anses
French agency for food, environmental and occupational health & safety

Quality management in veterinary testing laboratories

EU / OIE & FAO Reference Laboratory for Brucellosis
ANSES – Maisons-Alfort, France

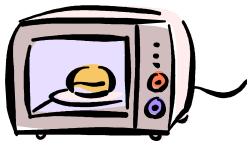
The 4th FAO-APHCA/OIE/DLD
Regional Workshop on Brucellosis Diagnosis and Control
in Asia and Pacific Region
- Proficiency Test and Ways Forward for the Region
Chiang Mai, Thailand, 19-21 March, 2014

Issues

- Quality in the field of veterinary laboratories: importance, means, recognition
- Management requirements (ISO 17 025)
- Technical requirements (ISO 17 025)

What is quality?

A word we use **everyday**…when talking about various everyday life things




Goods, services

Satisfaction of need, reliability, acceptability, durability, efficiency, comfort, warranty, cost, maintenance requirements, contract compliance, delay, function, value for money, equipment, safety, value for money,…




☞ A measure of **excellence** or a state of being **free from defects,** deficiencies and significant variations

✋Many factors involved….

Objective : to achieve **uniformity** of a product in order **to satisfy** specific **customers** or user requirements/needs

Importance of quality in veterinary testing laboratories

Analyses carried out

Results produced

Essential role of laboratories

- **Diseases prevention, surveillance and control plan**
- **Certification for trade of live animals and products of animal origin**

Results delivered **influence** actions implemented in the field

Results should be

accurate, reliable, understandable, trustworthy

Demonstration of competency and ability to generate consistent technically valid results is needed

→ Confidence is required

Quality in veterinary testing laboratories : the means

Achieved by the implementation of a **quality management system**
= a **set** of organisation, responsibilities, proceedings, processes, resources
aiming at **improving quality** of the produced results

- *Quality assurance = "systematic and planned process of ensuring that the service offered meets the stated requirements in all areas (internal or defined in recognised standards)"*
- *Quality control = systematic and planned monitoring of output to ensure the minimum level of quality have been met. In the lab., ensure test processes are working correctly and results are within the accepted range.*

- Implies an **organization** + **continuous improvement** of performance (controls)
- Includes technical, managerial and operational elements of testing and interpretation of test results

→ **mutual recognition** of test results

- Contribute to improve **harmonization** between regions, countries,…
- Significantly **improves the rigour** of the processes and reduces the risk of failures.

Quality in veterinary testing laboratories : the means

➢ Which standards, guides and references?

- ❖ General standards : ISO 17 000, ISO 9001 (quality management system only, no technical requirements)
  - ISO = The International Organisation for Standardisation (ISO) is an international collaboration of national standards setting organisations. Since 1947, ISO has developed and published commercial standards, many of which have become laws.
- ❖ **ISO 17025 (2005)** specific for testing and calibration laboratories
- ❖ **ISO 17043** interlaboratory proficiency testing
- ❖ **OIE Terrestrial Manual (2012) – Code**
  - esp. Chap 1.1.4. but also regarding recognized methods for each disease
- ❖ OIE quality standard and guidelines for veterinary laboratories : infectious diseases

→ **Internationally recognized, accepted, and reputable**

For further informations on standards

- ILAC (International Laboratory Accreditation Cooperation)
- and/or national standards and accreditation bodies of each country
- ISO publish useful references, guides,…that supplement the general requirements of ISO 17025

Quality in veterinary testing laboratories : the means

- Which recognition?
- **Certification**

"third party attestation related to products, processes, systems or persons."

