MA SC

ICAR Sub-Commitee on Milk Analysis

ICAR Reference Laboratory Network

- 4th Meeting, Niagara Falls, 16 June 2008

- Agenda -

8.00 : Opening - Welcome - Round table for presentation

8.20 : Introduction : ICAR Reference Laboratory Network history and objectives
ICAR analytical strategy - International anchorage & harmonisation *(O. Leray, Cecalait, FR)*

8.50 : Interlaboratory reference systems and centralised calibration – Prerequisites and standard optimum procedures *(O. Leray, Cecalait, FR)*

9.10 : Discussion

9.40 : The way to reference systems and centralised calibration for milk recording testing - Present status in Germany *(C. Baumgartner, MPR, DE)*

10.00 : Health break

10.20 : Reference system and centralised calibration for milk recording testing in Argentina *(R. Castañeda, Inti-Lacteos, AR)*

10.40: Reference system and centralised calibration for milk (payment) testing in USA, *(D. Barbano, Cornell University, USA)*

11.00 : Assessment of laboratory performances and analytical equivalence in milk testing in North America, *(P. Sauvé, Canadian Laboratory Services, CA)*

11.30 : Discussion

12.00 - Closure of the meeting

- INTRODUCTION - GENERAL OBJECTIVES -

History : **ICAR Session in Ottawa1994,**
=> Analytical Quality Assurance (AQA) policy by ICAR

General objective : Develop an **international AQA system for DHI** based on harmonised laboratory practices.

Goal : **Confidence, equivalence, comparability**
=> within / between countries,
=> worldwide : international genetic evaluation.

Implementation by MA SC (MTL WG) :
> Guidelines for the harmonisation of analytical practices :
Analytical methods, Quality Assurance,

> International network of reference laboratories for milk recording analytical performances

ROLES OF THE LABORATORY NETWORK

ICAR Reference Laboratory Network is expected to operate as **an** international platform for milk recording as to

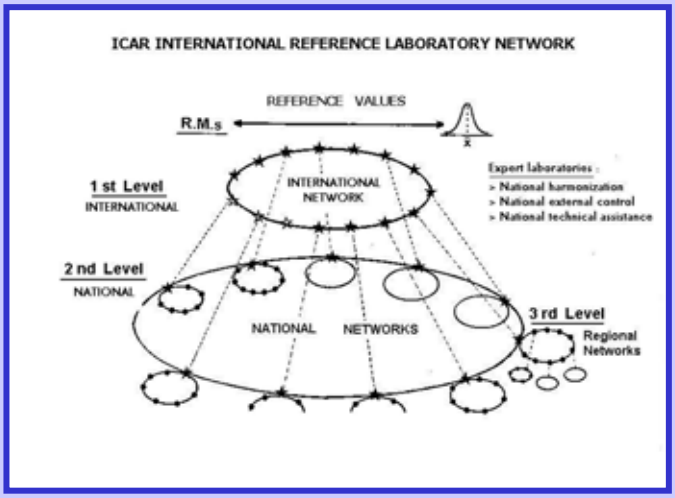
- diffuse/promote GLP and AQA based on international guides and standards => communication *(Internet, website)*

- provide precision traceability and anchorage to consensual international "true values" to routine labs via network members
=> analytical data harmonisation *(PTs, RMs)*

- a mean for developing collaborations for laboratory purposes
=> Co-operation *(Education, training)*

Model & explanation provided every year to ICAR member organisations

THEORETICAL STRUCTURE



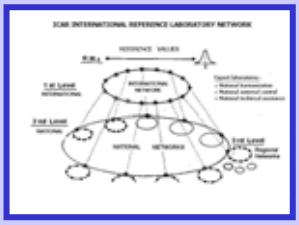
Missions / activities expected
- Eligibility criteria -

- 1- National ring test organizer
- 2- Reference Material supplier
- 3- Master laboratory for centralized calibration
- 4- Teaching and training in laboratory techniques
- 5- Information on analytical methods
- 6- Evaluation of analytical methods/instruments
- 7- Research on analytical methods
- 8- National regulatory control of analyses
- 9- Routine testing where only 1 or 2 labs/country

ICAR Reference Laboratory Network

Composition & evolution

from 1998 to 2008



ICAR Reference Laboratory Network

Membership in 2008

38 laboratory members from **32** countries as follows:

Argentina	(1)	Austria	(1)	Belgium	(2)	Canada	(1)
Cyprus	(1)	Czech Republic	(1)	Denmark	(1)	Estonia	(1)
Finland	(1)	France	(1)	Germany	(1)	Hungary	(1)
Ireland	(1)	Israel	(1)	Italy	(1)	Korea	(1)
Latvia	(2)	Lithuania	(1)	The Netherlands	(1)	New Zealand	(1)
Norway	(1)	Poland	(1)	Slovak Repub.	(1)	Slovenia	(1)
South Africa	(3)	Spain	(1)	Sweden	(1)	Switzerland	(1)
Tunisia	(2)	United Kingdom	(1)	U.S.A.	(2)	Zimbabwe	(1)

