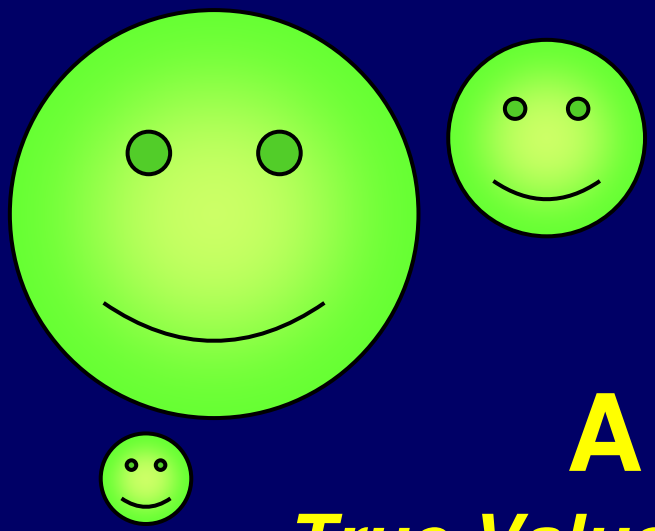
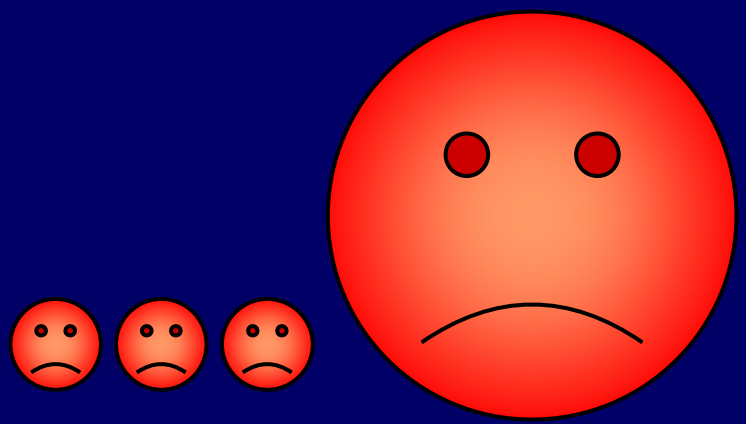
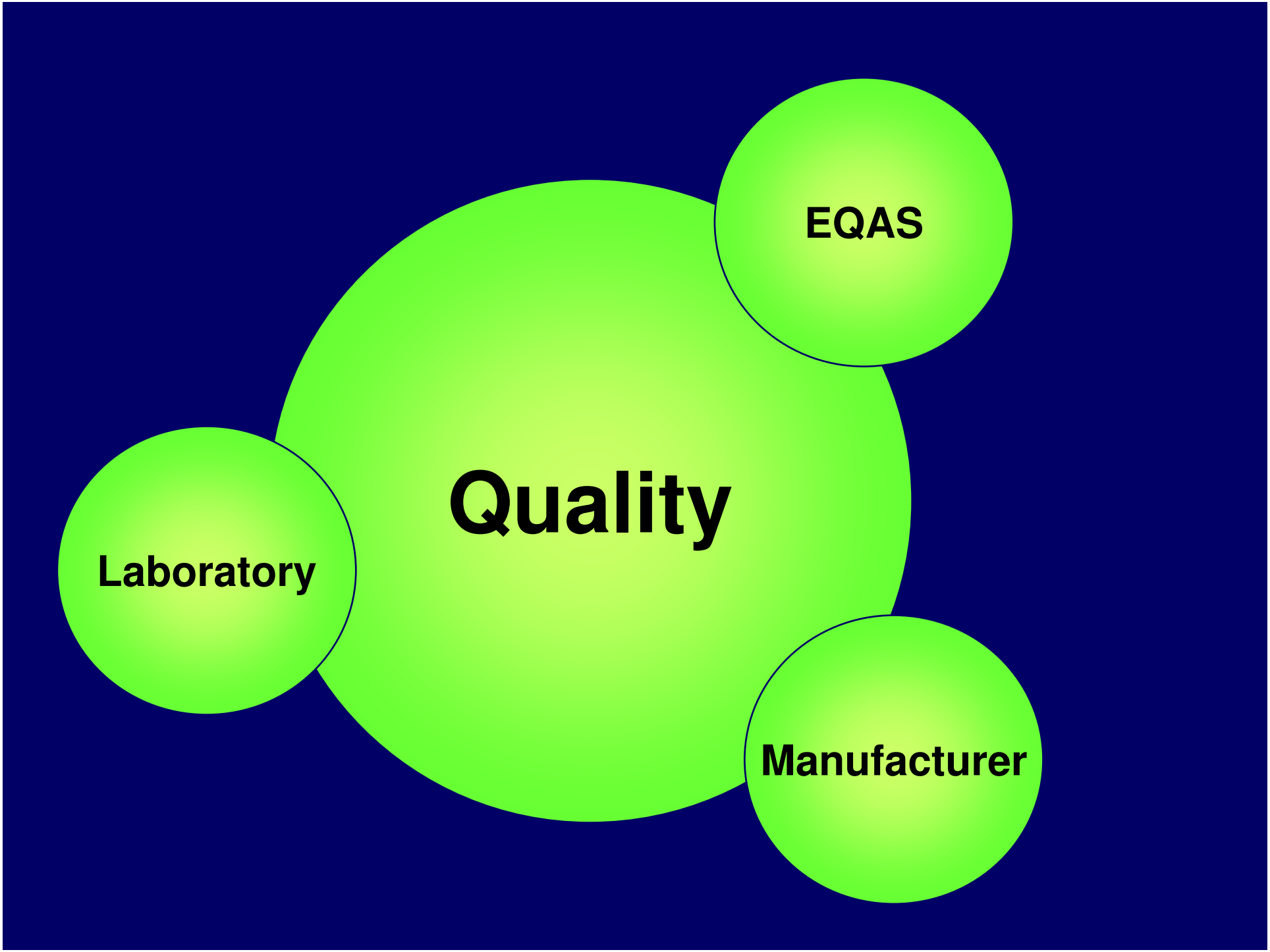


A Story of Smileys

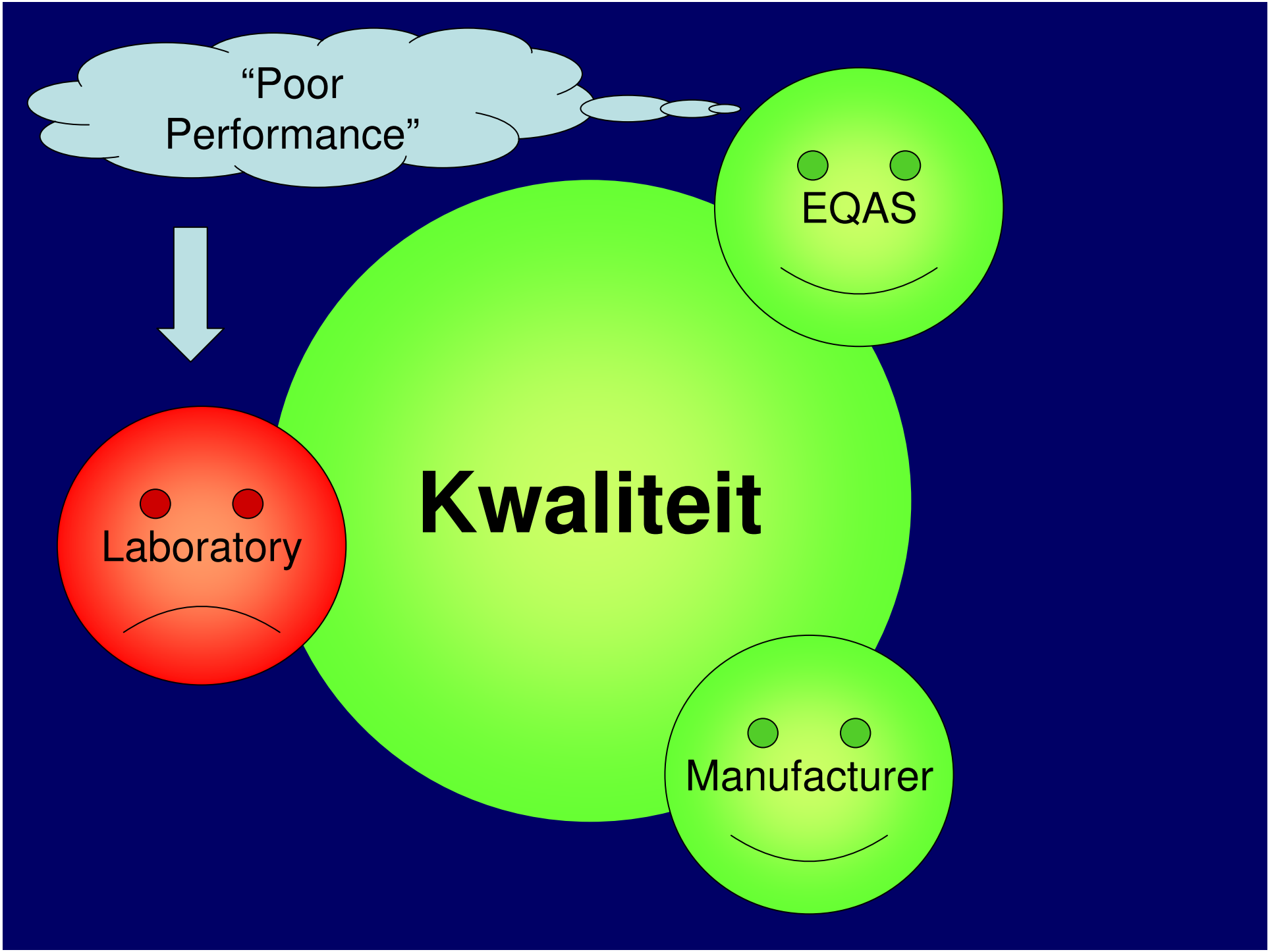
True Value Assignment to EQAS materials
A feasible task?

