical uncertainty = 16.12 %

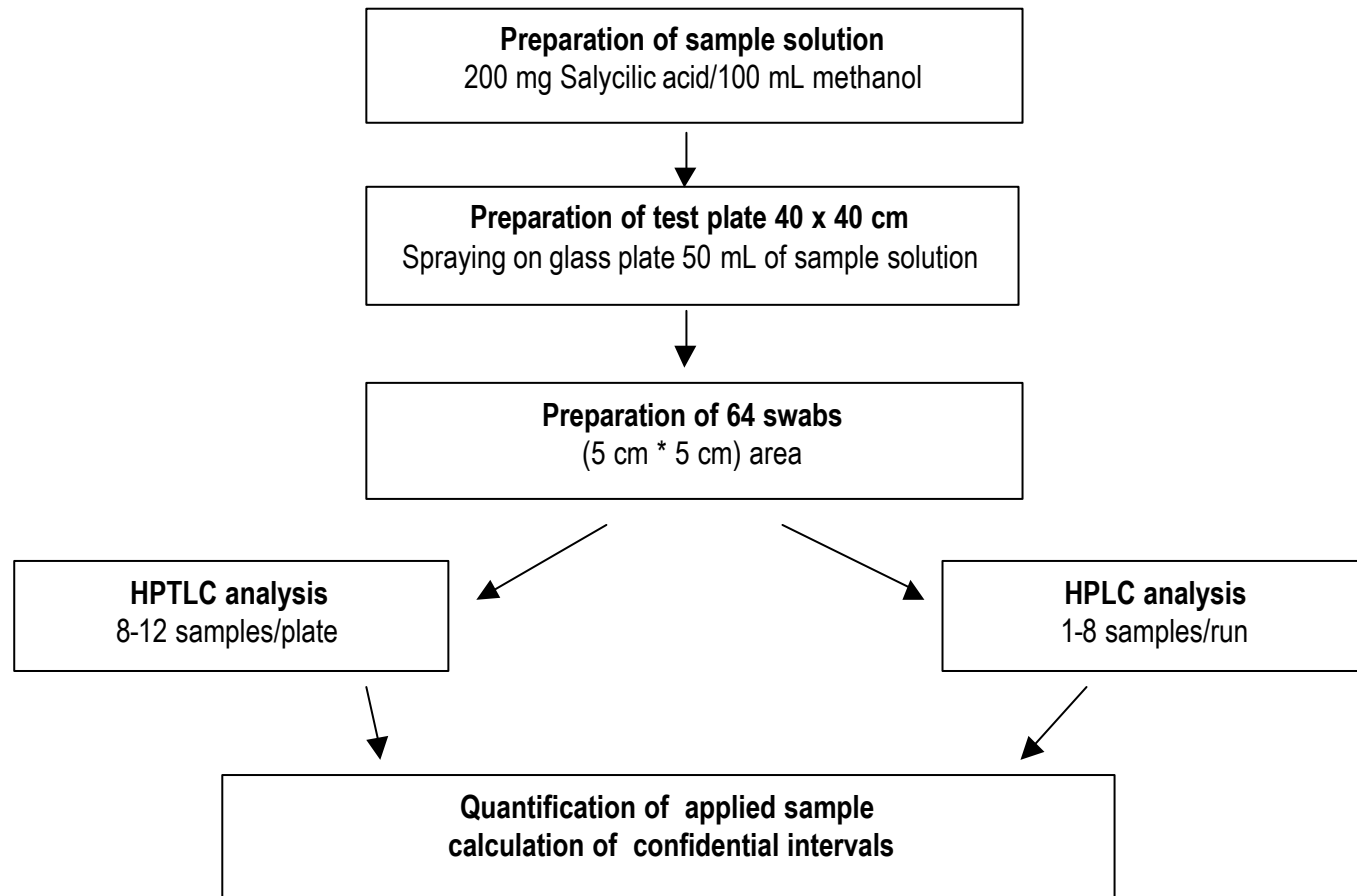
### TLC

Measuring uncertainty = 8.00 %

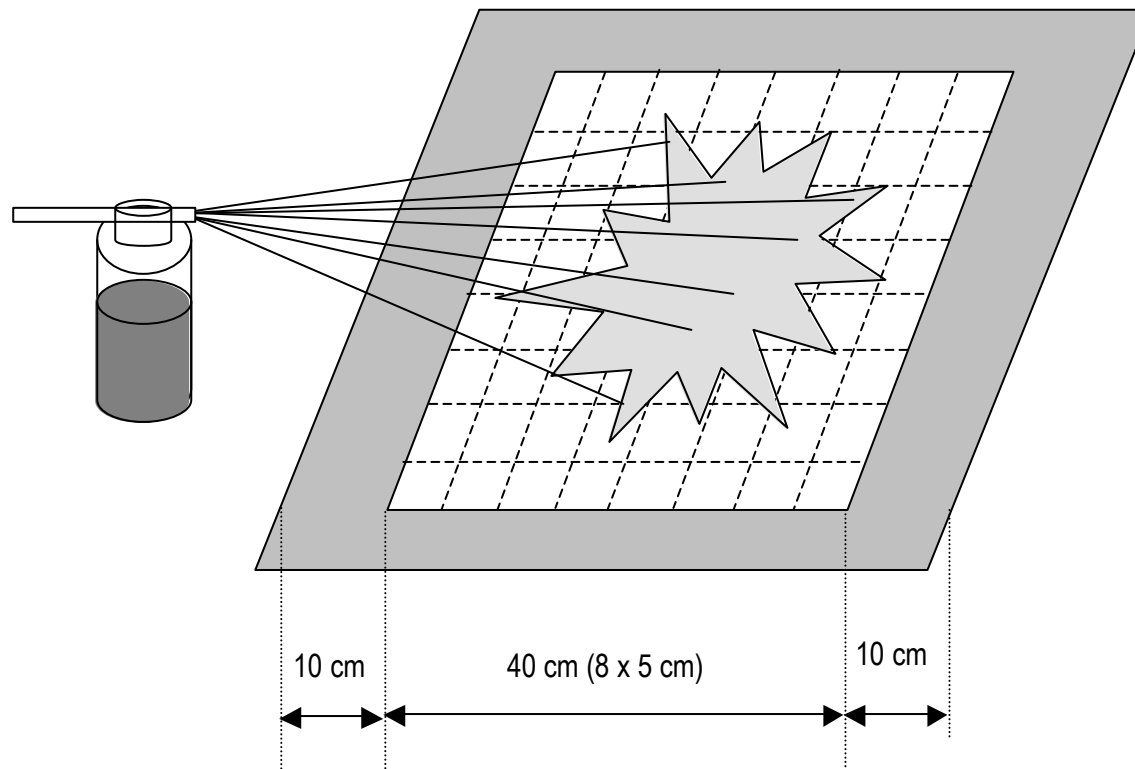
Sample uncertainty = 8.00 %

Analytical uncertainty = 11.31 %

## *The flowchart of prepared analytical method*



## *Preparation of test plate (with spraying)*



# Analytical methods

method	HPLC	HPTLC
<b>instrumentation</b>	HPLC pump Auto sampler HPLC Column	Development tanks HPTLC plates Micropipettes
<b>Identification &amp; quantification</b>	UV detector	TLC scanner III
<b>Necessary time</b>	7 minutes/injection	2 minutes/track
<b>Number of analysis</b>	158 injections (8/hour)	90 lanes/5 plates (18/plate)
<b>Price (all samples)</b>	900 Euro	300 Euro

## Analytical results

<b>Routine analysis (example)</b>		
<b>Sequence or Application plan</b>	3 SST 2 different swabs (2x) 4 calib. standards	10 different swabs 4 calib. standards
<b>N of injection/application.</b>	11	14
<b>price</b>	75 Euro	60 Euro
<b>Bias</b>	Small	No bias
<b>Back calculated values (%)</b>	32.6 mg (108,8 %)	29,6 mg (98.5 %)
<b>Analytical RSD</b>	28.0 %	30.0 %
<b>RSD of analytical method</b>	0.75 %	6.5 %
<b>t (p=0.95)</b>	2.13 (n = 2)	2.00 (n = 10)
<b>Confidential interval</b>	32.6 +- 35.1%	29.6 +- 17.0 %

## *Analytical results*

64 swabs were analyzed;

100 mg of Salicylic acid was applied on a plate.