→ **Conformity** to the standards requirements

→ Do not necessarily ensure or implies technical competence

- **≠ Accreditation process** (ISO 17000) = **COMPETENCE** > having and following documented procedures

= official recognition of **competence** in a specified subject or areas of expertise and **implementation of suitable quality assurance** system (meeting required standards) by a third party (duly recognized and respected **accreditation bodies**)

Choose a recognized accreditation body →Asia-Pacific Laboratories Accreditation Cooperation (APLAC)

Quality in veterinary testing laboratories

Type of testing

Purpose and requirements of results

Customer needs
(*e.g.* sensitivity and specificity of the test method, cost, turnaround time, strain/genotype characterisation)

Tolerance level of risk and liability

Specifities of each QMS depends on

Impact of a questionable or erroneous result

Leader of a network of labs
(assistance, overseeing);

Its business goals (e.g. any third party recognition and/or accreditation)

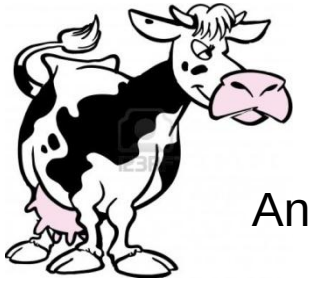
Its place in legal work or in regulatory programmes

☞A QMS has to be designed and maintained **in each particular context of each laboratory…**

Many common principles but generally not transposable from a lab to another

Choice of scope…

Quality in veterinary testing laboratories



Animal

Laboratory working in a well defined area, but its work depend on others actors

- ☞ Importance in a larger system
- ☞ Quality sensitization

e.g. refuse a poor quality sample

Sampling process

Sample

Competent authority

Trade control

Shipment

Laboratory

Material

Reagents

Analyst

Storage

1

Sample

2

Analysis

3

Result report

Traceability

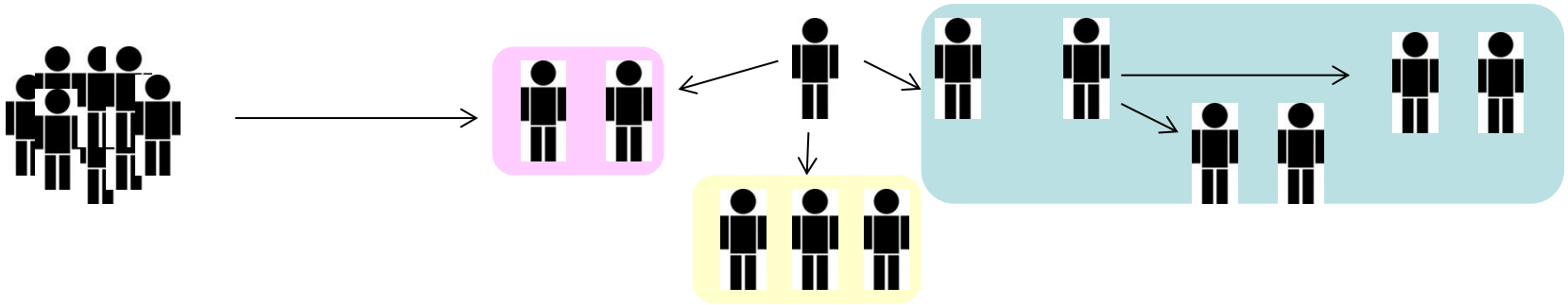
Fit for purpose (client needs)