(n) : number of member(s)

among which : 38 members for cow
16 members for goat
14 members for sheep

ICAR Reference Laboratory Network

- Evolution since 1998 -

Evolution of the composition and national roles from 1998 to 2007 (end of year)

YEAR	NRTO	RMS	MLCC	TLT	IAM	EAMI	RAM	NRCA	DHIA	PAYMENT	Other anal.	Members
1998	15	16	13	13	16	1	11	2	2	1	1	23
1999	17	18	17	14	17	1	12	2	3	1	1	28
2000	16	21	19	15	19	1	13	3	5	1	1	33
2001	19	22	19	18	21	3	15	5	6	2	1	35
2002	20	23	19	19	23	8	15	8	11	5	1	37
2003	21	26	19	21	24	12	16	9	14	7	3	38
2003	21	26	19	21	24	12	16	9	14	7	3	38
2004	25	26	18	20	24	14	16	9	16	9	3	38
2005	24	24	17	19	22	13	15	10	15	8	3	37
2006	24	24	17	20	22	14	15	10	15	10	3	36
2007	22	24	18	22	24	17	17	13	17	13	3	38

NRTO = National Ring Test Organiser
TLT = Training in Laboratory Techniques
RAM = Research on Analytical Methods
Membership = Officially nominated by ICAR National Committees

RMS = Reference Material Supplier
IAM = Information on Analytical Methods
NRCA = National Regulatory Control of Analyses

MLCC = Master Laboratory for Centralised Calibratio
EAMI = Evaluation of Analytical Methods/Instruments
DHIA = Dairy Herd Improvement Analyses
Payment = Analyses for milk payment

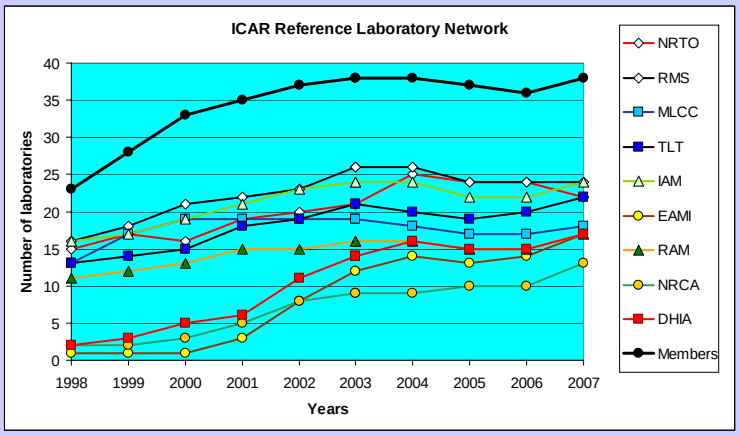
Evolution of the proportions of national roles from 1998 to 2007 (end of year)

YEAR	NRTO	RMS	MLCC	TLT	IAM	EAMI	RAM	NRCA	DHIA	PAYMENT	Other anal.	Members
1998	68	73	59	59	73	5	50	9	9	5	5	100
1999	63	67	63	52	63	4	44	7	11	4	4	100
2000	48	64	58	45	58	3	39	9	15	3	3	100
2001	54	63	54	51	60	9	43	14	17	6	3	100
2002	54	62	51	51	62	22	41	22	30	14	3	100
2003	55	68	50	55	63	32	42	24	37	18	8	100
2004	66	68	47	53	63	37	42	24	42	24	8	100
2005	65	65	46	51	59	35	41	27	41	22	8	100
2006	67	67	47	56	61	39	42	28	42	28	8	100
2007	58	63	47	58	63	45	45	34	45	34	8	100

Eligibility criteria declared in 2008

Criteria number N	Proportion %	Lab number with N	Lab % with N	Lab number with at least N	Lab % with at least N
8	100%	5	13%	5	13%
7	88%	4	11%	9	24%
6	75%	4	11%	13	34%
5	63%	4	11%	17	45%
4	50%	7	18%	24	63%
3	38%	3	8%	27	71%
2	25%	2	5%	29	76%
1	13%	4	11%	33	87%
0	0%	5	13%	38	100%

Evolution of membership and missions/activities from 1998 to 2008



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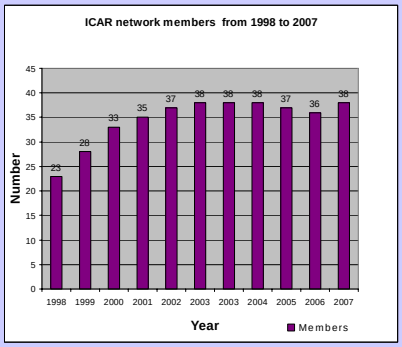

