

Analytical results for decisions!

What can analytical results really tell?

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Outline

- Analytical Chemistry for decisions
- Material flow – information flow - decision
- What actually is the measurand?
- Central role of uncertainty
- Real purpose of validation
- Guard bands and decision rules
- Non-technical issues

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What kind of decisions?

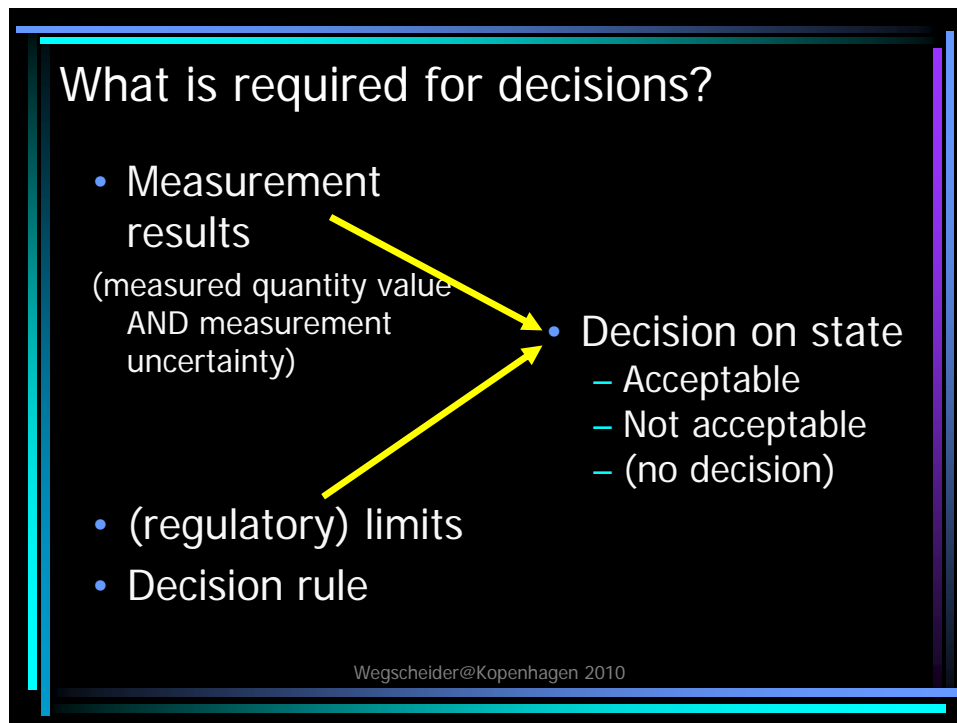
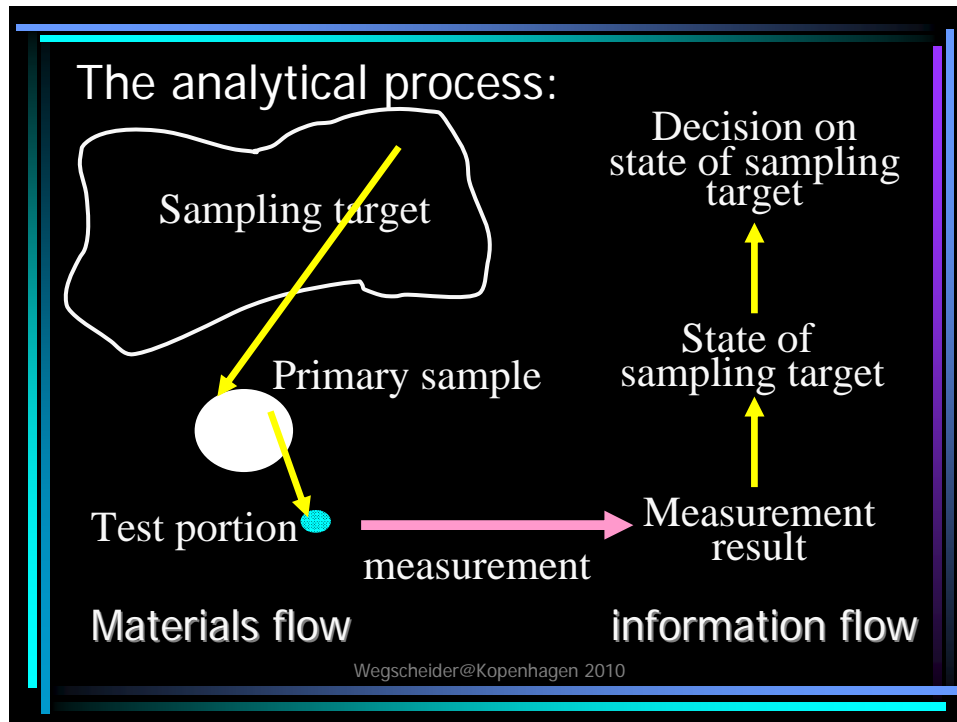
- Too low a content
- Too high a contaminant
- Out of specifications
- Within specifications
- Further studies required
-