During the spraying procedure 28.32 mg of Salicylic acid was deposit on glass frame around the plate.

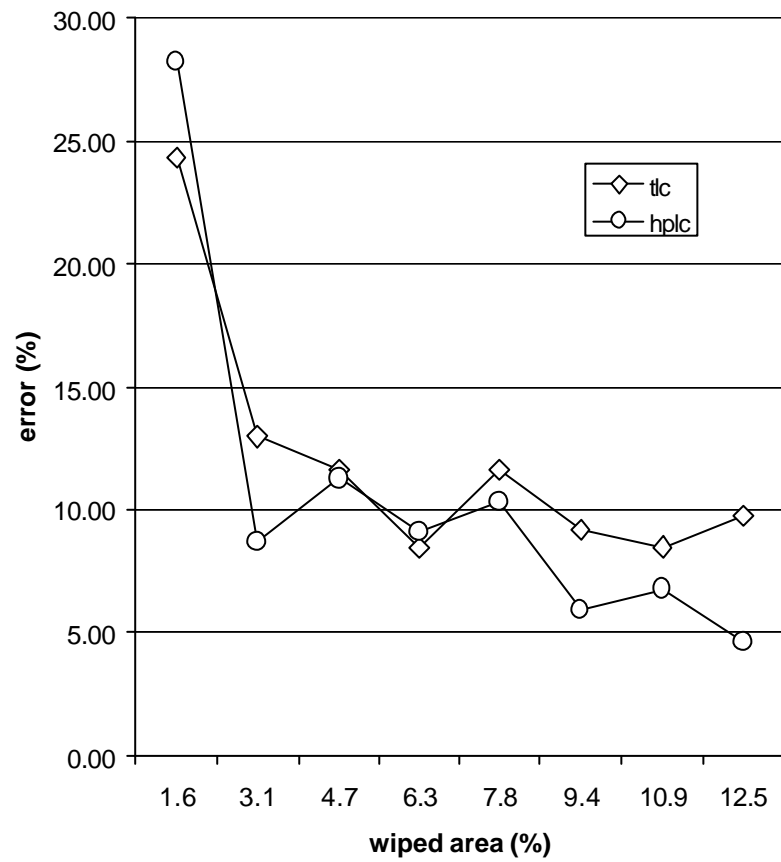
## Results of TLC measurement (mg/swab)

- Total amount of applied sample is 71.68 mg.
- Measured value, sum of all swabs is 66.21 mg,
- Recovery (TLC) = 92.4%.
- Average = 1.03 mg/swab,
- RSD = 28.53%

## Results of HPLC measurement (mg/swab)

- Total amount of applied sample is 71.68 mg.
- Measured value, sum of all swabs is 62.99 mg,
- Recovery (HPLC) = 87.9%.
- Average = 0.98
- mg/swab, RSD = 28.16%