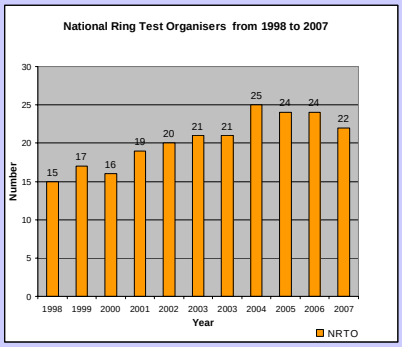

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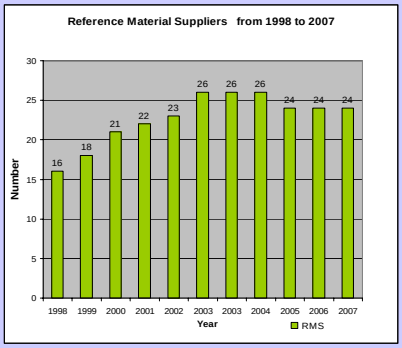

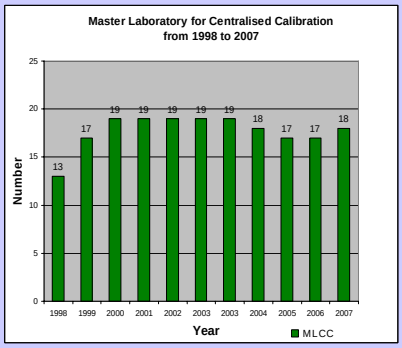

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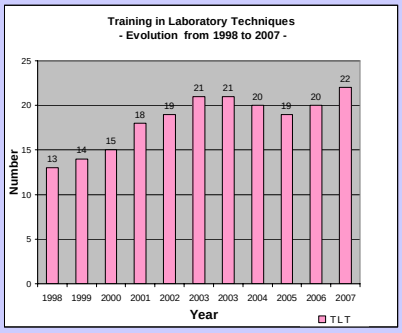

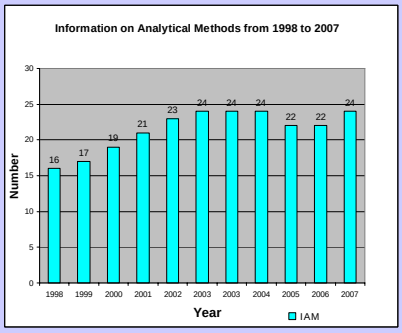

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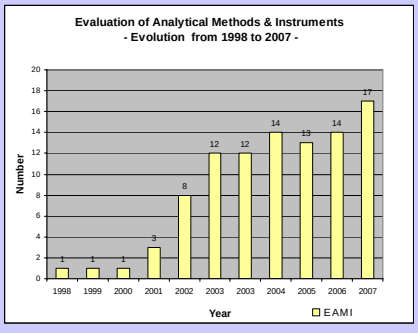
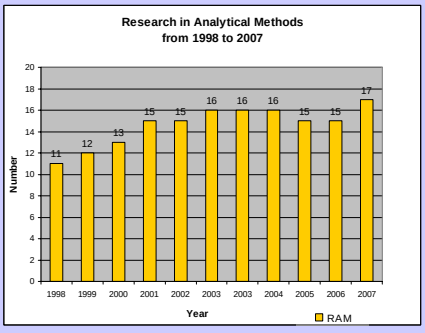
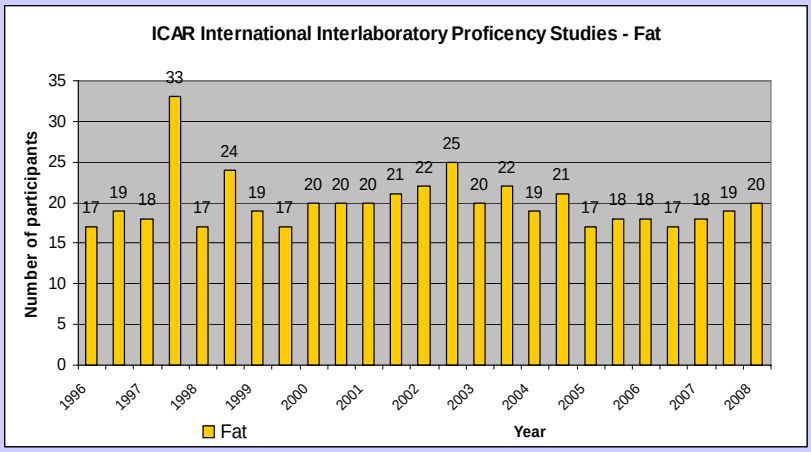




International interlaboratory proficiency studies

From 1996 :	International proficiency scheme organised by ICAR
Frequency :	twice a year
Participants :	members of ICAR ref lab Network
Analytical methods :	- reference methods to calibrate routine methods for fat, protein and lactose
	- methods for urea somatic cell counting
Type of milk :	cow milk