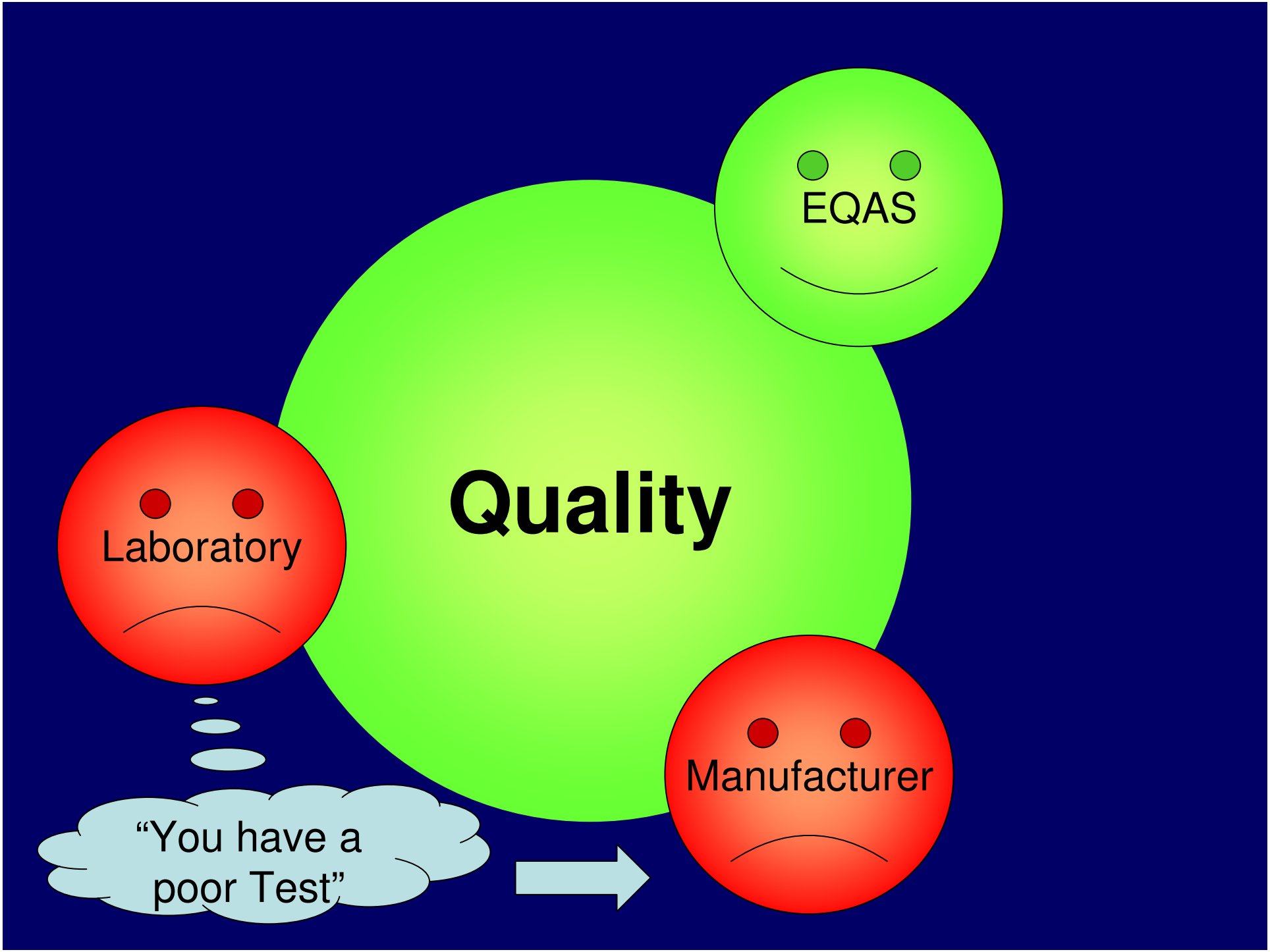
Cas Weykamp
Queen Beatrix Hospital, Winterswijk, The Netherlands
Milan, CIRME International Meeting, 30 November 2010