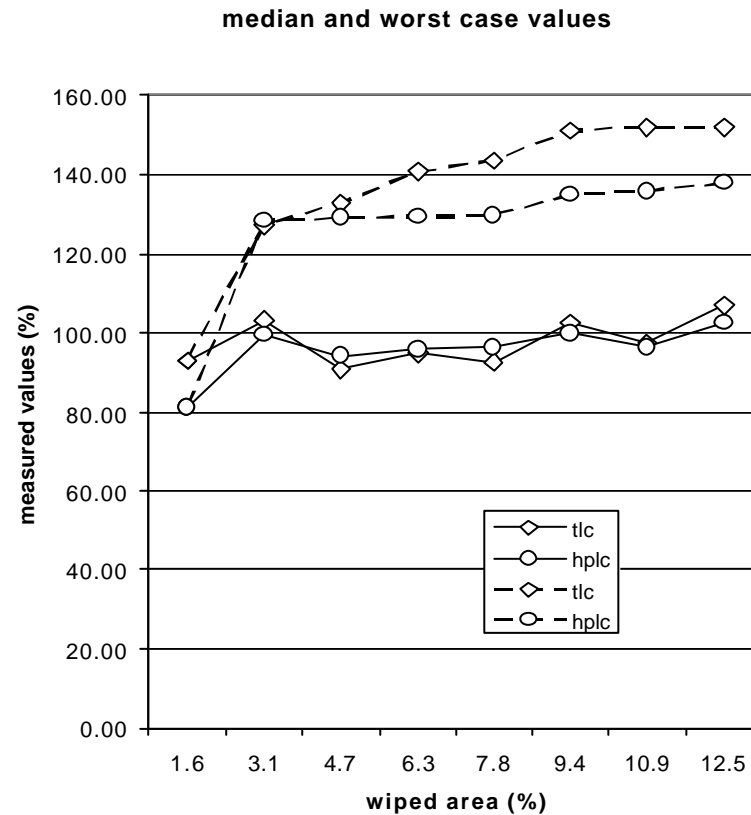
## Results (recovery)



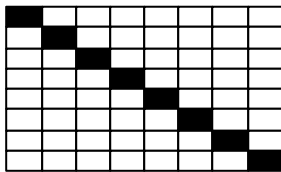
## *Results (recovery)*

- Difference between true values and measured values as the function of different number of collected swabs.
- Swab area was 25 cm<sup>2</sup>,
- From 1 to 8 swabs were merged in one sample.
- Wiped areas represented 1.6 to 12.5 % of total area. Swab positions were selected randomly. Plotted values represent the average of eight trials.

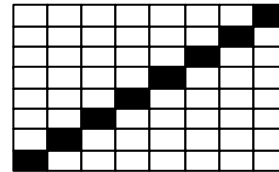
# Recovery (Median & Worstcase)



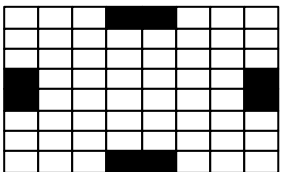
# Recovery as a function of sampling



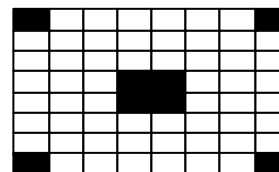
**a.)**  
Average 95.31  
Median 101.30  
Max 134.26



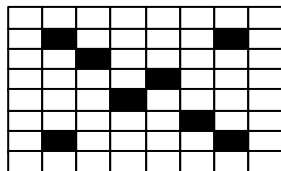
**b.)**  
Average 98.21  
Median 98.63  
Max 150.79



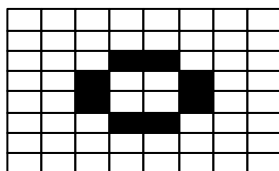
**c.)**  
Average 84.26  
Median 82.05  
Max 105.25



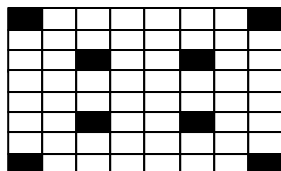
**d.)**  
Average 101.20  
Median 93.47  
Max 160.82



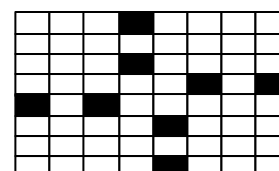
**e.)**  
Average 116.02  
Median 118.44  
Max 160.82



**f.)**  
Average 122.19  
Median 120.17  
Max 161.09



**g.)**  
Average 84.81  
Median 76.83  
Max 129.58



**h.)**  
Average 100.43  
Median 101.87  
Max 125.34

## *Recovery*

- The difference between true value, and measured values expressed in percentage.
- Recovery 1 was obtained when average value of 8 swabs was used for quantification;
- Recovery 2 was calculated from median
- Recovery 3 from the maximum concentration of 8 swabs.
- Swabs positions were selected according to presented templates (a – h).