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Decisions must be based

- On a sound logic and good scientific basis
- but what is this ?
- and how do we know ?

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What actually is the measurand?

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Definition of the measurand

- Large contribution to uncertainty
- (potentially) different definition in testing laboratories and inspection laboratories

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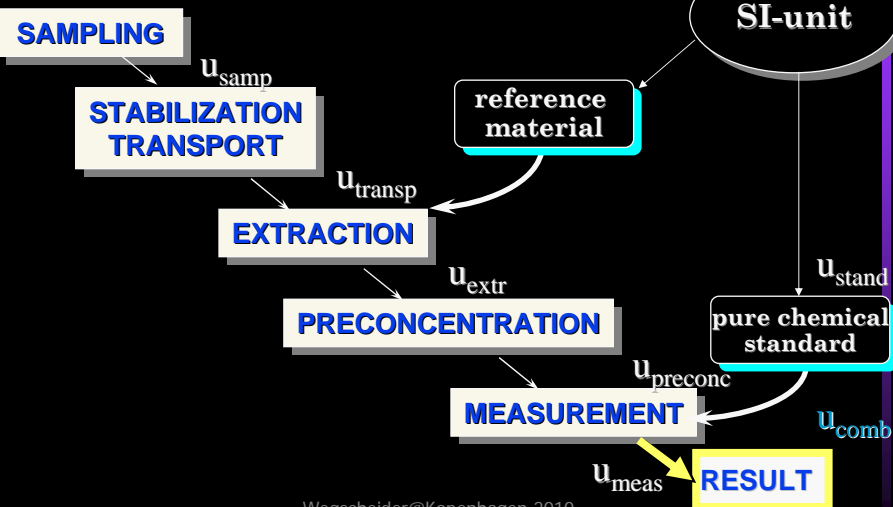
Definition of the measurand

- Phosphorus (P) in phosphate
- P in o-phosphate
- P in dissolved o-phosphate in water
- P in dissolved o-phosphate in a water body of a certain extension (in size and in time)

Uncertainty in the definition of the measurand increases greatly from top to bottom

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Uncertainties of standards and procedures



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Two key components to traceability:

- standards

$$\pm u_{st}$$

- uncertainty

$$\pm u_{pr}$$

combined uncertainty:

$$u_x = \sqrt{u_{st}^2 + u_{pr}^2}$$

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Real purpose of method validation

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Traditional roles of method validation

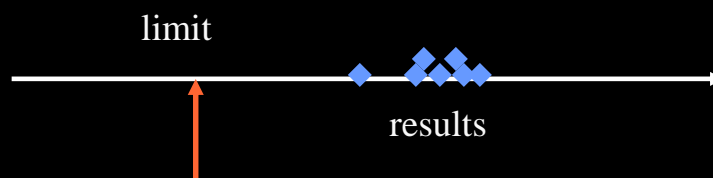
- Establish performance characteristics
 - Linearity
 - Limits of detection/determination
 - Precision: repeatability, intermediate precision
 - Effect of concomitants
- Present data for approval of method
- Produce control limits for everyday operation