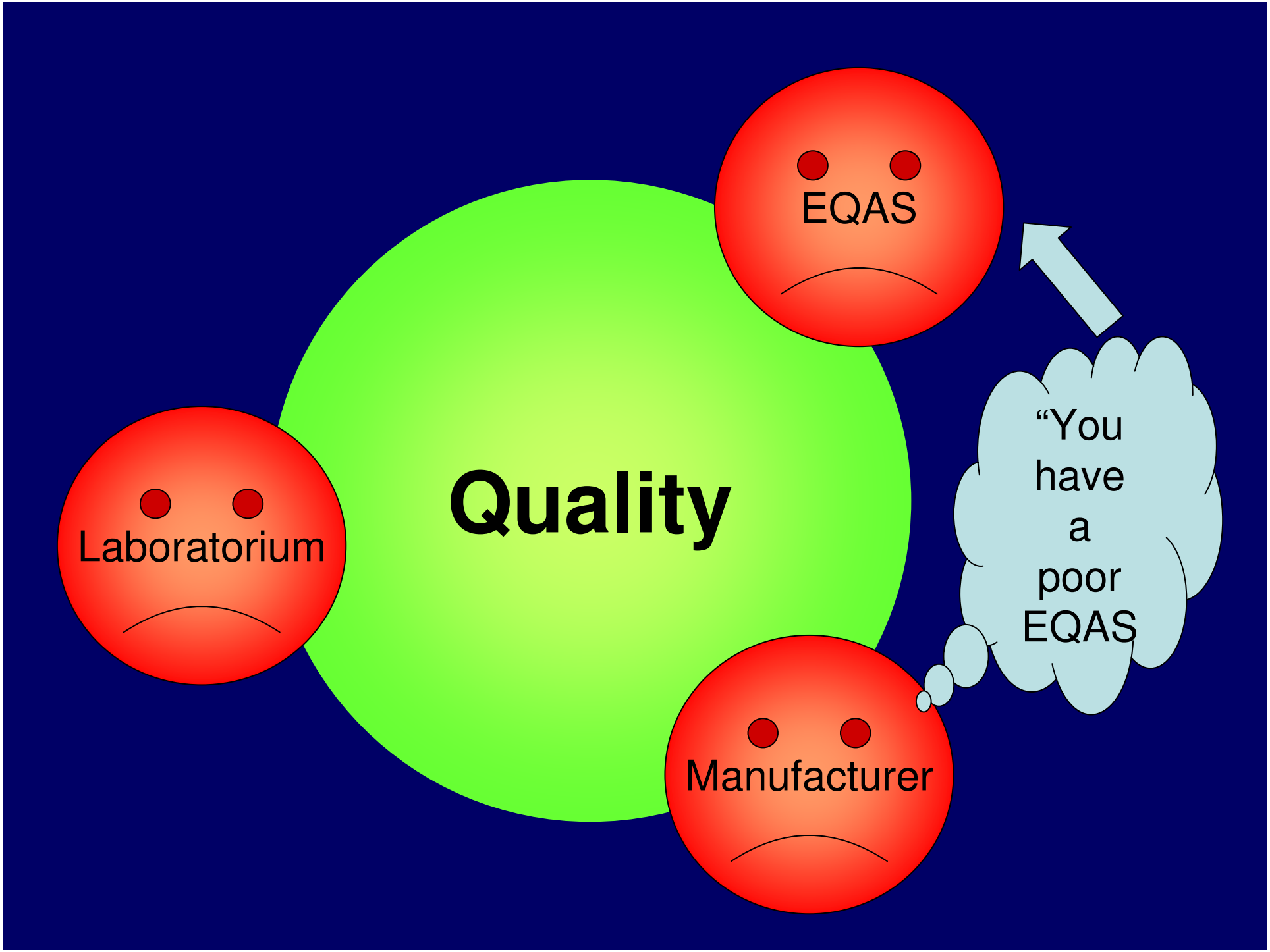


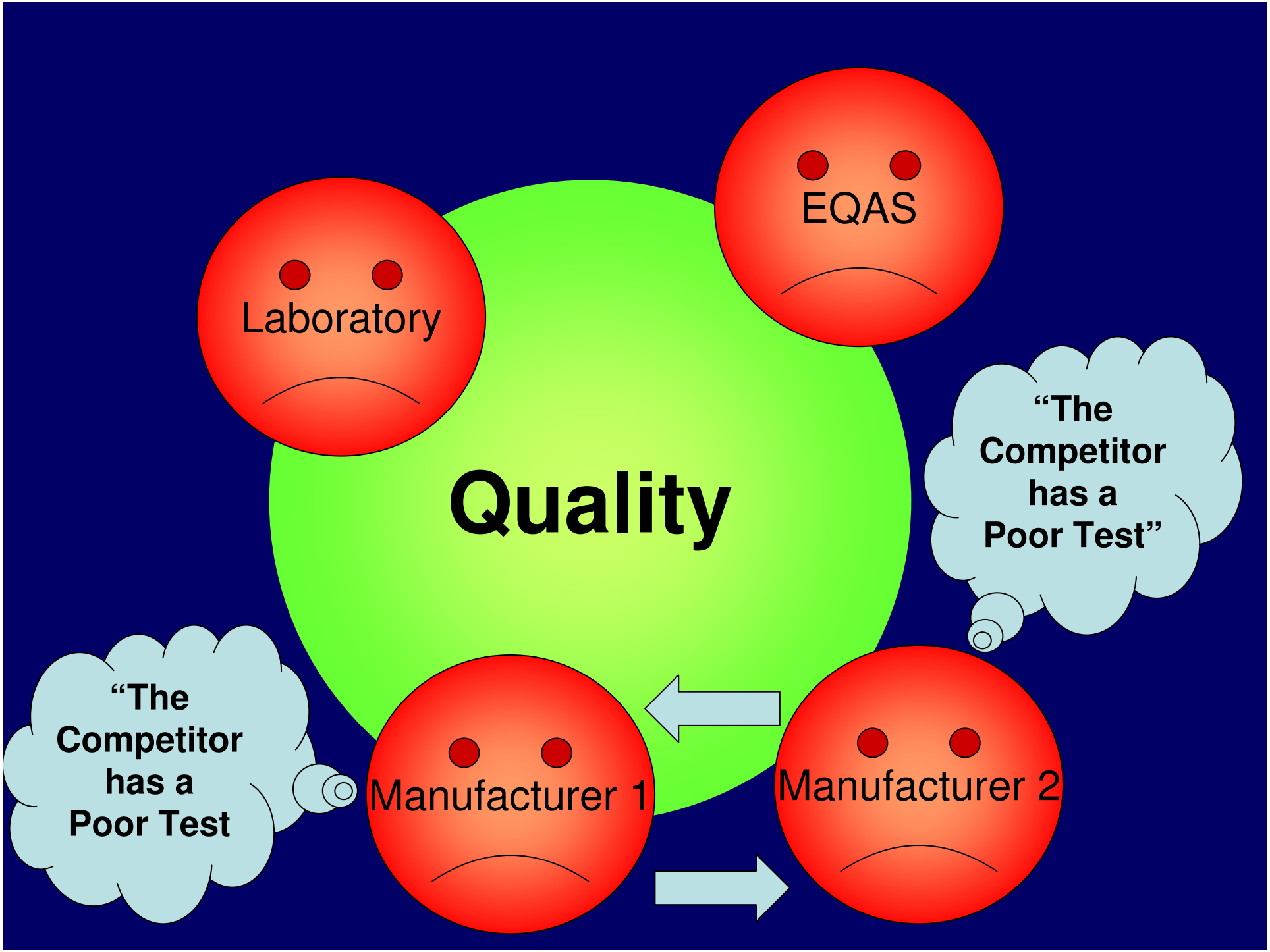

EQAS
Quality
Laboratory
Manufacturer

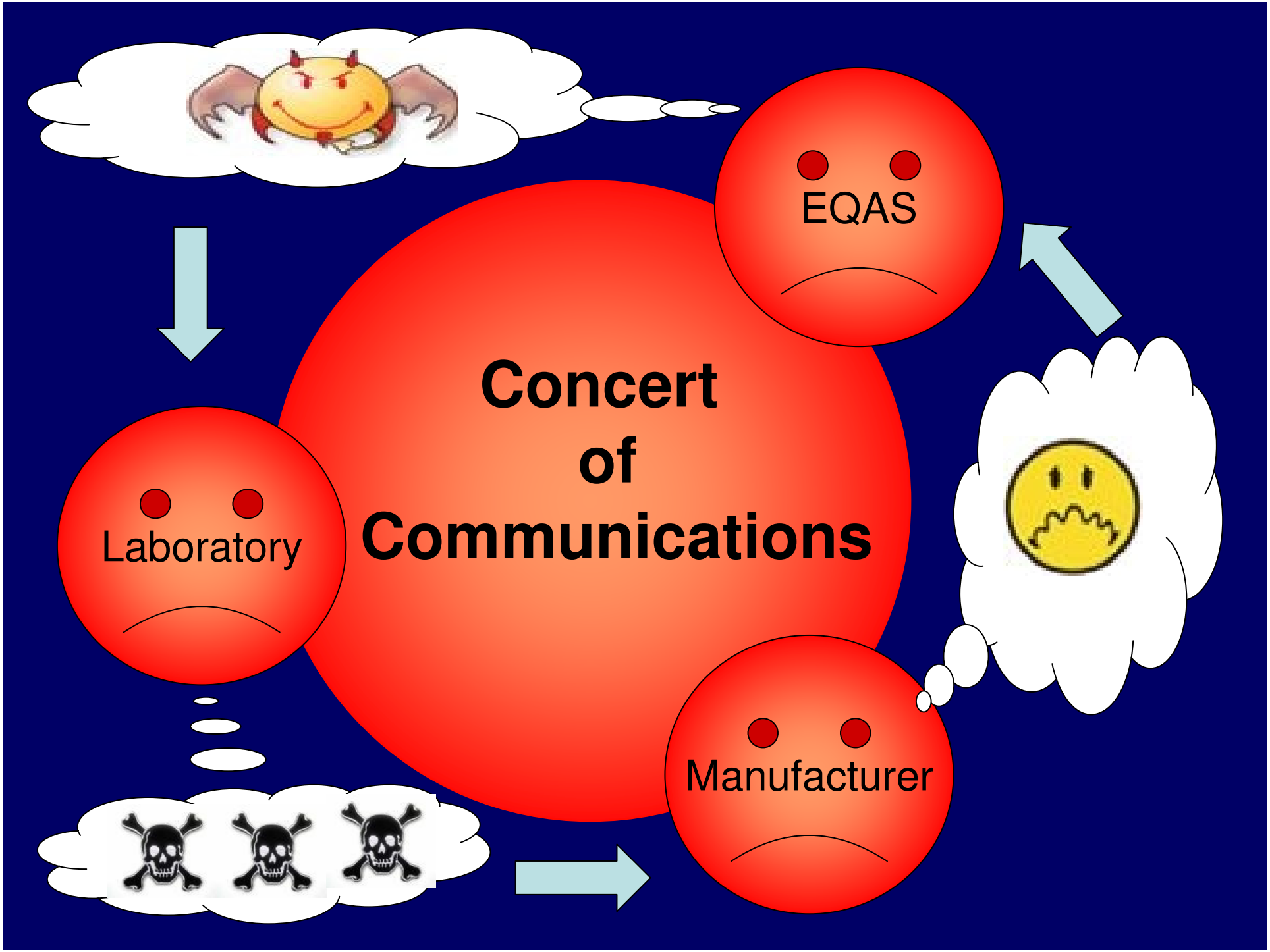
Quality OK….
EQAS
Laboratory
Quality
Manufacturer
….All
Smile