Procedures

MANAGEMENT REQUIREMENTS

Management requirements

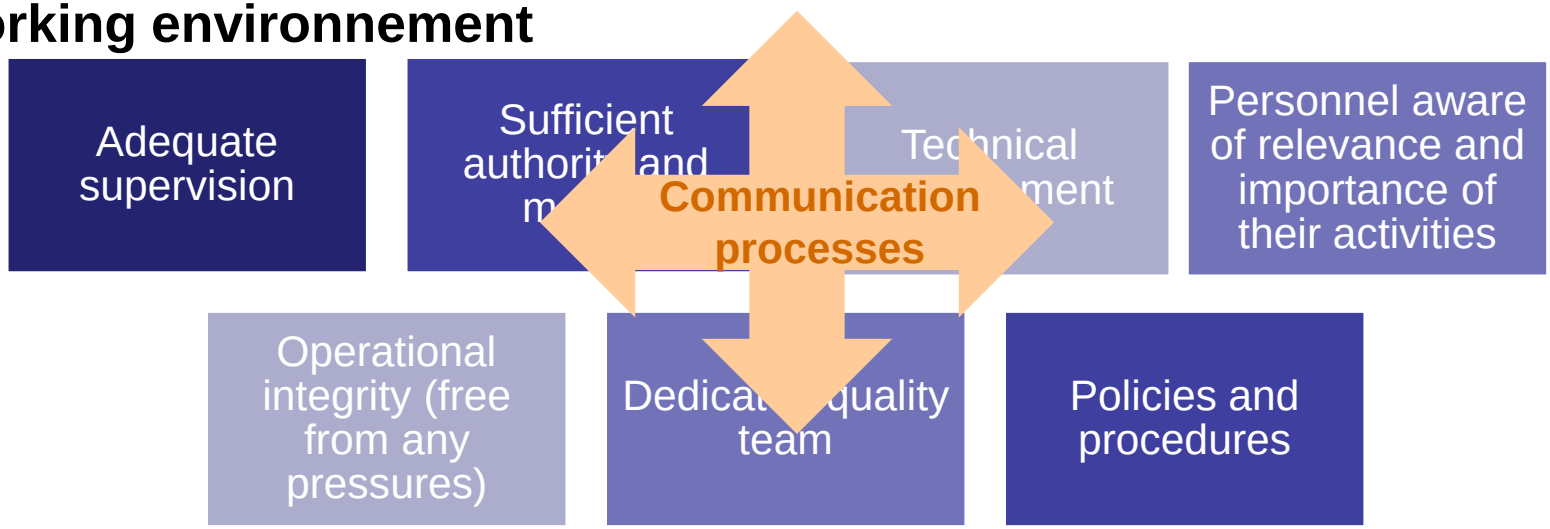
- Prerequisite…ressources are needed, quantity depends on the lab. activities
  - Personnel: managerial and technical staff (in small labs indivuals may have more than one function)
  - Adequate material
  - Sufficient funds
- **Defined organisational/management system and structure**
  - responsabilities, authority, inter-relationships and job description of the personnel
  - relationship between management, technical operations, support services and quality activities



- Laboratory's place within larger organization,

Management requirements

Working environnement



The ideal ….dedicated quality team or department

= quality manager + backups + documentation

Engagement for quality (up to a defined level) and check its application

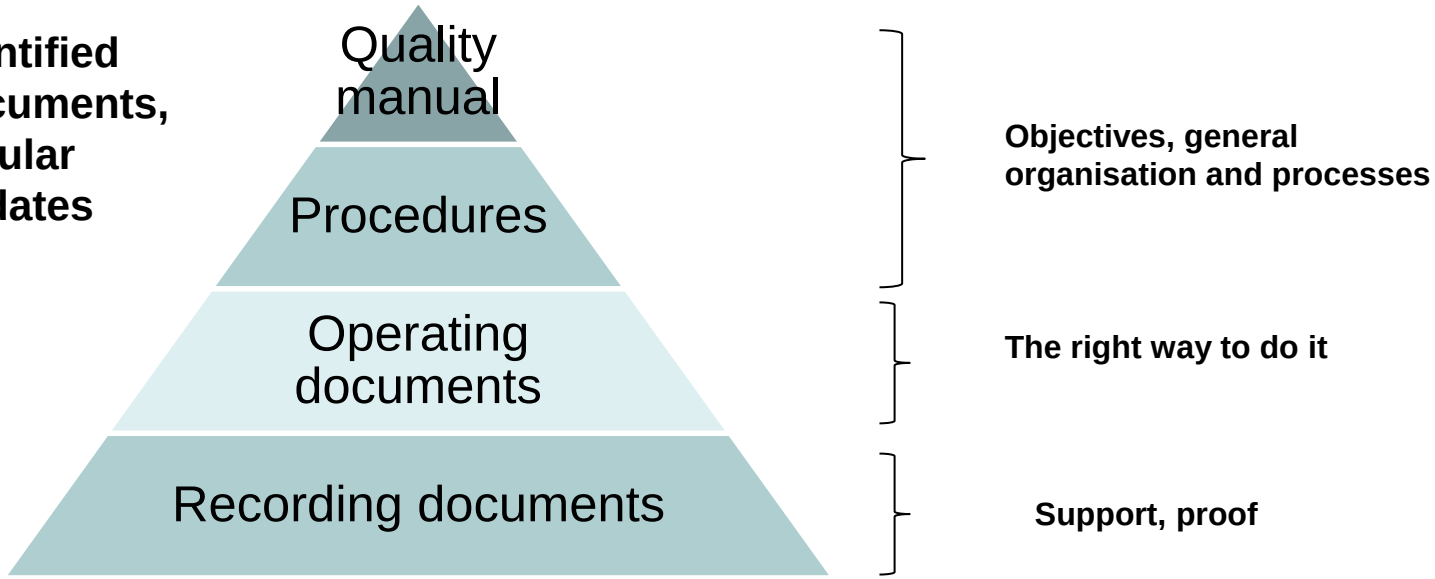
- Provide quality support
- Responsible for their improvment → keep a strong link with managerial and technical personnel (communication +++)
- Check their application (internal audit)

