Contribution of EQA in the evaluation and follow-up of serological methods in Virology

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CTCB

- CTCB is a non-profit-making association of medical biologists that proposes EQA programs in several fields of medical biology. It is accredited (NF EN ISO/CEI 17043) by the French accreditation committee (COFRAC)

- The virology laboratory of Toulouse University Hospital, in charge of biological expertise and samples preparation for serological and molecular programs of Virology, is also accredited (NF EN ISO 15189)

- Accreditation of medical analysis laboratories is now mandatory in France. Internal validation of the methods used in laboratories is a critical point of the accreditation process

Validation of methods in Virology

➢ In virology, serological methods are used to detect viral antigens and more frequently serum antibodies against virus

➢ Although results are generally expressed in a qualitative way (NEGATIVE / POSITIVE), these methods are regarded as quantitative because interpretation is based on a continuous and quantifiable signal (absorbance, chemiluminescence unitsÅ)

➢ The aim of this presentation is to illustrate the potential contribution of EQA to validate serological methods in virology with some examples from our experience in CTCB programs
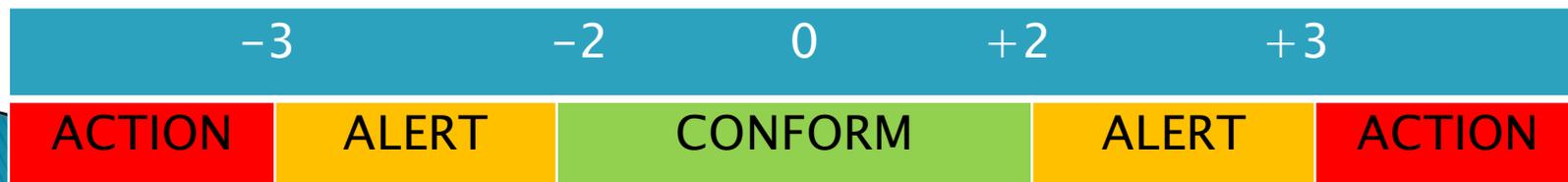
Accuracy

Accuracy is evaluated by the interpretation of the bias expressed by the z-score

Since numeric results are rarely standardised, comparison must be performed by peer groups using the same reagent

But even with the same reagent, results expression may vary. Thus it is necessary to obtain relative values such as ratios or index and not raw data

➢ Statistical treatment
  ◦ Elimination of absurd values (over MEDIAN +/- 50%)
  ◦ Determination of strong **MEAN (Ms)** and **STANDARD DEVIATION (SDs)** for each reagent (norm ISO 13 528) > **Assigned values of the peer group**

➢ Determination of the « z » score : **(Result Ë Ms) / SDs**

−3	−2	0	+2	+3
ACTION	ALERT	CONFORM	ALERT	ACTION

Accuracy

Example : IgG antibodies against rubella virus

Votre résultat quantitatif	Seuil	Votre technique : ABBOTT - Architect			
		N	Moyenne	Ecart-type	CV
= 37,1	10	91	27,05	1,68	6,22

Votre score : > 3

Result

Assigned values

Lower Limit of detection

- Lower limit of detection is a critical point that needs to be evaluate for the choice and follow-up of methods

- For some parameters, and particularly in the field of Virology, the Common Technical Specifications published in 2009 fixed precise exigencies for obtaining C.E. approval

- For example the lower limit of detection for HIV p24 Ag assays is 2 IU/mL against the WHO standard. Thus we used this standard to prepare a sample adjusted at this level in HIV serological EQA programs

Lower Limit of detection

Example : HEV IgG antibodies

FALSE NEGATIVE

1   Sérologie HEV

1.1   Sérum 1331 - IgG

Analyse des réponses qualitatives

Trousses	N	%	Négatif	Douteux	Positif =Assigné
ADALTIS - EIAgen HEV G	6	37,5	6	0	0
DIAPRO - HEV IgG EVG.CE	1	6,25	0	0	1
WANTAI - HEV Elisa IgG	9	56,3	0	0	9
TOTAL	16	100%	6	0	10

IgG prevalence in Midi-Pyrénées:15%

IgG prevalence in Midi-Pyrénées: 50%

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Comparison of methods

➢ **Some serological assays in Virology results are expressed in international units (anti-HBs or anti-rubella antibodies)**

➢ **Data analysis are interesting but disturbing since it demonstrated a lack of correlation between assays although they are calibrated upon the same standard**

Comparison of methods

Example : Rubella IgG (IU/mL)

Analyse des réponses quantitatives

Trousses	N	N*	Min*	Max*	Moy r	ET r	CV r
ABBOTT - Architect	95	95	35,8	49,7	43,2	2,24	5,2
ABBOTT - Axsym	8	8	39,5	63,7	57,2	6,43	11,2
BECKMAN - Access	16	16	47,7	90	71	13,6	19,2
BECKMAN - Unicel DxI 600/800	39	39	48,1	94	69,5	8,02	11,5
BIOMERIEUX - Vidas Rubéole IgG II	57	57	58	93	75,7	7,47	9,9
BIORAD - Platelia	3	3	93	110	101	9,78	9,7
DIASORIN - Liaison XL	10	9	32,8	49	41,5	5,4	13
ORTHO - Vitros	10	10	69,2	113	85	12	14,2
ROCHE - Cobas 6000	72	72	145	181	172	6,11	3,6
ROCHE - Elecsys / e411 / e601 / Modular	53	53	120	211	172	7,35	4,3
SIEMENS - Advia Centaur	33	33	86,5	153	104	7,3	7
SIEMENS - Immulite 2000	21	21	48	73	60,6	3,72	6,1

Medical diagnostic devices vigilance

2.1 Sérum 1112 (Dépistage) - Anticorps HBc "IgG ou Totaux"

Analyse des réponses qualitatives

Trousses	N	%	Négatif	Douteux	Positif =Référence
Autre	2	0,63	0	0	2
ABBOTT - Architect	80	25,1	1	0	79
ABBOTT - Axsym	21	6,58	0	0	21
ABBOTT - Prism	1	0,31	0	0	1
BECKMAN - Access	15	4,7	0	0	15
BECKMAN - UniCel Dxi 600 / 800	37	11,6	0	0	37
BIOMERIEUX - Vidas	22	6,9	13	9	0
BIORAD - Monalisa	1	0,31	0	0	1
BIORAD - Monalisa plus	6	1,88	0	0	6
DIASORIN - ETI-AB-Corek-2	1	0,31	0	0	1
DIASORIN - Liaison	1	0,31	0	0	1
ORTHO - Vitros	12	3,76	0	0	12
ROCHE - Cobas 6000 / Modular	69	21,6	2	0	67
ROCHE - Elecsys / Cobas e411	17	5,33	0	0	17
SIEMENS - Advia Centaur	27	8,46	17	0	10
SIEMENS - Enzygnost	1	0,31	1	0	0
SIEMENS - Immulite 2000	3	0,94	0	1	2
SIEMENS - Immulite 2500	3	0,94	0	3	0
TOTAL	**319**	**100%**	**34**	**13**	**272**

Acceptable ⟵ (BIOMERIEUX - Vidas)

⟵ (SIEMENS - Advia Centaur) **Discrepancy had been attributed to a reagent batch number. The supplier was informed and a declaration of medical diagnostic devices vigilance was sent to the French authorities.**

Thank you for your attention.