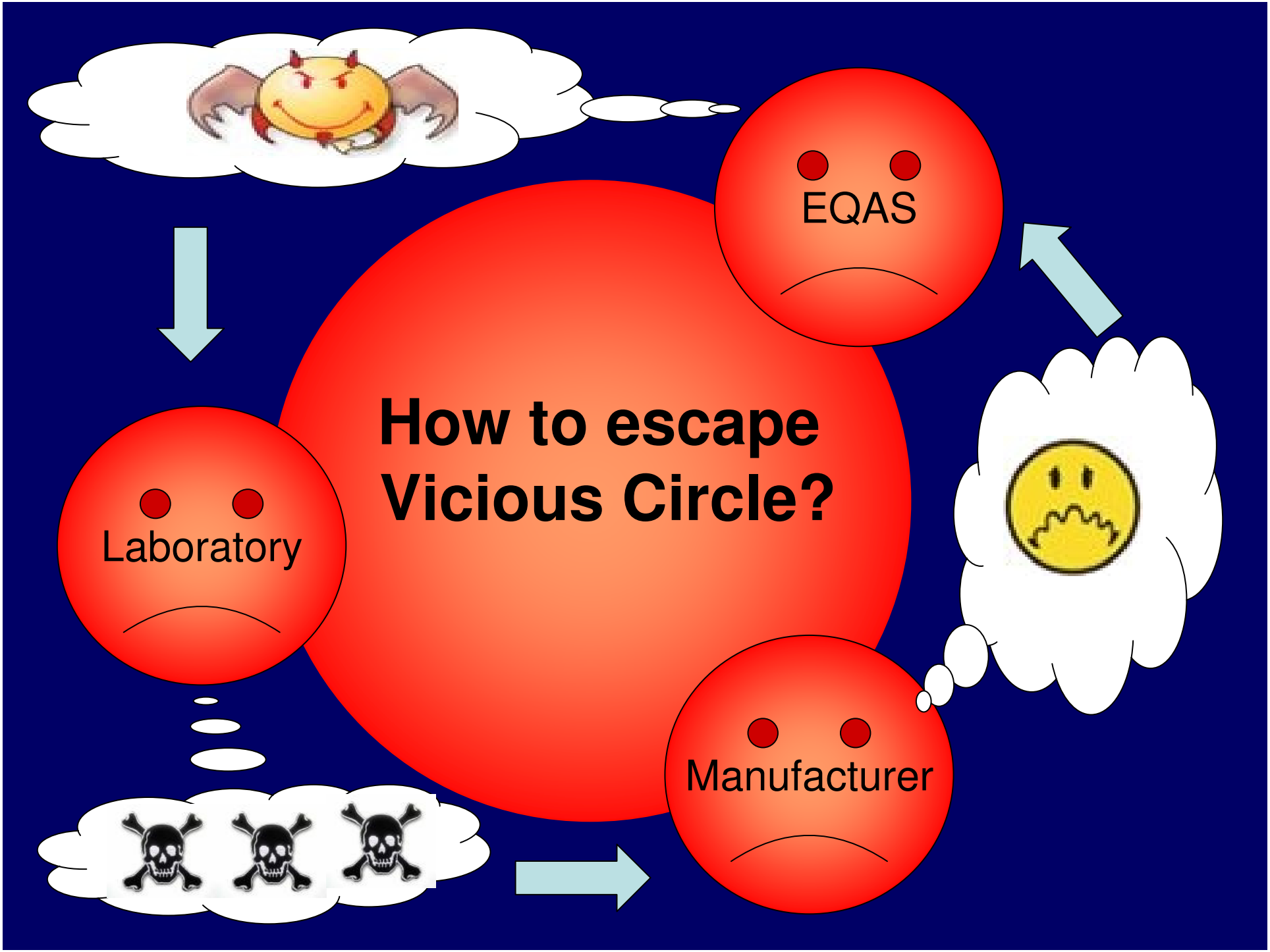

“Poor Performance”
EQAS
Laboratory
Kwaliteit
Manufacturer

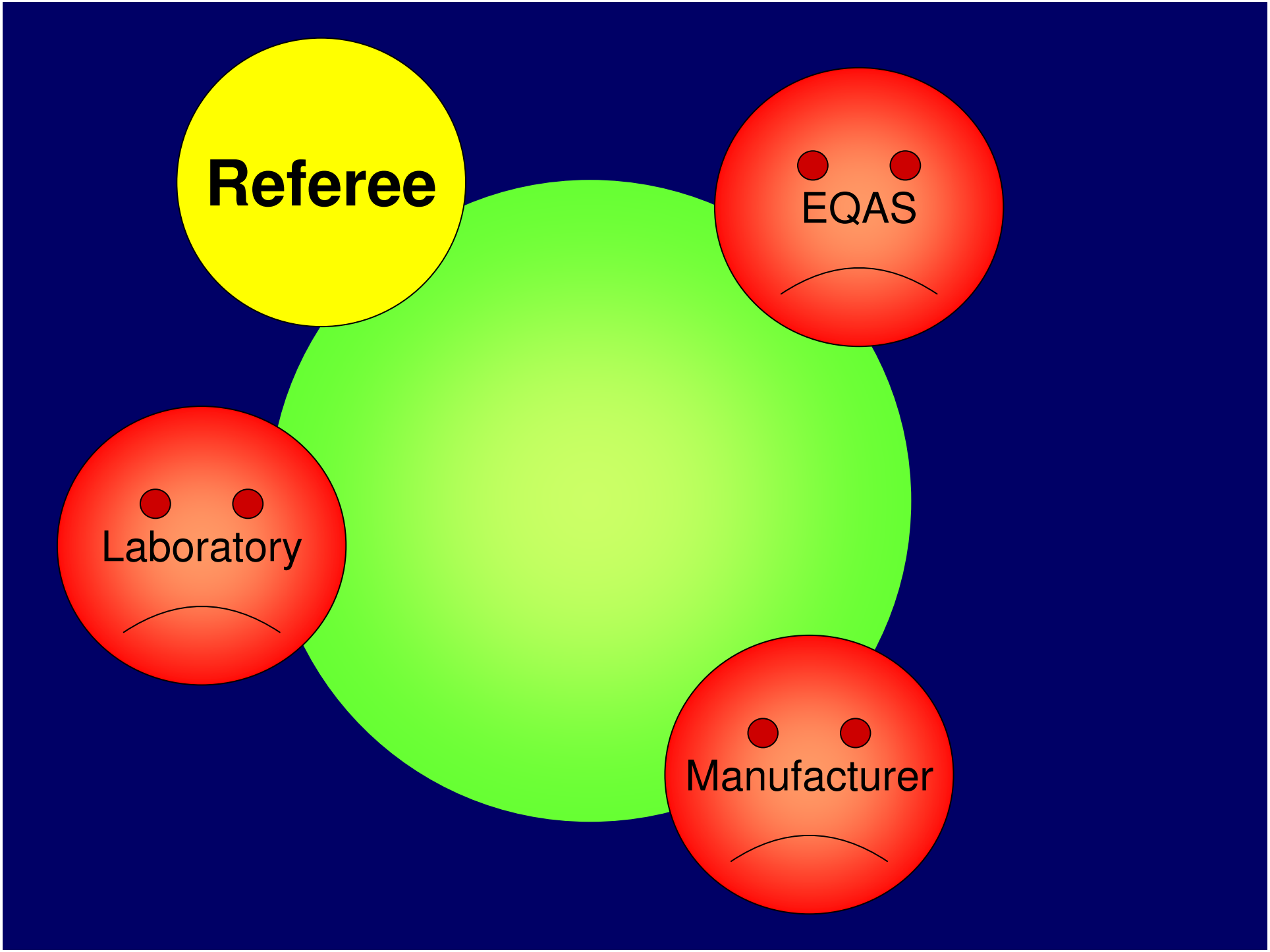

EQAS
Quality
Laboratory
Manufacturer
“You have a poor Test”