Participation in international proficiency studies from 1998 to 2008



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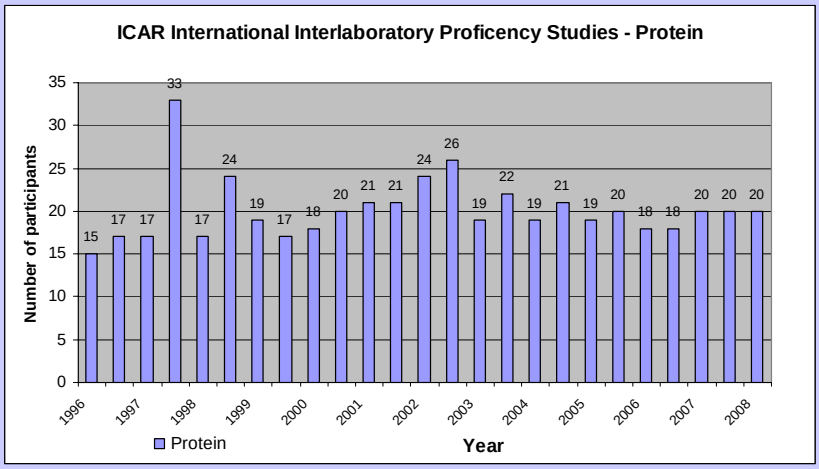
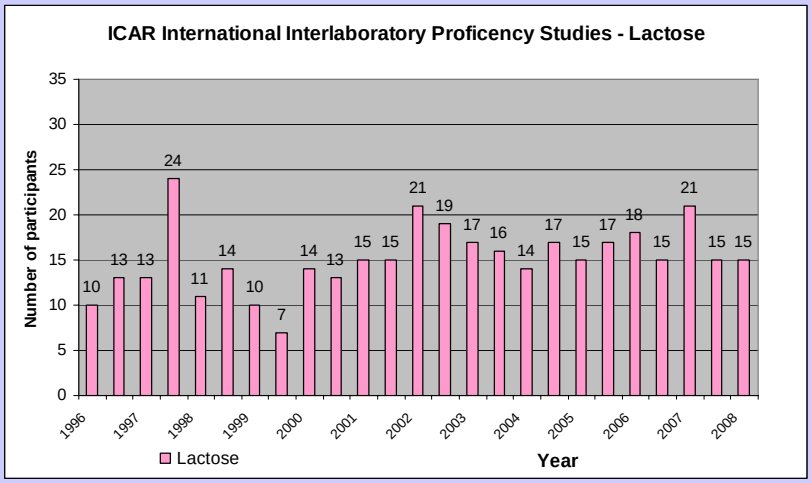
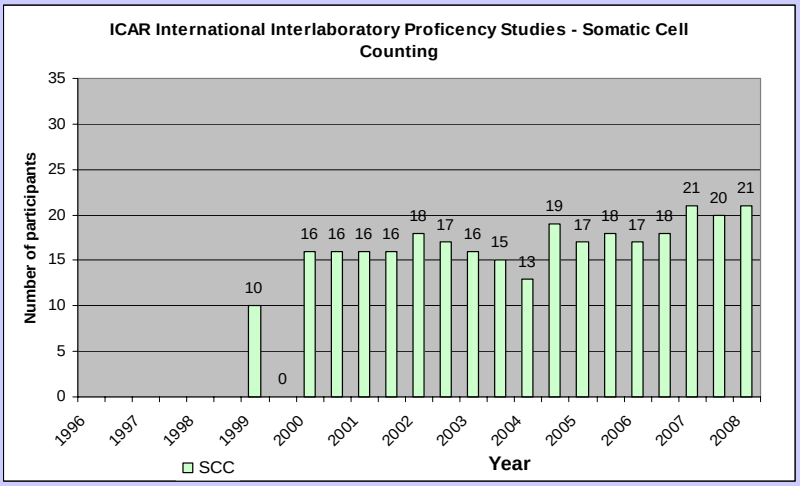


Participation in international proficiency studies from 1998 to 2008



Participation in international proficiency studies from 1998 to 2008



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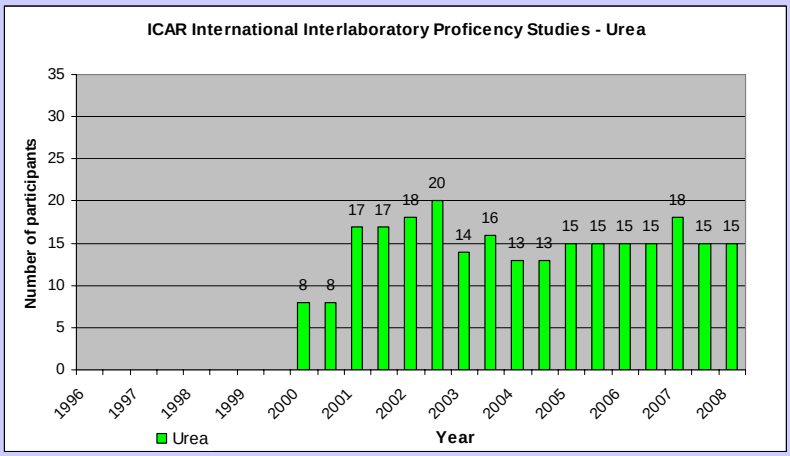


