Az Damiaan
Dicht bij het leven

10th EUROPEAN MEETING ON MOLECULAR DIAGNOSTICS
October 11 – 13, 2017
Noordwijk aan Zee

PITFALLS AND SOLUTIONS FOR THE VERIFICATION OF THE FILMARRAY® MENINGITIS/ENCEPHALITIS PANEL (BIOMÉRIEUX)

Ben Vanmassenhove(1), Anne-Sophie Hervent(1), Lies Persijn(1), Liesbeth Vynckier(1), Vanlaere Elke(2), Philippe Van Lint(3), Gudrun Alliet(1)

(1) Az Damiaan, Oostende (2) Az Sint-Lucas, Gent, (3) GZA, Antwerpen (Belgium)

Background

The objective of this study is to evaluate the analytical performance of the FilmArray® (FA) Meningitis/Encephalitis (ME) Panel (BioMérieux). The FA system is an easy sample-in-result-out system for the simultaneous qualitative detection of nucleic acids in cerebrospinal fluid from 6 bacteria, 7 viruses and 1 yeast that can cause ME. In Belgium there is only reimbursement for herpes simplex virus 1 and 2 (HSV), varicella zoster virus (VZV) and enterovirus (EV) if the assay is performed under ISO15189:2012 accreditation. Therefore the verification was in the first instance done for only those 4 viruses.

Methods

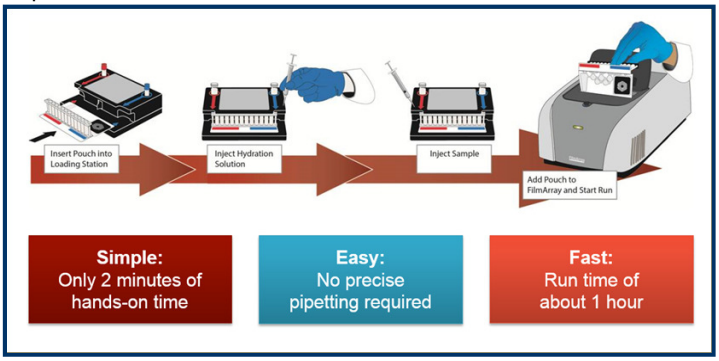
The assay was checked on two different FilmArray® systems for analytical accuracy and reproducibility following the Belgian guidelines (Raymaekers *et al.*, Acta Clinica Belgica, 2011).

- Analytical accuracy

One pool including all 14 pathogens (ZeptoMetrix), 18 external quality controls (12 EV, 2 HSV-1, 1 HSV-2, 1 VZV positive and 2 negative controls), 4 quantified, but not certified, commercial controls (Qnostic, Vircell) and 1 clinical sample were tested on both systems.

- Reproducibility

2 QCMD (Quality Control for Molecular Diagnostics) samples with a high Cq value for EV (33.5) and HSV-1 (34.5) and 2 Qnostic samples diluted to more or less 3 times the limit of detection (LOD) for HSV-2 (4000 copies/ml) and VZV (5000 copies/ml) were tested on 3 different days by 3 different operators.



Results (1)

- The internal extraction and inhibition controls were all positive. No sample was inhibited. One system missed 6 external quality controls (3 EV, 2 HSV-1 and 1 VZV) and the Vircell HSV-1 control (3333 copies/ml). Both systems could not detect the quantified HSV-1 Qnostic control (4500 copies/ml: 3 times limit of detection). No false-positive results were observed.
- The triplicates of the 4 pathogens gave the same positive result.

Results (2)

Sample	Target	Device 1	Device 2
Zeptometrix	14 pathogens	OK	OK
QCMD EV14-10	EV68	OK	OK
QCMD EV14-01	EV71	OK	neg
QCMD EV14-07	Coxsackie A9	OK	neg
QCMD EV14-09	Coxsackie A16/B5	OK	OK
INSTAND 372044	Coxsackie B3	OK	OK
INSTAND 372045	Coxsackie A21	OK	OK
INSTAND 372025	Echovirus 30	OK	OK
INSTAND 372026	Coxsackie B4	OK	OK
INSTAND 372027	Echovirus 7	OK	OK
UKNEQAS 2446	Coxsackie A24	OK	OK
UKNEQAS 3024	Coxsackie A4	OK	neg
UKNEQAS 3025	Coxsackie A9	OK	OK
UKNEQAS 3021	HSV-1	OK	neg
INSTAND 363061	HSV-1	OK	neg
UKNEQAS 3022	HSV-2	OK	OK
UKNEQAS 3026	VZV	OK	neg
UKNEQAS 3023	neg	OK	OK
QCMD NG14-04	neg	OK	OK
clinical sample	HSV-1	OK	OK
Vircell	HSV-1 (3333 c/ml)	OK	neg
Qnostic	HSV1 (4500 c/ml)	neg	neg
Qnostic	HSV-2 (4000 c/ml)	OK	OK
Qnostic	VZV (5000 c/ml)	OK	OK

Conclusion

Although the FA ME panel is FDA and CE-IVD approved, we advise to do a more extended verification of each separate system in the lab for each pathogen in the panel. Appropriate samples and external quality controls should be well chosen (low positive). In our evaluation the positivity of the internal extraction and inhibition controls were not always a guaranty for good accuracy. As there is a lack of certified quantified reference material it is difficult to check the stated LOD of the package insert. One system did not meet our criterion for accuracy and was sent back to the manufacturer for thorough technical inspection. The other system was successfully implemented in our daily routine.

Acknowledgements: we thank all lab technicians for their contributions.