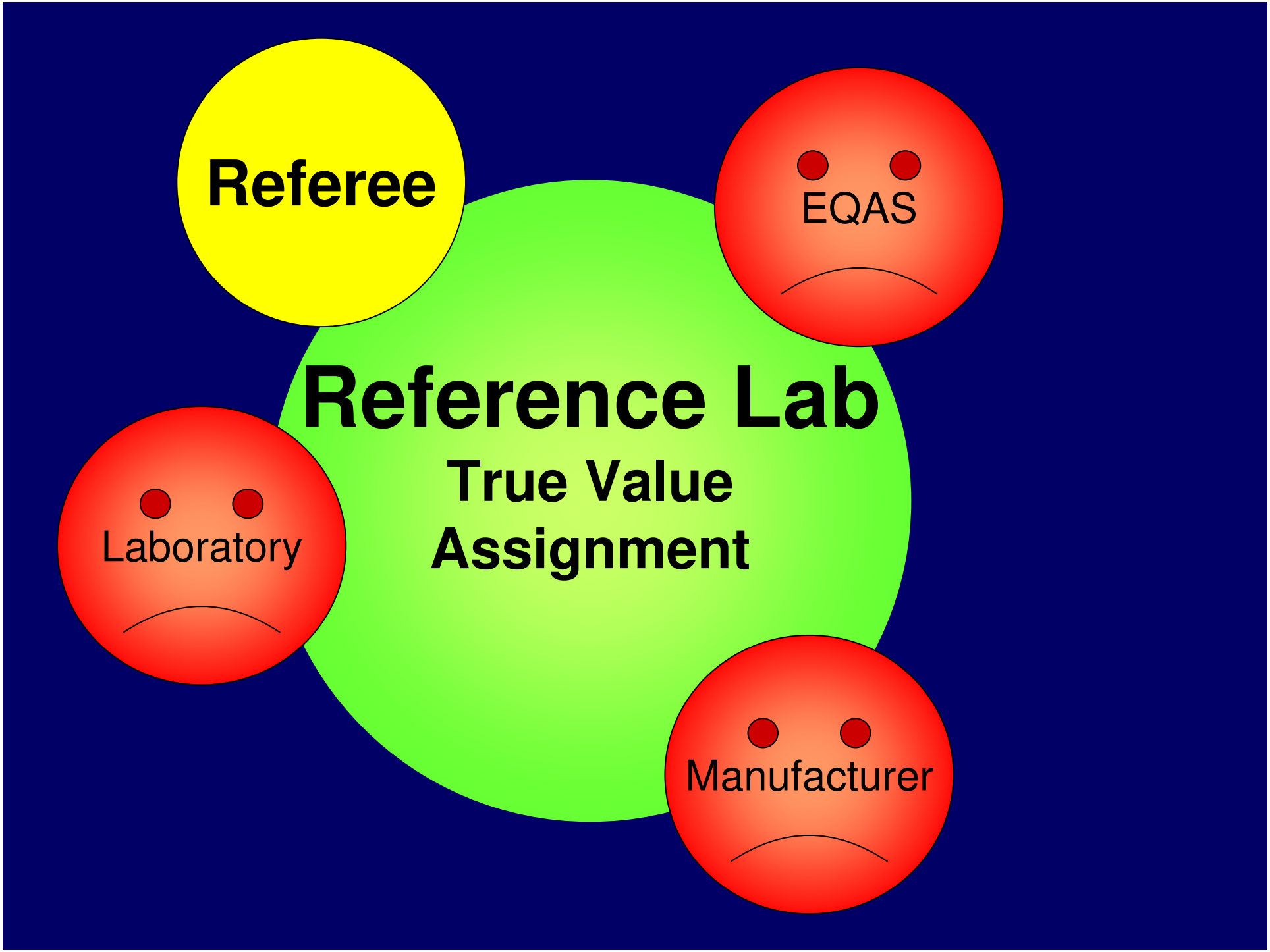

EQAS
Quality
Laboratorium
Manufacturer
“You have a poor EQAS

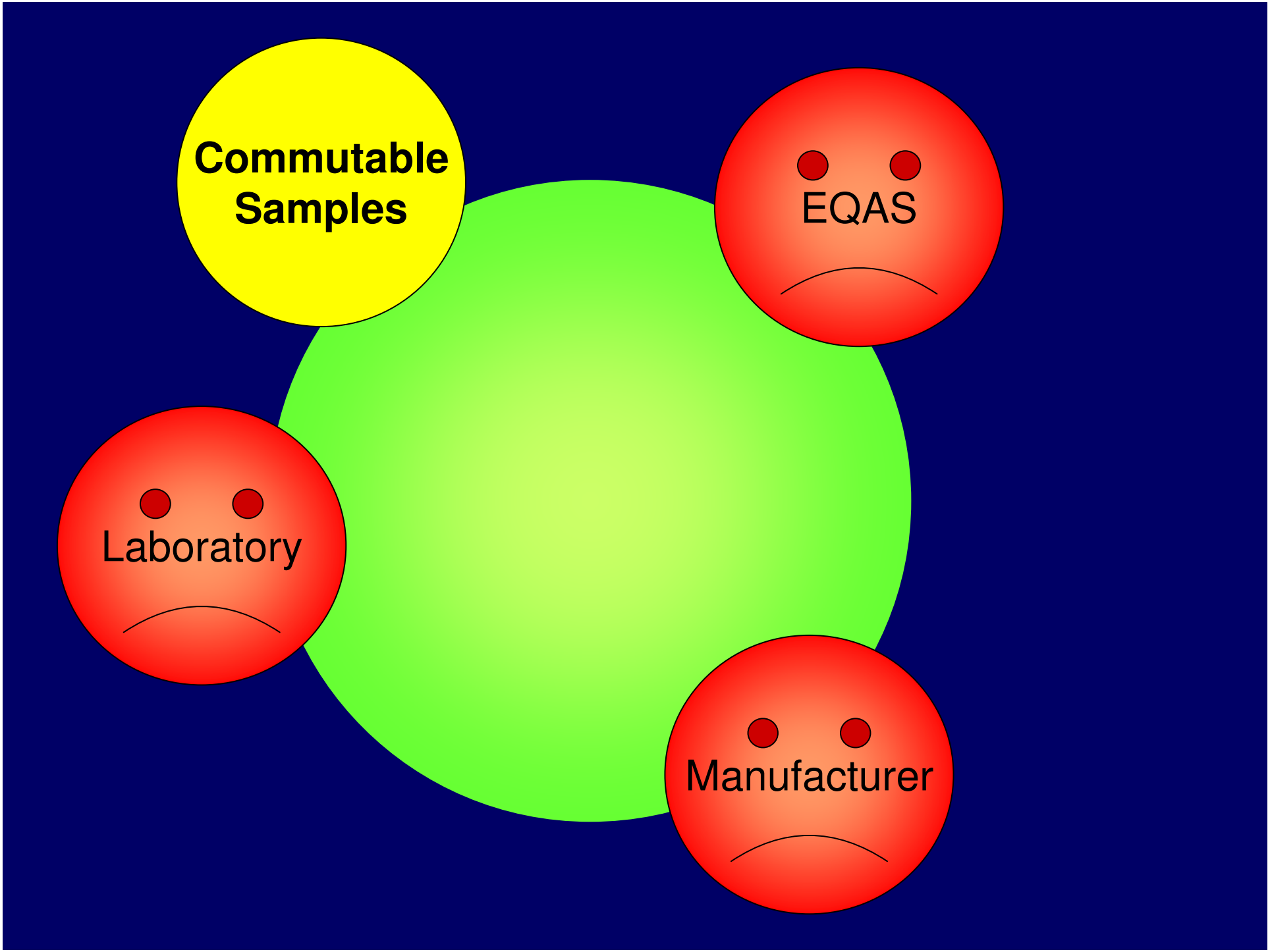

EQAS
Laboratory
Quality
"The Competitor has a Poor Test"
"The Competitor has a Poor Test
Manufacturer 1
Manufacturer 2

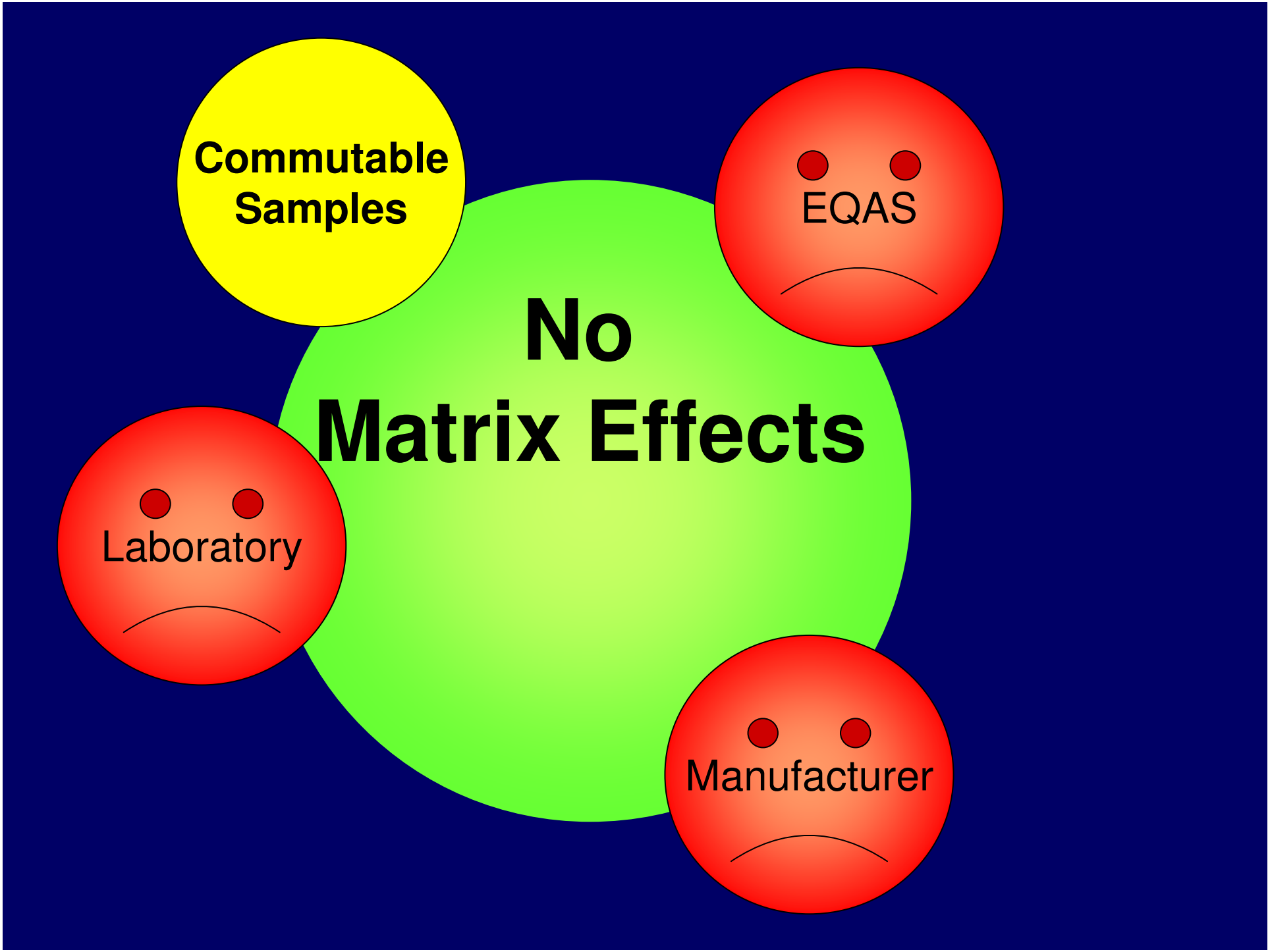

EQAS
Concert
of
Communications
Laboratory
Manufacturer


EQAS
How to escape
Vicious Circle?
Laboratory
Manufacturer


Referee
EQAS
Laboratory
Manufacturer


Referee
EQAS
Reference Lab
True Value
Assignment
Laboratory
Manufacturer


Commutable Samples
EQAS
Laboratory
Manufacturer


Commutable Samples
EQAS
No Matrix Effects
Laboratory
Manufacturer

Essentials EQAS

* Design EQA

* Commutable Specimens

* True Value Assignment

Design EQA

What we do not want……

EQA with ad hoc available specimens
On the Market

……But

Make a design for an EQA
Manufacture specimens in
Our ISO 13485 certified production unit