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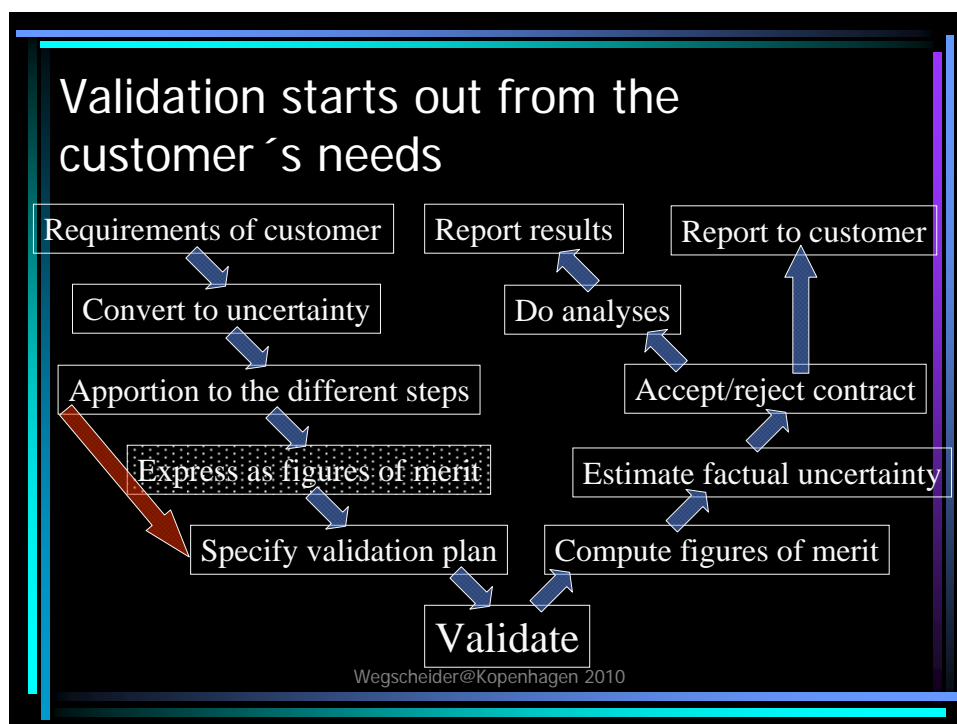
What **should** be the role of validation ?

As analytical chemistry is about making decisions

- validation should support the decision making process



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Sometimes this is prescribed even by modern legislation:

COMMISSION DIRECTIVE 2009/90/EC of 31 July 2009 ... technical specifications for chemical analysis and monitoring of water status

„Member States shall ensure that the minimum performance criteria for all methods of analysis applied are based on an uncertainty of measurement of 50 % or below ($k = 2$) estimated at the level of relevant environmental quality standards and a limit of quantification equal or below a value of 30 % of the relevant environmental quality standards.“

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Worked Example in validation:

Fe_2O_3 in MgO

For certain industrial applications of MgO the upper limit of Fe-oxide needs to be controlled very tightly

- Definition of the need of the customer translated to analytical quality criteria including cost and time

In this application an upper limit of 0.5 % was guaranteed by the supplier, the customer found 0.64 %, the supplier 0.41 %.

from W. Wegscheider, in B. Neidhart, W. Wegscheider: Quality in Chemical Measurements, Springer Verlag, 79-87 (2000)

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Deriving minimum performance characteristics from requirements

As the differences from one another was about 0.1 % Fe_2O_3 (0.41%, 0.50%, 0.64%) the proposed method needs to have the following characteristics:

- overall uncertainty (including sampling): <0.03 %
- uncertainty at required level of concentration from analysis itself: ~0.01% **o.k.**
- limit of quantitation (with matrix): <0.03 % **o.k.**
- limit of detection (with matrix): <0.01 % **o.k.**
- selectivity/interferences: CRM **o.k.**
- linearity: at least 0.3-0.7 % **o.k.**