CONCLUSION ON THE NETWORK IMPLEMENTATION

Nominations by national organisations :

- **Number :** Stability from 2003 around 38 members
  ⇒ growth completed

- **Qualification :** Increase of mission numbers (eligibility criteria)

International Proficiency Testing schemes :

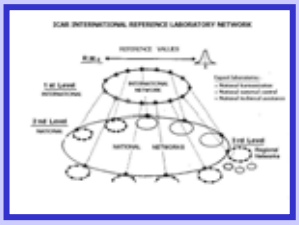
- Regular participation of about 50% of laboratory network members

- Improvement of performance from 2003

ICAR AQA Strategy

International anchorage & harmonisation

Olivier Leray, Cecalait, France



ICAR analytical anchorage

Intent

> to establish links from local/national/regional levels to the international level

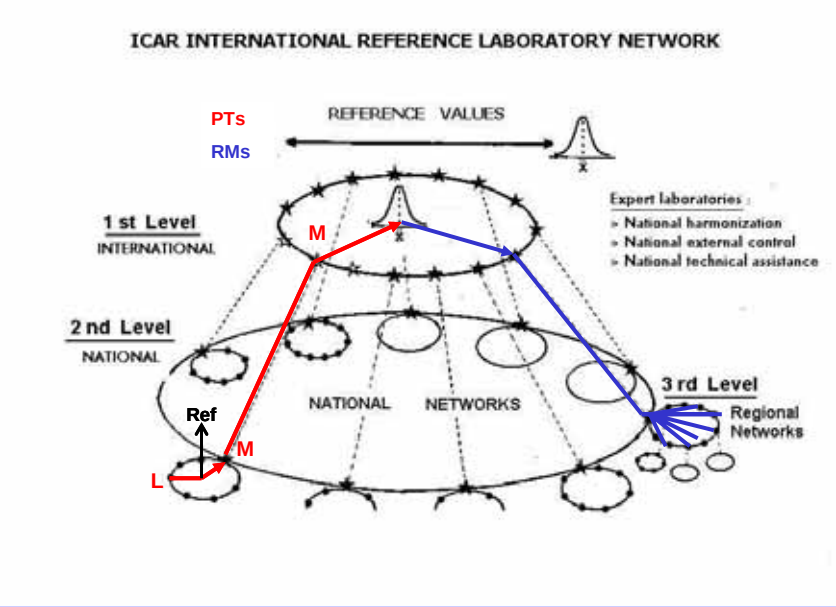
> to harmonise laboratories on a international collective reference

Means

> Guidelines, standards, GLP, AQA

> Interlaboratory proficiency studies ⇒ lab trueness traceability

> Reference materials ⇒ trueness improvement



Requirements for the reference

1- Technical :

⇒ Use of international reference methods (IDF/ISO)

⇒ Compliance with precision figures of the methods

2- Statistical : Unbiased and low uncertainty

⇒ sufficient number, representativeness of participants

3- Political/economical : recognition for the purpose

⇒ consensus of participants / organisations based on representativeness

For international genetic evaluation (Interbull), it should be built from results of laboratories from different countries !!!

Possible uses of interlaboratory proficiency studies

1- Measuring laboratory performance

2- Measuring result uncertainty

3- Comparing laboratories (assess equivalence)

4- Providing traceability to international reference

5- Qualifying/selecting reference/expert laboratories

6- Assessing/certifying reference materials

1- Measuring laboratory performance

Laboratory L

- participates with p laboratories, q samples in n replicates
- the estimate of sample S true value is $\bar{X}_S$
- means of n replicate (average) are x_{Lk}
- level score (individual bias) is $d_{Lk} = \bar{x}_{Lk} - \bar{X}_S$

Laboratory score = Average of q level scores :

$$\bar{d}_L = \sum \bar{d}_{Lk} / q \quad \text{also} \quad \bar{d}_L = \bar{x}_L - \bar{X}$$

Additionally:

- standard deviation of repeatability sr_L
- standard deviation of differences sd_L
- Euclidian distance (equivalent to SEP) $D = (\bar{d}_L^2 + sd^2)^{1/2}$

Within lab reproducibility : $sR_L^2 = sr^2.(1-1/n) + \bar{d}_L^2 + sd^2$

Evaluation example : ICAR PT scheme (10 samples in duplicates)