Commutable Specimens

General Chemistry

- Frozen Human Sera
- Spiked Recombinant Human Enzymes
- Spiked Minerals
- Shipment Dry Ice
- Commutabilty “Spy” Sample

Immunochemistry

- Lyophilised human serum
- Made commutable with CLP no. 5

HbA1c

- Lyophilised human lysate red cells
- Made commutable with CLP No. 3

(matrix effect 1 method of 3 mmol/mol – 0.3%)

True Value Assignment

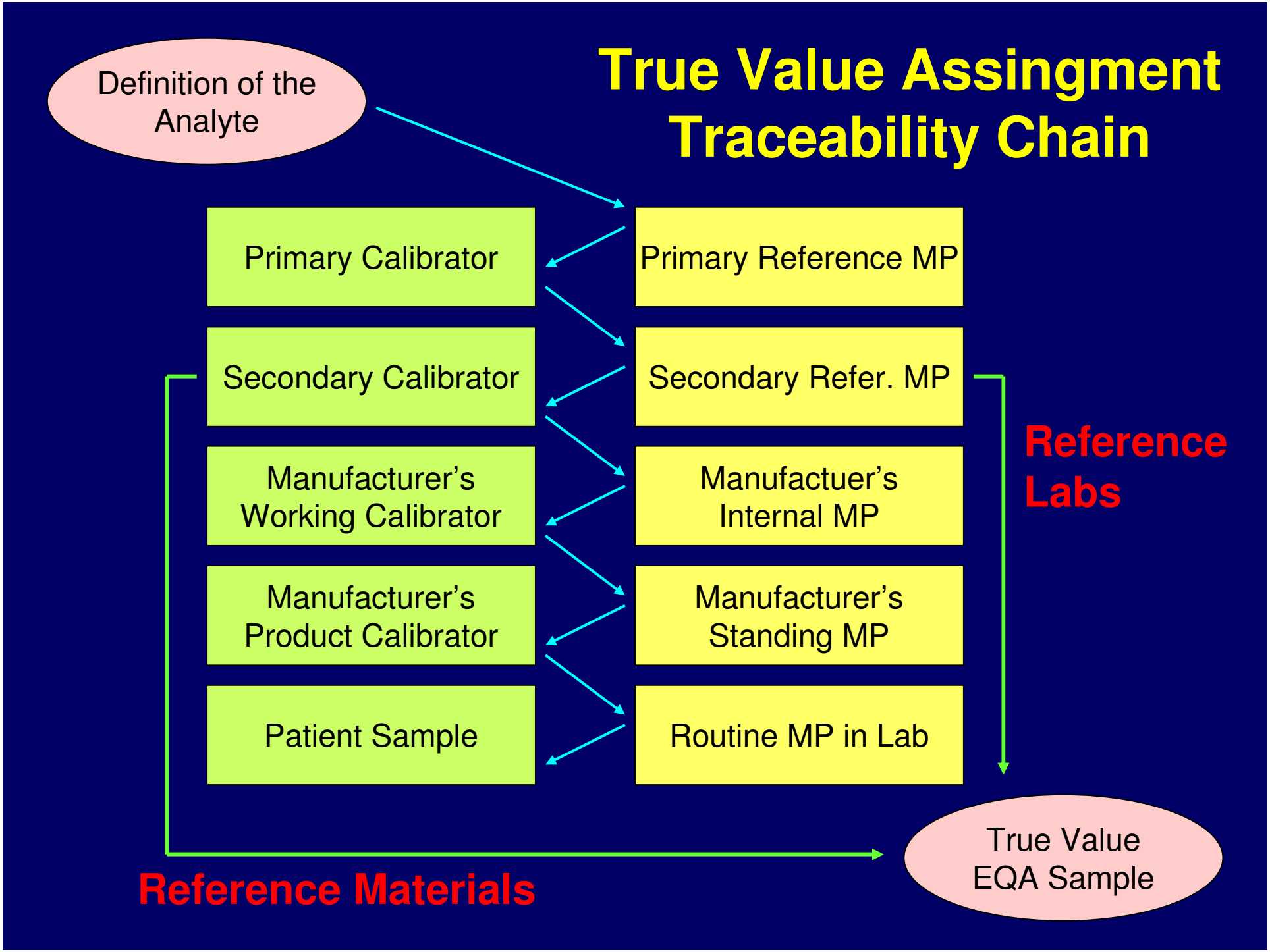
Concept

* Traceability Chain

Tools

* Measured with JCTLM endorsed Reference Measurement Procedure by Reference laboratory
* Calibrated with JCTLM endorsed Certified Reference Material

True Value Assingment Traceability Chain



Analyte	*Reference Lab/ Material*
Ca – Cl – K – Na – Glucose Total Protein – Li – Mg	Prof Reinauer, Dr. Kaiser Düsseldorf, Germany
Bilirubin	Prof. Schumann, Hannover, Germany
Creatinine	Prof. Siekmann, Dr. Kessler Bonn, Germany
HbA1c	Dr. Weykamp, Winterswijk, The Netherlands
Cholesterol – HDL	Prof. Lindemans Rotterdam, The Netherlands
ALAT – ASAT – GGT – LDH CK – Amylase	Dr. Franck The Hague, The Netherlands
IgG – IgM – IgA – Transf – Hapto AAT – AAT – C3c – C4	CRM 470a; IRMM

A nice Concept……..

……But does it work in Daily Practice?

Time for Examples

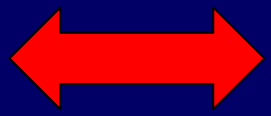
ALAT: True Value 61 U/L

Manufacturer	n	Mean	Interlab CV
Abbott	18	59	3%
Beckman	41	60	3%
Roche	128	59	2%
Siemens	21	60	3%
Overall	208	59	3%

Successfull Nation wide Standardisation
To IFCC Reference Measurement Procedure

GGT 2009: True Value 78 U/L

Manufacturer	n	Mean	Interlab CV
Abbott	18	77	3%
Beckman	45	68	12%
Roche	117	78	3%
Siemens	22	77	3%
Overall	202	75	3%



Observation: Problem Beckman users
Action SKML: Letter to Labs and Beckman
Result: Corrective Action Beckman/Labs

GGT 2010: True Value 85 U/L

Manufacturer	n	Mean	Interlab CV
Abbott	17	84	3%
Beckman	42	84	4%
Roche	128	85	3%
Siemens	21	86	3%
Overall	208	85	3%

Corrective Action Successfull
Nationwide Standardisation to IFCC
Reference Measurement Procedure restored

LD: True Value 393 U/L

Method Group	n	Mean	Interlab CV
IFCC	109	384	2%
Lactate	42	371	9%
Pyruvate	52	714	9%
Overall	not relevant		

Nationwide Confusion
SKML: Advise to standardise to IFCC RMP
Dispute: Quality versus Change Ref.Range

Creatinine: True Value 94 µmol/L

Method Group	n	Mean	Interlab CV
Jaffe	70	104	6%
Jaffe Comp.	42	101	8%
Enzymatic	107	94	3%
Overall	not relevant		

Enzymatic: Excellent
SKML: Advise Enzymatic Methods
Dispute: Quality versus Costs