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Estimation of Uncertainty from Sampling

- *about 500 g laboratory sample delivered*
- *sampled "according to ISO" by customer*
- *max. concentration about 1 % Fe in dark pieces*
- *min. concentration below LOD in light pieces*
- *many larger grains: ca 1 cm³ corresponds to 3 g*
- *total of 500 g/3 g \approx 160 pieces*
- *80 pieces give a relative uncertainty of 9 %*
- *at the 0.5 % level this is 0.045 % (0.02 % requ. !!!)*

- **CONCLUSION:**
- *the laboratory sample must be about 2000 g*

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The Numerous Interfaces of Analytical Chemistry and Law

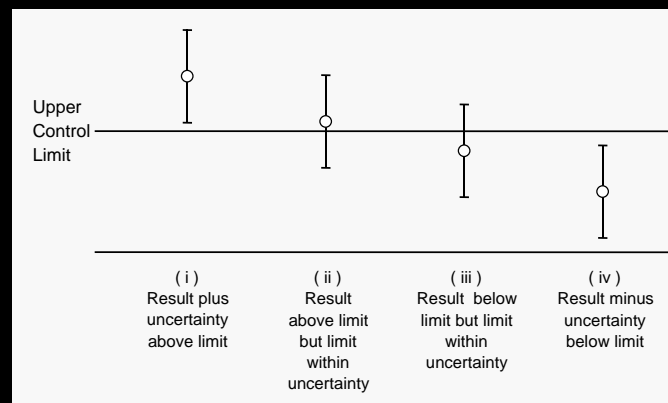
- ❖ *Pre-normative: what to regulate*
- ❖ *Normative: how to regulate, setting legal limits*
- ❖ *Operation of Legal System*
 - ❖ *Administrative: testing for legal limits*
 - ❖ *Civil Court*
 - ❖ *Criminal Court*