DETERMINATION of FAT in RAW (cow) MILK - page 1/6

Tableau I : **Ranking of the laboratories**

Units : g / 100 g

Nb	%	N°	d	Sd	D
1	5	1	+ 0,002	0,004	0,004
2	10	6	+ 0,001	0,005	0,005
3	15	8	+ 0,003	0,004	0,005
4	20	18	+ 0,004	0,004	0,005
5	25	3	- 0,002	0,005	0,005
6	30	13	- 0,000	0,005	0,005
7	35	10	- 0,001	0,005	0,005
8	40	12	- 0,006	0,005	0,008
9	45	2	+ 0,004	0,008	0,009
10	50	20	- 0,007	0,007	0,010
11	55	14	+ 0,007	0,007	0,010
12	60	17	+ 0,009	0,005	0,010
13	65	15	+ 0,005	0,010	0,011
14	70	11	- 0,009	0,007	0,012
15	75	7	+ 0,009	0,009	0,013
16	80	16	+ 0,002	0,013	0,013
17	85	5	+ 0,011	0,007	0,014
18	90	9	+ 0,001	0,017	0,017
19	95	19	- 0,023	0,008	0,024
20	100	4	- 0,023	0,012	0,026

(NC : OUT of RANKING because of insufficient data number)
(Nb : laboratory rank; % : relative rank)
(N° : laboratory identification number)
(d et Sd : mean and standard deviation of the differences (laboratory -reference))
(D : Euclidian distance to YX-axis origin = SQUARE ROOT.(d^2 + Sd^2))

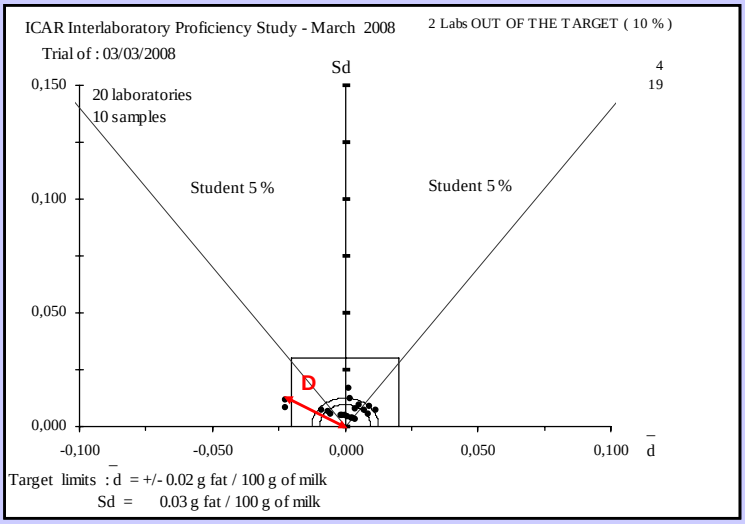
The table should be studied in parallel with figure 2 where the laboratories are located according to an acceptability area (or target) the limits of which are :

+/- 0,02 g / 100 g for $\bar{d}$ and 0,03 g / 100 g for Sd

The reference values are the average values of 20 laboratories having used the extraction method and after outlier discarding using Grubbs test at 5 % risk level.

Note : Limits are only indicative and so far do not constitute standard values; they indicate what is normally reachable by labs for their self evaluation.

Evaluation example : ICAR PT scheme (10 samples in duplicates)



2- Measuring test result uncertainty

Estimation from several ($N_t \geq 8$) last successive PT trials

ISO 5725-2: *(replacing laboratory variable by trials)*
Precision of Laboratory L ⇒ $\mathbf{sr_{L,ref}}$ and $\mathbf{sR_{L,ref}}$

ISO 5725-6: Reference method for *q samples and n replicates*

uncertainty $= \pm u_{0.975} .[sR_{L,ref}^2 - sr_{L,ref}^2.(1-1/nq)]^{1/2}$

(in calibration) $\approx \pm u_{0.975} .(sR_{L,ref}^2 - sr_{L,ref}^2)^{1/2}$ (1)

ISO 8196: Routine (alternative) method

uncertainty $\approx \pm u_{0.975} . (sR_{L,alt}^2 + s_{y,x}^2)^{1/2}$ (2)

From (1) + (2) ⇒ Overall uncertainty of routine testing results

$$\mathbf{\approx \pm u_{0.975} .(sR_{L,ref}^2 - sr_{L,ref}^2 + sR_{L,alt}^2 + s_{y,x}^2)^{1/2}}$$

3- Comparing laboratories

Same PT study

With scores of laboratories L1 and L2

$$\bar{d}_{L1} = \bar{x}_{L1} - \bar{X} \quad \text{and} \quad \bar{d}_{L2} = \bar{x}_{L2} - \bar{X}$$

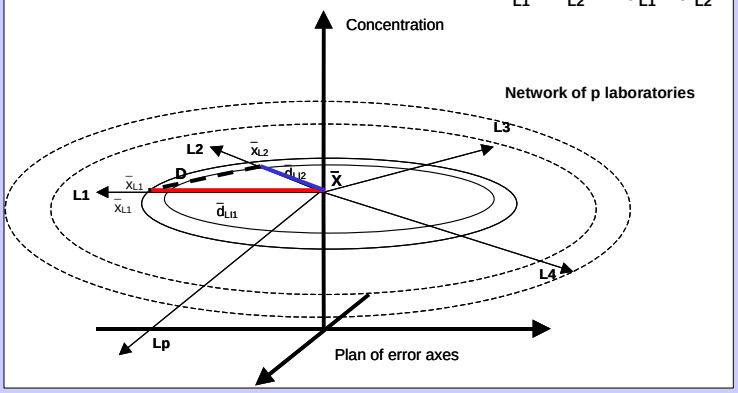
Between lab performance comparison is made through the difference

$$\bar{d}_{1,2} = \bar{x}_{L1} - \bar{x}_{L2} \quad \Leftrightarrow \quad \bar{d}_{1,2} = \bar{d}_{L1} - \bar{d}_{L2}$$