Management requirements

Documentation system

- Describe the whole organisation and means to achieve it : relevant, easy to update, always up-to-date
- Policies regarding quality (incl. quality policy statement) →quality manual
- Maintained up-to-date and aimed at continuous improvment → document control
- Ensure availability of the documents and good understanding of the personnal

Identified documents, regular updates



Management requirements

Customer relation (mostly V.S.)

- Adequate review of the requested work (is the analysis requested is fit for purpose? is lab. able to do this test?)
- Information on subcontracting
- Notification of nonconformities
- Resolution of complaints

Supplier relation : assessement for critical material supply

Traceability – record

Documentation – IT

Depend on the objectives

Management reviews

Non conformities and improvement

- Detection of non conforming tests and results
- Investigation to identify the origin
- Corrective/preventive actions implemented
- Continous improvement (audit results, data analysis, ….)
- Internal audit

TECHNICAL REQUIREMENTS

Step 1 : the sample

- Designated (authorized) **personnel** should take care of it
- Different types (depend on the analysis requested → customer relation)
- **Criteria of approval** (T during shipment, packaging, quality of the sample = suitable for testing)
- **Identification** (unique code or Nb) / recording of the corresponding informations
  - Client, animal identification, circomstances of testing….
- **Storage** :
  - protect the integrity
  - prevent spoilage, loss or damage
  - During all the analysis period