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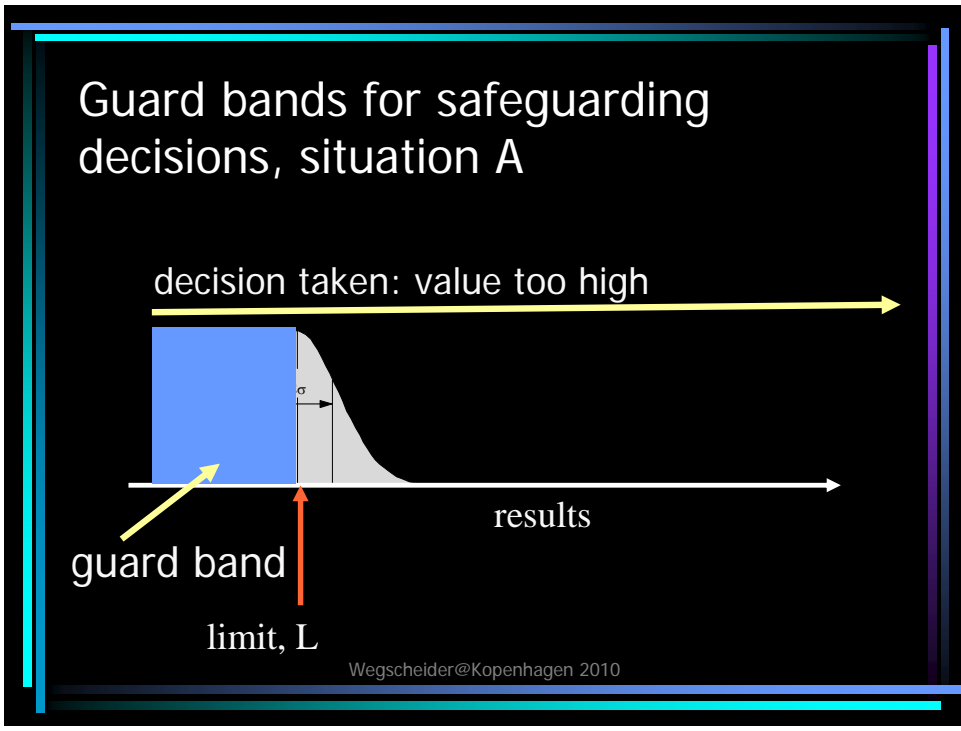
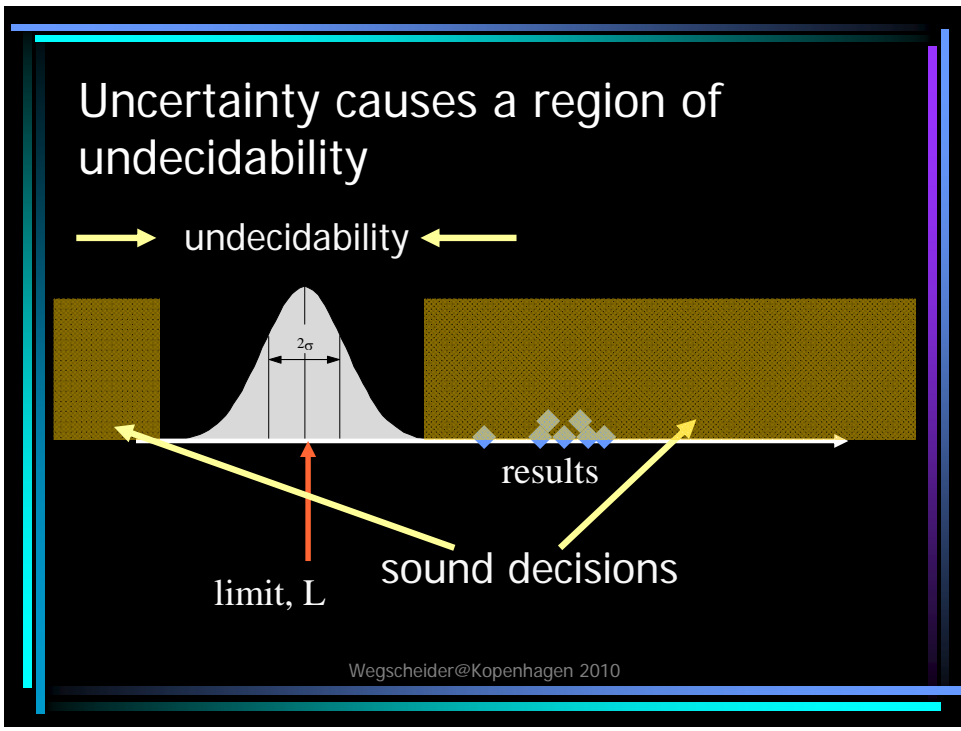
Guard bands and decision rules

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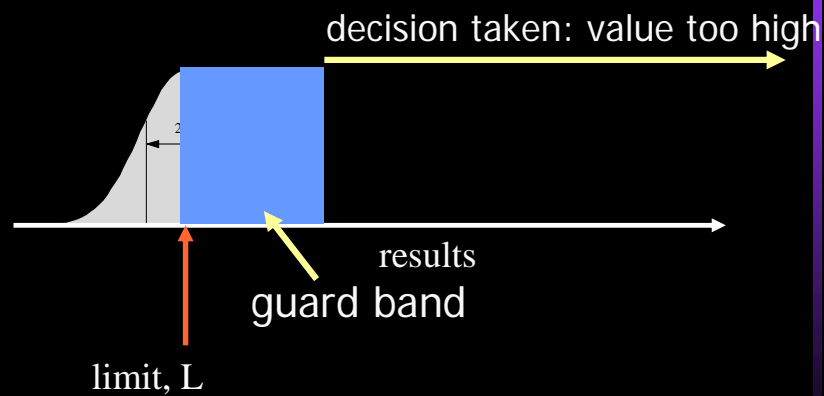
Results, uncertainty, control limits



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Guard bands for safeguarding decisions, situation B



The real difference between situation A and situation B is:

Who has the burden of proof ?

