UMR 15

Review on ring trials organised within EPIZONE and perspectives for standardisation

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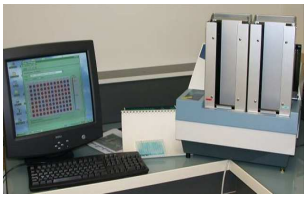
Summary:

Theme 4 of EPIZONE is dedicated to the development and standardisation of the diagnostic tools for epizootic diseases. To achieve this objective, regular ring trials are organised within the network. However, to our knowledge, they are designed and organised by different laboratories with no established standards. In agreement with a recent report on the Euroepan network of excellence (1), we believe that EPIZONE could somehow play a role in improving quality, particularly in the present case, for the standardisation of ring trials designed for the comparison and validation of diagnostic methods. As a starting point, we decided to review three European ring trials into which we took part (AIV/RRT-PCR, BT/ELISA & PCR(2), ASF/ELISA & PCR), one that we are currently organising for EPIZONE (PPR/ELISA & PCR) and three others that we have organised in 2008 either at the international, European or national level (AIV/RRT-PCR, Culicoides/PCR, BT/ELISA). From this evaluation, it is possible to make suggestions for harmonisation. EPIZONE could promote the definition of guidelines for the organisation of such ring trials, taking into account the international standards available (3, 4).

Key-words: ring trials, quality assurance, standards, diagnostics.



CIRAD contribution:		Participation					Organisation				
							Europe				France
Ring trials:		AIV	BT		ASF		AIV	Culicoides	PPR		BT
Method		rRT-PCR	ELISA	PCR	ELISA	PCR	rRT-PCR	PCR	ELISA	PCR	ELISA
Participants number		39	35	29	28	23	5	11	7	7	81
Sample type		virus	sera	blood	sera	virus	virus	crude lysate extracted DNA	sera	RNA virus	sera
Total number of samples		10	10	10	8	12	20	38	15	5	20
Sample status:	Negative	1 N	2 N	2 N	3 N	3 N	9 N	6 N	3 N	1 N	5 N
	Positive	9 P	8 P	8 P	5 P	8 P	9 P	32 P	8 P	4 P	6 P
	Doubtfull	-	-	-	-	1 D	-	-	-	-	8 D
	Mock	0	0	0	0	0	2	0	1	1	1
Number of samples for	Detectability (analytical sensitivity)	0	0	0	0	0	11	0	3	0	5
	Dose/effect	0	0	0	0	0	0	0	0	0	5
	Repeatability	0	0	0	0	0	0	0	0	0	6
Necessary volume for two tests		yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
Random coding of the samples		no	no	no	no	no	yes	yes	yes	yes	yes
Official final reporting	- global analysis of results	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
	- individual analysis with conforming and non conforming	no	no	no	yes	yes	yes	no	yes	yes	yes

PROPOSITIONS

Standardisation of the ring trials within EPIZONE could be based of a recommended set of samples, a list of criteria to be evaluated and a template for the final result reporting.

I – RECOMMENDED SET OF SAMPLES:

► **Number of samples**: the risk of not detecting an anomaly is directly determined by the number of samples included in the set. The table shows the risk interval according to the number of samples in the set (confidence interval of 95 %):

Number of samples	Number of results corresponding to the expected results	Risk of not detecting an anomaly
5	5	0 % à 45 %
10	10	0 % à 25 %
28	28	0 % à 10 %
60	60	0 % à 5 %

A compromise must be found between a lower risk and a reasonable number of samples: our suggestion would be **20-25 samples**.

► **Sample status :** since it is impossible to assess the specificity of a participant using a low number of negative samples, we recommend to include more positive and positive limits in the set. Only few negative samples are to be included.

► **Codification:** the samples should be randomly codified.

► **Volume :** The volume of samples should be limited to three repetition of the test.

II- CRITERIA TO INCLUDE:

According to the OIE and ISO guidelines for Laboratory Proficiency Testing (3, 4), the criteria to be assessed should be:

► **Sensitivity:** capacity to detect a true positive sample.

► **Specificity**: capacity to score as negative, a true negative sample.

► **Detectability**: capacity to detect a minimum quantity of the target

► **Dose/Effect response**: for quantitative results only, capacity to generate a linear curve for serial dilutions.

► **Repeatability**: capacity to generate identical results on repetitions of the same sample.

III- REPORTING

The **final report** should include an overall analysis of the ring trial with an anonymous result reporting and a statement on conforming and non conforming results to individual laboratory participant.

References:

1- Expert group on the future of Networks of Excellence, Final report, A. Bonaccorsi, M. Horvat, T. Maimets, P. Papon, September 2008. http://ec.europa.eu/research/reports/2008/pdf/expert-group-on-the-future-of-noes_final-report.pdf

2- Bluetongue virus: European Community inter-laboratory comparison tests to evaluate ELISA and RT-PCR detection methods C.A. Batten, K. Bachanek-Bankowska, A. Bin-Tarif, L. Kgosana, A.J. Swain, M. Corteyn, K. Darpel, P.S. Mellor, H.G. Elliott and C.A.L. Oura : Veterinary Microbiology , Volume 129, Issues 1-2, 25 May 2008, Pages 80-88.

3- OIE Quality Standard and Guidelines for Veterinary Laboratories 2nd Ed., 2008, B. Vallat, OIE

4 - Proficiency testing by interlaboratory comparisons -- Part 1: Development and operation of proficiency testing schemes ISO/CEI GUIDE 43-1: 1997.