Comparison between laboratories L_1 & L_2

Figure 1 – Between laboratory comparison through an interlaboratory study

$$D = \bar{x}_{L1} - \bar{x}_{L2} = \bar{d}_{L1} - \bar{d}_{L2}$$



4- International laboratory anchorage

Parallel national and international PT studies

Thanks to scores of the reference laboratory M

in national study $\bar{d}_{MN}$

in international study $\bar{d}_{MI}$

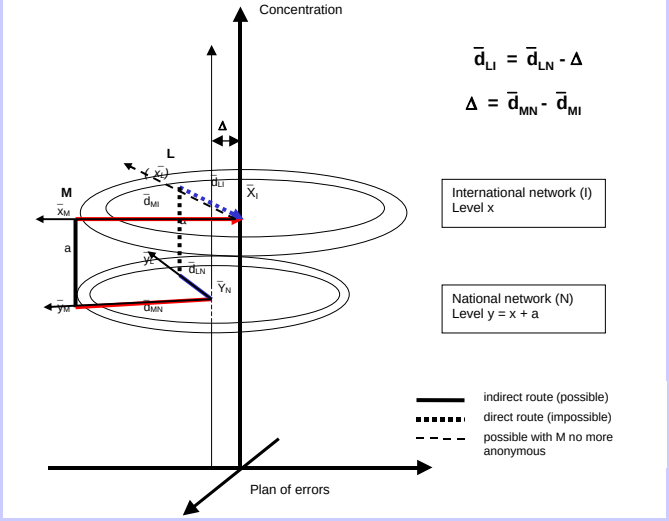
the virtual error between reference $\Delta = \bar{d}_{MN} - \bar{d}_{MI}$

the effective score of Lab L in the national study $\bar{d}_{LN} = \bar{x}_L - \bar{X}_N$

the **virtual international score of Laboratory L** is

$$\bar{d}_{LI} = \bar{d}_{LN} - \Delta = \bar{d}_{LN} - \bar{d}_{MN} + \bar{d}_{MI}$$

4- International laboratory anchorage



3- Indirect laboratory comparison

Different PT studies

Thanks to scores of reference laboratories M1 and M2

in national studies $\bar{d}_{MN1}$ and $\bar{d}_{MN2}$

in international studies $\bar{d}_{MI1}$ and $\bar{d}_{MI2}$

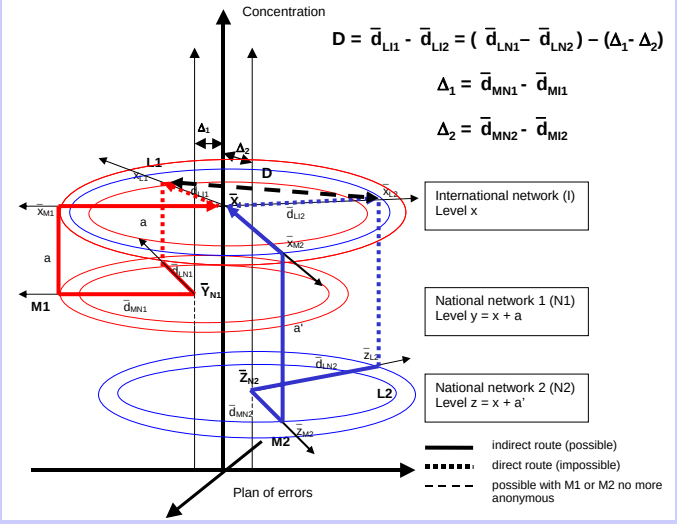
the virtual bias between reference $\Delta_1 = \bar{d}_{MN1} - \bar{d}_{MI1}$ and $\Delta_2 = \bar{d}_{MN2} - \bar{d}_{MI2}$

the effective scores in national studies $\bar{d}_{LN1} = \bar{x}_{L1} - \bar{X}_{N1}$ and $\bar{d}_{L2} = \bar{x}_{L2} - \bar{X}_{N2}$

the **virtual international difference between laboratories L1 and L2** is

$$D = \bar{d}_{LI1} - \bar{d}_{LI2} = (\bar{d}_{LN1} - \bar{d}_{LN2}) - (\Delta_1 - \Delta_2)$$

Comparison between laboratories L_1 & L_2



5- Qualifying/selecting reference laboratories

Required regular good performance in PTs

RMs certification :

> Regular score compliance in a number of successive trials

Laboratory anchorage :

> Regular score compliance throughout time

> Constant bias (better 0) ⇔ $sR_{L,ref} \approx sr_{L,ref}$

Means of success : Trueness adequacy and stability ensured through RMs and special training, competence, caution.