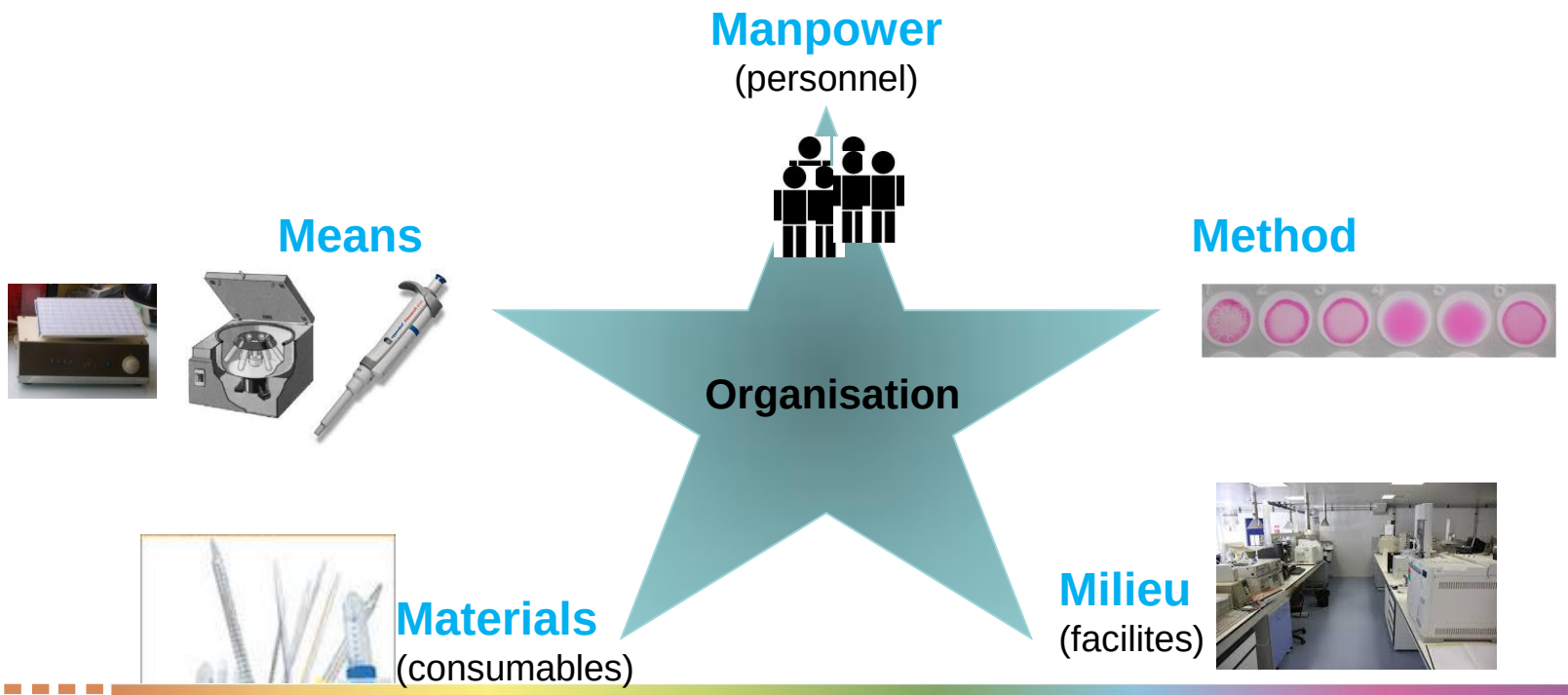
Ex. : serum for brucella anti-bodies detection in RBT should be refused if poor quality (temperature damage, contamination, appearance)

If not refused, risk of false agglutinates with plasma, high degree of haemolysis → caution with the results

Storage of sera after reception : fridge or freezer?

Step 2 : the analysis

- Designated (habilitated) **personnel** should take care of it
- Different **methods** (depend on the objective→ customer relation)
- Factors involved **5M**



Step 2 (analysis): MILIEU (environnement)

→ No impact on test performance and results

- **Facilities** : design and layout
- **Room conditions** → monitoring & control (record if influence on tests)
- **Cleaning** (hygiene)
- **Access** → limitation?
- Effective **separation** between neighbouring areas with incompatible activities (prevent cross contamination)

Ex: Air conditionning for test performance standardisation (RBT) if temperature ↑, agglutination ↑ (sensitivity ↑)
Incubation of iELISA at « room temperature »…need for RT incubator
Circulation of personnel in the laboratory (where DNA is amplified: risk of cross contamination)
Containment level of activity rooms (security and quality)

Step 2 (analysis): MATERIALS (consumables & reagents)

- **Supply** : requirements (fit for purpose, no impact on test result), supplier, warranties
- Checks upon reception
- Identification, labelling
- **Storage** (conditions, time) / stock monitoring / use before expiry date (if any)
- Preparation if needed, packaging (aliquots)

Ex: tips (fit for pipettes used in the laboratories, filter if needed), plastic tubes, U-bottom 96 wells microplates use in CFT, rose Bengale plates

Appropriate cleaning/disinfection process for reusable consumables)

Quality of reagents when standardization is required

Step 2 (analysis): METHOD

« appropriate test methods »
→selection, development/calibration, validation

- **How to choose ?**

☞ **Suitability** (species of interest, intended use, perf. characteristics…)

☞ **Acceptability**/scientific and regulatory bodies, acceptability/ customer,

☞ **Feasibility** given laboratory resources

Also : safety factors, cost of test, availability of reference standard

☞ To the extent possible, methods endorsed or published by reputable technical org.