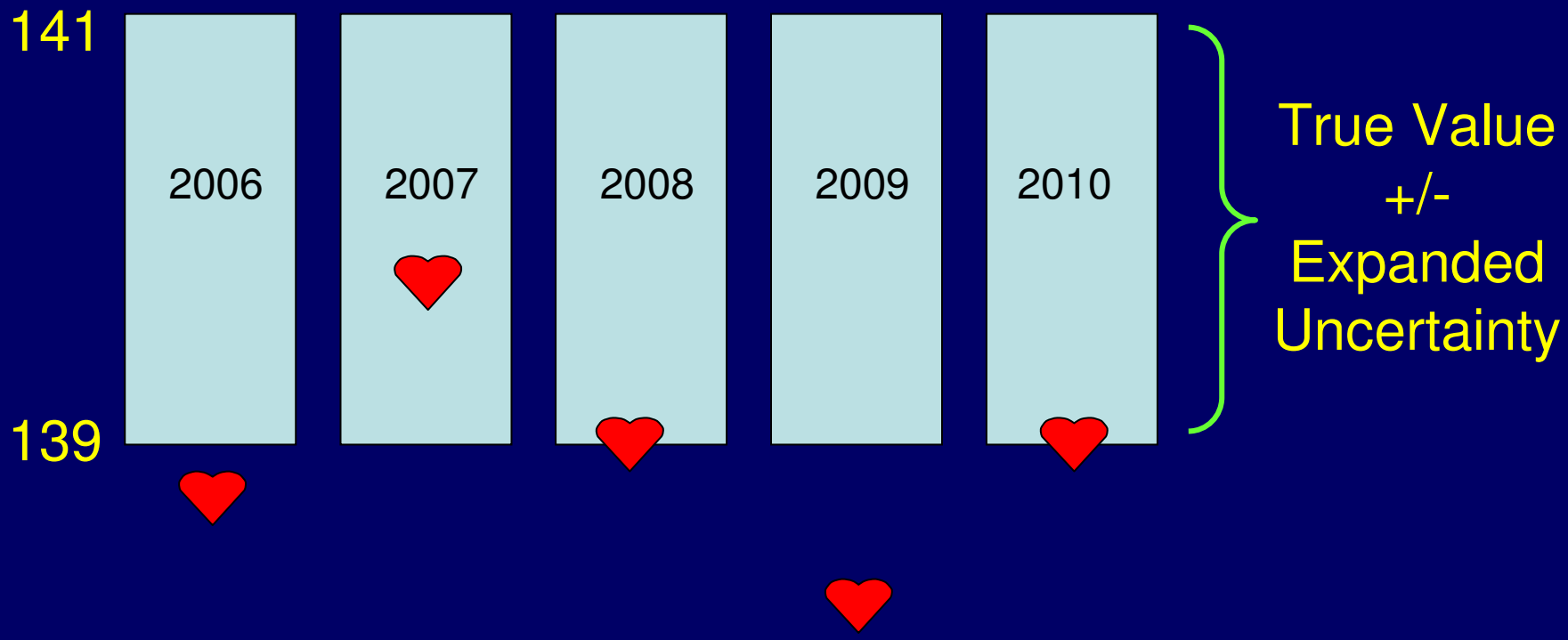
Creatinine e-GFR: True Value 53

Method Group	Mean	% Labs e-GFR >10%
Jaffe	50	21%
Jaffe Comp.	50	18%
Enzymatic	53	9%
Overall	not relevant	

e-GFR wrong due to Creatinine Method…..
……but also due to wrong MDRD equation
Action EQA: paper collaboration clinicians

Na: True Value 140 mmol/L

Ion Selective Methods



Substantial Uncertainty in True Value
Over 5 years: Significant Deviation ISM
But is this clinically relevant?
Present Status: under investigation

Immuno Chemistry

2003: Lyophilised Sample

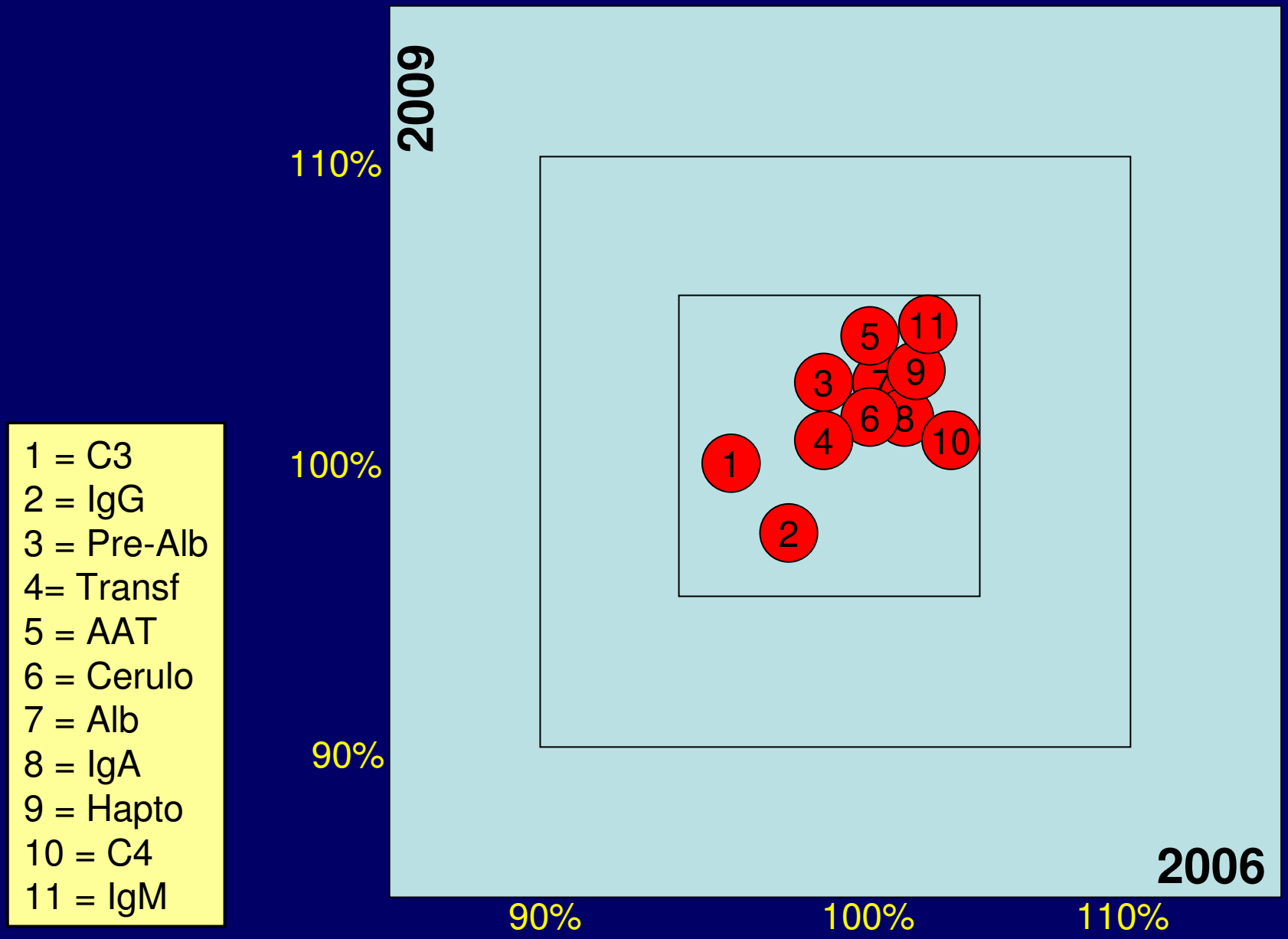
Calibrated: CRM 470

In EQA 2006 en 2009

Do labs measure True Value?

Method	n	Recovery		Interlab CV	
		2006	2009	2006	2009
AAT	50	101	104	8%	7%
Albumine	49	101	104	5%	6%
C3c	43	97	101	5%	6%
C4	43	104	101	5%	8%
Ceruloplasmin	23	100	101	9%	13%
Haptoglobin	79	101	104	5%	5%
Prealbumin	12	101	103	6%	4%
Transferrin	84	100	100	4%	5%
IgG	92	98	98	4%	6%
IgA	89	103	101	7%	6%
IgM	89	104	103	6%	7%
Overall		101	102	6%	7%

Recovery Proteins 2006 and 2009: Mean All Labs



1 = C3
2 = IgG
3 = Pre-Alb
4= Transf
5 = AAT
6 = Cerulo
7 = Alb
8 = IgA
9 = Hapto
10 = C4
11 = IgM

Conclusion

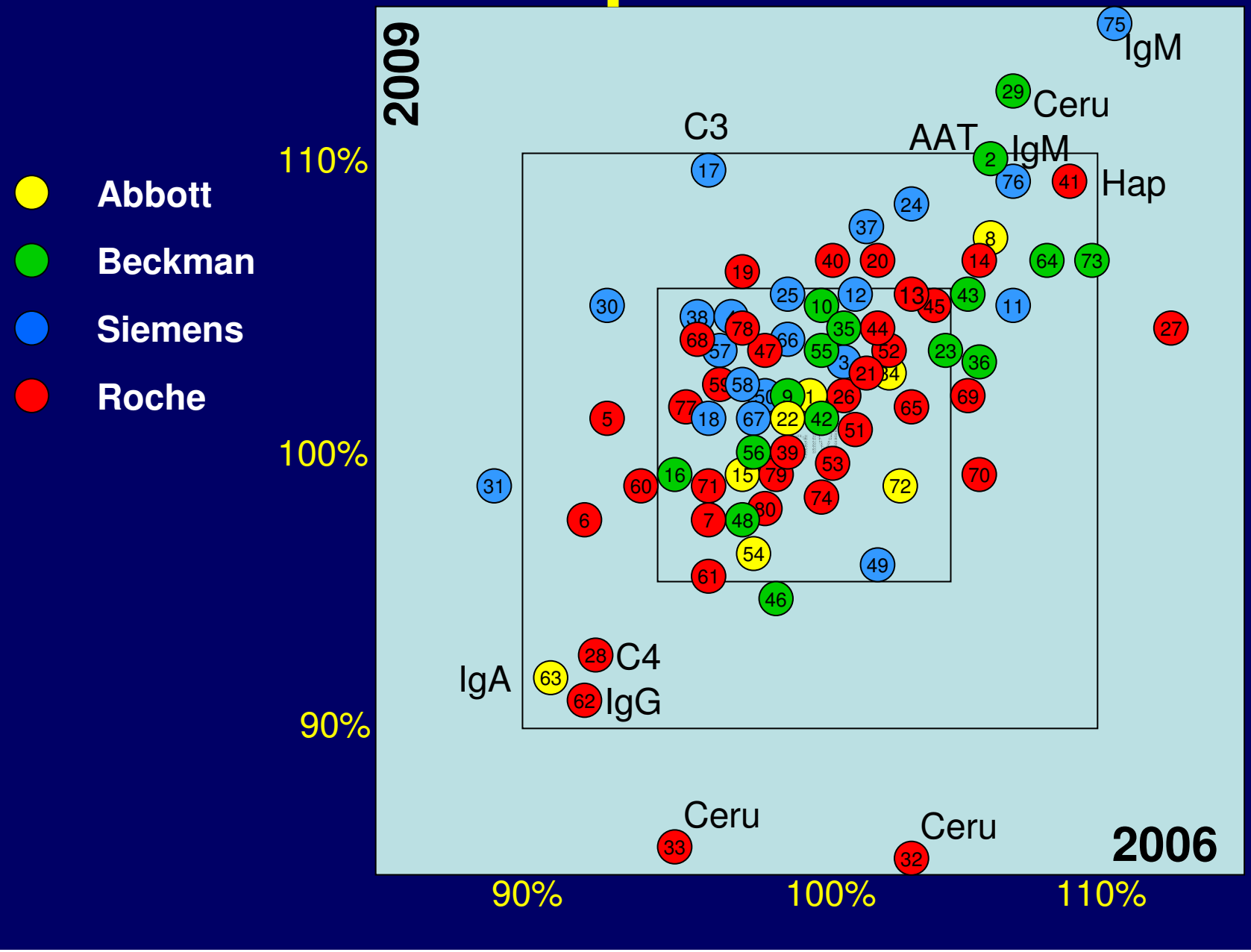
Overall:

Long-term Excellent Traceability

But:

Per Manufacturer?

11 Proteins – per Manufacturer



Conclusion

In general: OK

But:

Some Manufacturers may

Investigate

Traceability some proteins

HbA1c

* Long term Efforts IFCC WG and NGSP

* 2010: All Manufacturers Traceable IFCC RMP

* Effect on Quality?

HbA1c

* Long term Efforts IFCC [illegible] NGSP

* 2010: All Manuf[illegible]raceable
  IFCC [illegible]

* Effect[illegible] ?

HbA1c

* Long term Efforts IFCC V… …GSP

* 2010: All Manufac… …able
  IFCC RM…

* Effect or…

Cas do not talk to long on your hobby-horse

HbA1c: Trend Quality in 15 years

Year	*Deviation Target**	*Intralab CV*	*Interlab CV*
1993	----	5.2%	22.0%
1999	+3 (+0.3%)	4.9%	11.2%
2002	-1 (-0.1%)	3.4%	8.5%
2005	-2 (-0.2%)	2.9%	6.9%
2010	0 (0.0%)	1.9%	3.5%

* Mmol/mol (%NGSP)

EQA with True Value shows….

Method Manuf. X	Method Manuf. Y	Method Manuf. Z
Lab A	Lab G	Lab M
Lab B	Lab H	Lab N
Lab C	Lab I	Lab O
Lab D	Lab J	Lab P
Lab E	Lab K	Lab Q
Lab F	Lab L	Lab R

….Poor performing Individual labs

EQA with True Value shows

Method Manuf. X	Method Manuf. Y	Method Manuf. Z
Lab A	Lab G	Lab M
Lab B	Lab H	Lab N
Lab C	Lab I	Lab O
Lab D	Lab J	Lab P
Lab E	Lab K	Lab Q
Lab F	Lab L	Lab R

….Poor performing Methods/Manufacturers

EQA with True Value shows

Method Manuf. X	Method Manuf. Y	Method Manuf. Z
Lab A	Lab G	Lab M
Lab B	Lab H	Lab N
Lab C	Lab I	Lab O
Lab D	Lab J	Lab P
Lab E	Lab K	Lab Q
Lab F	Lab L	Lab R

….Poor Performing Profession

Many Examples showing that EQA programmes with commutable samples and traceable target values are effective….

….but what are the limitations of this concept?

Limitations (1)

1. No RMP or CRM for many analytes
2. Costs EQA organisers (samples/targeting)
3. Burden Reference Labs (accreditation)
4. How to handle Uncertainty?

Limitations (2)

5. Criteria Performance (state of the art, biological variation, clinical decision)

6. Reluctance to change (clinicians/costs)

7. Qualitative Tests?

8. Lack of knowledge (Traceability?)

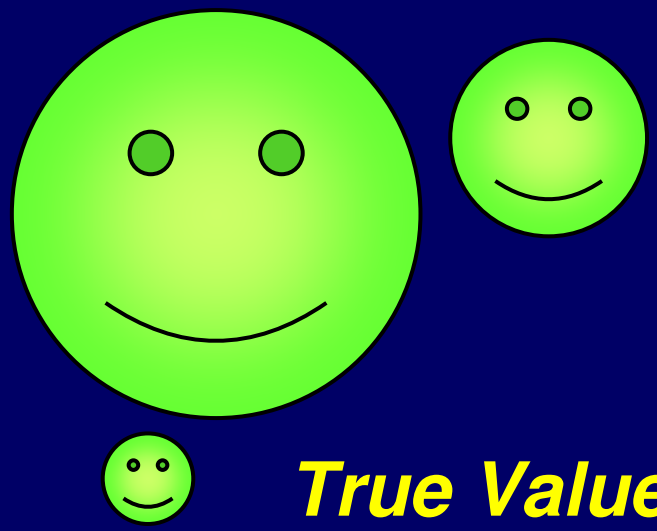
Summary

An EQA Programme, using commutable samples and traceable targets (true value assignment):

* Can irrefutably identify
  - poor performing individual labs,
  - poor performing methods/manufacturers
  - overall poor performance of the profession

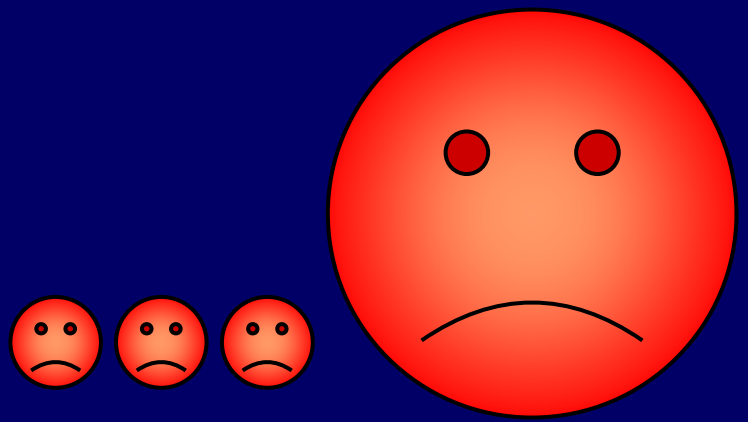
* Is an excellent tool to monitor Standardisation and harmonistaion efforts

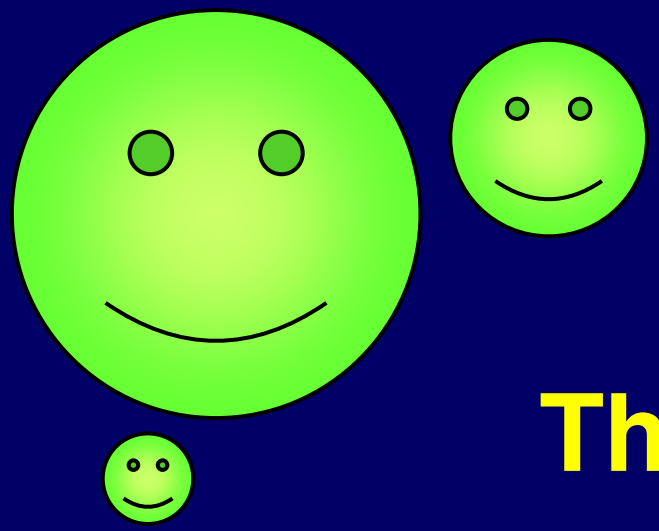
* In the long term: improves Quality

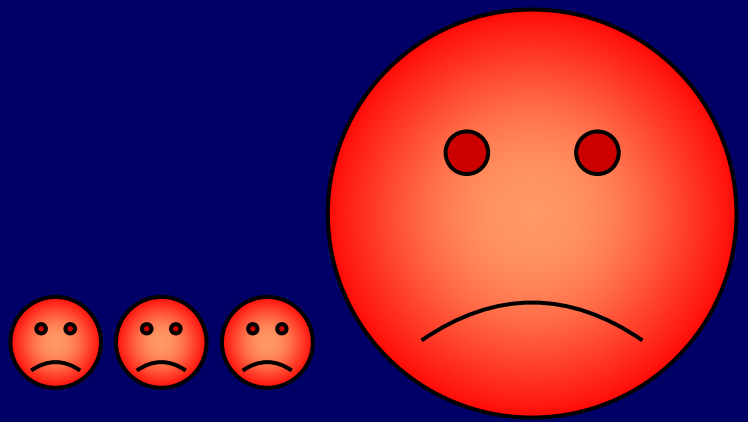


True Value Assignment to EQAS materials
A feasible task?

Yes!





Thank you for Your Attention…..

….And keep on Smiling!