6- Assessing/certifying reference materials

Focus is given to reference values determination and reference material quality

ICAR protocol :

> Experimental design for PTs also possible for RMs

> Both tools are dedicated to calibration :
⇒ same concentration ranges
⇒ same sample numbers

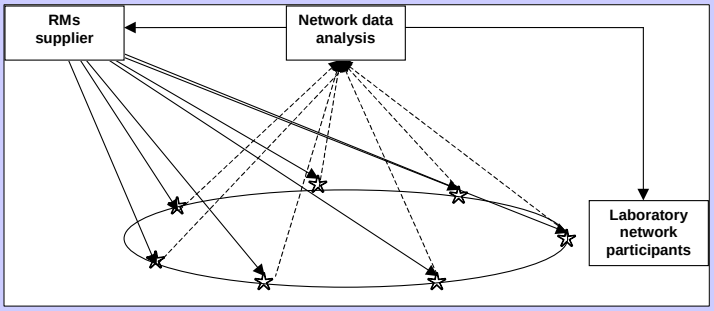
Combined use is possible provided respective specific caution :

- Reference values: according to **ISO 5725-4** with uncertainty

- Laboratories : Qualified / selected on performance for the lowest uncertainty

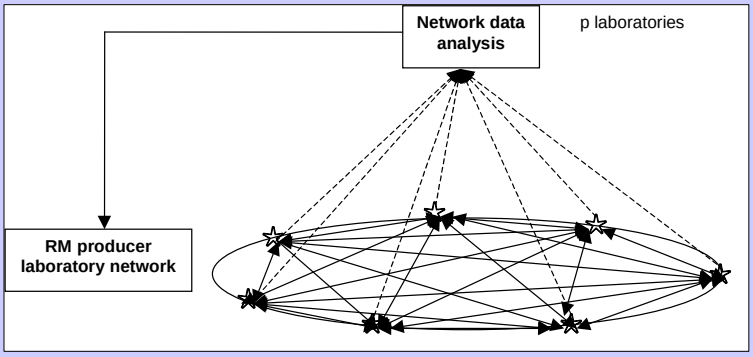
- Experimental design: Consider long term homogeneity/stability

Example : Central RM system



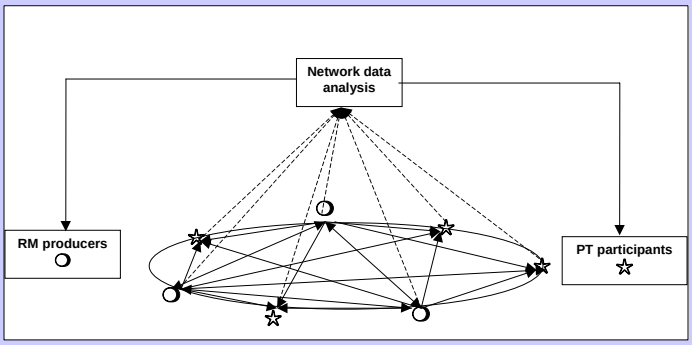
General model : Numerous laboratories and samples ; robust reference

Example : Multiple RM system = crossed system



Specific model : Homogeneous laboratory groups ; numbers of laboratories and samples limited ; good performance must compensate small laboratory number ; consensus on group reference better than individual

Example: Mixed system



Intermediate model : Heterogeneous laboratory groups ; a few laboratories address samples to a larger group ; samples number still limited ; more robust reference

Conclusion

International anchorage

can provide objective elements on :

- the overall accuracy & uncertainty of milk testing
- the (degree of) analytical equivalence within ICAR

⇓

ICAR International Reference Laboratory Network

corner stone for analytical harmonisation in milk recording

- Agenda -

8.00 : Opening - Welcome - Round table for presentation

8.20 : Introduction : ICAR Reference Laboratory Network history and objectives
ICAR analytical strategy - International anchorage & harmonisation *(O. Leray, Cecalait, FR)*

8.50 : Interlaboratory reference systems and centralised calibration – Prerequisites and standard optimum procedures *(O. Leray, Cecalait, FR)*

9.10 : Discussion

9.40 : The way to reference systems and centralised calibration for milk recording testing - Present status in Germany *(C. Baumgartner, MPR, DE)*

10.00 : Health break

10.20 : Reference system and centralised calibration for milk recording testing in Argentina
(R. Castañeda, Inti-Lacteos, AR)

10.40: Reference system and centralised calibration for milk (payment) testing in USA,
(D. Barbano, Cornell University, USA)

11.00 : Assessment of laboratory performances and analytical equivalence in milk testing in North America,
(P. Sauvé, Canadian Laboratory Services, CA)

11.30 : Discussion

12.00 - Closure of the meeting

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