APPROVED (recognised) METHODS

By regional, national, international standard-setting bodies or other standard specification
Prescribed test for trade (OIE Manual 1.1.4./1. 1. 5 and Code)
Regular up-dating (if any)

Step 2 (analysis): METHOD

- **How to perform ?**

☞Qualified & authorized **personnel** using written instructions **(procedure)**

- Relevant references
- Test description (analyte, …)
- Reagents
- Material specifications
- Safety considerations
- Equipment calibration
- Standard material references
- Sampling and sample preparation,
- Criteria for sample/result acceptance,
- Control inclusion,
- Record procedure…

Step 2 (analysis): METHOD

- **How to perform ?**

☞**Optimisation and standardisation** of the method → **setting up** in the lab.

- For new methods
  - Optimisation : establishes critical specifications and performance standards
- Critical specifications for equipment and reagents
- Robustness (**CCP** and **acceptable ranges**)
- Quality control : **CCP monitoring**
- Criteria of test results **acceptance, interpretation** and **reporting**

☞Test proficiency should be **regularly controlled**

☞ **Use of external reference material, ILPTs**

Critical points for RBT?

Way of control?

Antigen and serum at room T	→ specify a time during which reagents should be placed at RT and check by the analyst (bench work sheet)
Homogenization (esp. antigen)	→ procedure & intensity of + control?
Identical volumes of serum and Ag	→ volumetric control of the pipettes
No freezing of the antigen	→ control/mapping of incubators
No reading after 4 minutes	→ timer calibration

Positive control in each series of test / expected results (control card)

Step 2 (analysis): METHOD

In-house validation : evaluation of test fitness for a given use by establishing performance characteristics

☞Using documented, optimised and fixed validation procedure

Extent and depth of the validation:

Internal methods : exhaustive validation is required (ex: in-house iELISA)

≠ Standard methods should not be competely re-validated (ex: RBT if antigen approriately standardized)

See Chap. 1.1.4./5 OIE Manual

Step 2 (analysis): METHOD Uncertainty of the test method

☞**Uncertainty** Measurement of Uncertainty (MU) is “a parameter associated with the result of a measurement that characterises the dispersion of values that could reasonably be attributed to the measure” (Eurachem, 2000).

Should be estimated for quantitative / qualitative methods (if possible)
Testing in repeatability conditions ex: CFT, iELISA

All the major sources of **uncertainty** should be identified

✋ Definition of acceptable ranges for each CCP

→ **quality control procedures** targeted at each CCP

Storage conditions, sample processing, reagent quality, preparation and storage, volumetric and weight manipulation, equipment effects

→ monitoring the validity of tests with **internal controls (calibrated against reference materials)**

Step 2 (analysis): METHOD Traceability measurement

Reporting/recording :

- General information: date, analyst,…
- Test results
- Control results
- Materials and reagents used during the test

Every useful information to help evaluate the impact / finding the origin of a potential problem

Ex: when volumetric accuracy of a pipette is not satisfactory , evaluation of the impact on previous analyses should be conducted

Step 2 (analysis): MEANS/EQUIPMENT

Choice and **supply** (requirements, fit for purpose, …)

→ checks upon reception

Calibration required before use (fridge 5±3° C on every racks)

Inventory and record (identification, labelling, life-sheet,…)

Traceability of any **intervention** (maintenance, cleaning, fixing…)

Planned regular **calibration**

Step 2 (analysis): MEANS/EQUIPMENT

Use by authorised/qualified **personnel**

Metrological controls (calibration and verification acc. to standards and adequate procedures)

→ for all materials with a significant impact on analysis results

Scales, pipettes, sensors, incubators, spectrometers, thermocylers, timers

→Weight, volume, temperature, pH, wavelength, time

Ex: choice & control of pipettes for RBT, incubators in iELISA

Step 2 (analysis): MANPOWER

Job description ↔ adequate **qualification/training**

Authorization process : what is to be known and how (hands-on training), evaluation