- *Is it necessary to prove that the value is exceeded ?*

OR

- *Is it necessary to prove that the value is within limits ?*

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Consequences of decision situation A vs. decision situation B

Probability of an event E (true state) given an
analytical result R:

$$P(E|R) = \frac{P(R|E)P(E)}{\sum_{i=1}^n P(R|E_i)P(E_i)}$$

Simplification as we have just two states:

- event E_1 : too high
- event E_2 : **NOT** too high

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Probability of exceeding, situation A

$$P(E_H|R) = \frac{P(R|E_H)P(E_H)}{P(R|E_H)P(E_H) + P(R|E_L)P(E_L)}$$

$$P(R|E_H) = 0.05$$

$$P(E_H) = 0.5$$

$$P(R|E_L) = 0.95$$

$$P(E_L) = 0.5$$

$$P(E_H|R) = \frac{0.05 * 0.5}{0.05 * 0.5 + 0.95 * 0.5} = \frac{0.025}{0.025 + 0.475} = 0.0125$$

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Probability of exceeding, situation B

$$P(E_H|R) = \frac{P(R|E_H)P(E_H)}{P(R|E_H)P(E_H) + P(R|E_L)P(E_L)}$$

$$P(R|E_H) = 0.95$$

$$P(E_H) = 0.5$$

$$P(R|E_L) = 0.05$$

$$P(E_L) = 0.5$$

$$P(E_H|R) = \frac{0.95 * 0.5}{0.05 * 0.5 + 0.95 * 0.5} = \frac{0.475}{0.025 + 0.475} = 0.95$$

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Probative Standard

Definition:

Degree of the judge's conviction which is necessary for the fact finding

- *Regular probative standard*
- *Reduced probative standard: preponderance*
- *Increased probative standard*

from Rechberger, Fres. J. Anal. Chem. 2000

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Degrees of Legal Probative Standards:

Paternity

- Increased Probative Standard:
for disproval of marital status, proof is required of the impossibility or improbability verging on certainty that the child was fathered by the mother's husband
- Regular Probative Standard:
should only be one man be affected by the presumption of paternity, then improbability rules which argues against the assumption of this paternity
- Reduced Probative Standard (preponderance):
the most probable among several men under consideration

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Complications in practice

- *Not all possible events/substances E_i are known*
therefore also not all responses R to these substances
- *Not all prior probabilities $P(E_i)$ are known*
- *Not only the one (analytical) result is available*
- *There is usually more than one piece of evidence*
but the correlations between evidences and/or results
are not quantified

Conclusion:

the judge must make a subjective evaluation of all evidence: "freedom of evidence"

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Odds on event E given result R:

$$O(E|R) = \frac{P(E|R)}{P(\neg E|R)}$$

- High ratios mean highly selective evidence from result of measurement
- low ratios mean low „selectivity“

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Very high Odds of $>10^5$: PCR

Evidence has produced a hair from the helmet used in a bank robbery

a) *hair is confirmed to be from suspect*

➤ *suspect must have worn this helmet*

b) *hair is not from suspect*

➤ *other people must also have worn this helmet*

Conclusion:

even very high odds do not necessarily translate into “high probative standards”

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Non-technical limits of Analytical Chemistry: *Doping at Olympic Games*

- Innsbruck 1976:
 - Gold medal was given back to an acquitted long distance skier:
 - J.F.K. Huber had proven that the drug level in serum can be established by a hand-shake
- Sydney 2000:
 - many previously acquitted athletes are admitted: „too strong a dose, it would kill the man“

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Conclusions for court decisions

- Judge objectifies his subjective conviction by reasoning his ruling
- Regular probative standard is the high probability
- Whether legal requirements for ruling are adequate must be left to the judge

but

on the way there are many opportunities for analytical chemistry

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Conclusions

- No uncertainty without definition of the measurand
- Validation is for estimating uncertainty
- No guard band without uncertainty
- Beware of decision rule
- Do not forget the non-technical issues

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Literature

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