Regular competence evaluation

Maintenance of a **training programme** relevant to present and anticipated needs of the laboratory→ continuous improvment

Ex: qualification follow-up: ILPT, internal double-blind test

Step 2 Analysis

Results validity control :

- Internal controls : blank, +/- controls (expected results)
- Traceability control
- If not consistent with expected results : no results issued

→ Non-conformities investigation

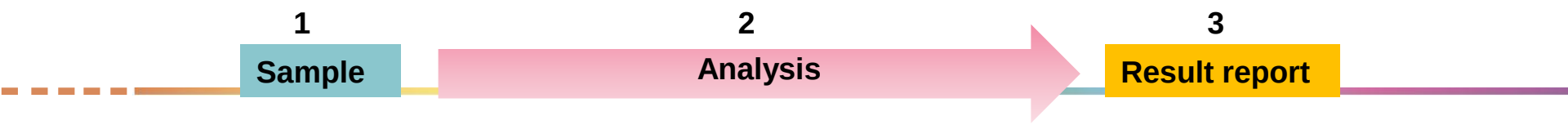
Step 3 Results report

Reporting:

Results **accurately, clearly, unambiguously, objectively** expressed in the report → Understandable for the customer

Report with **a unique number**, identification of customer and sample, name of the method, date of reception and analysis, interpretation if needed, signature

If corrected : **edition of a new report** clearly identified



Steps 1,2 and 3

Continuous improvement

Non-conformities identification

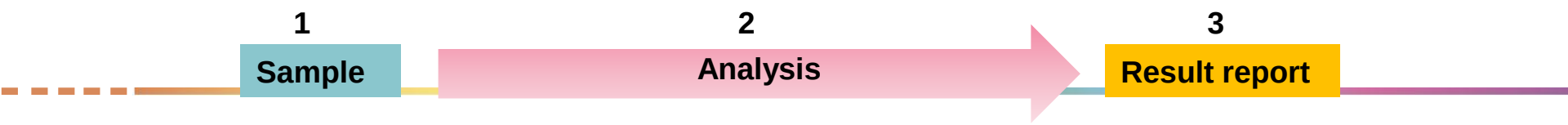
→ investigation of the **origin/consequences**

→ **corrective/curative** actions

Ex: customer claim

Ensure corrective action **efficiency**

Consider **preventive** action (prevent a new occurrence of the problem)



Steps 1,2 and 3

Flexibility of the system…?

Derogation : written authorization to stray from procedures

→ Preliminary impact analysis is required

Ex. use of 20 µL instead of 30 µL in RBT provided pipette is well calibrated

→ Flexibility is accepted up to a certain level

→ Management review at least once a year: feedbacks, reports, complaints, suitability?, corrective/preventive actions, recommendations

Conclusion

Quality is a….**TOOL !**

- Ensure operational performance **:**

Write what you do and Do what you have written

→ one language, everybody's personal commitment

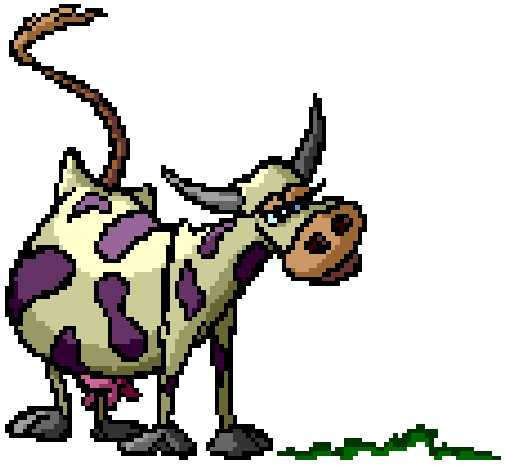
→ not to be enforced, consensus is necessary

- Cost optimization : do the right thing the right way at first try
- Anticipation of new developments

Quality is a long, long way

Not ready-to-go, continuously improved

The first step is the hardest one



ขอบคุณครับ

Thanks for your attention…