Proficiency of laboratories in the detection and quantification of Cytomegalovirus by molecular methods

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INTRODUCTION

The prevalence of Cytomegalovirus (CMV) is high (40-80%) in populations throughout the developed world. While CMV is normally a latent lifelong infection that is completely asymptomatic in those infected with the virus, this is not the case in persons with compromised immune systems such as AIDS patients and organ transplant recipients. In such patients CMV infection is much more serious and is recognised as one of the most important viral causes of mortality and morbidity in these groups.

Early detection of a CMV viral load in these patients may allow for the infection to be halted before clinical symptoms are apparent. Additionally changes in viral load in the patient may indicate the need to modify treatment strategies to prevent further disease progression. Both of these scenarios require rapid and accurate diagnostics tests.

Here we report on the results of a six year international proficiency testing (PT) study on the detection and quantification of CMV by molecular methods.

AIMS

- Determine trends in the Performance of participants in the detection and quantification of CMV by molecular methods

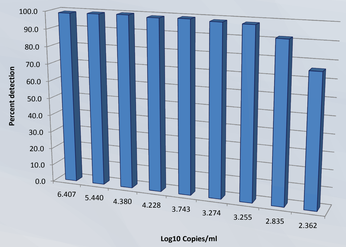
METHODS

- The QCMD PT programme was distributed annually to participants worldwide. Participants were given five weeks to test the blinded panel. Data were collected through a dedicated online system, before being analysed by QCMD
- CMV was present at a range of concentrations from 10^2 to 10^8 Copies/ml, and each panel contained at least one negative sample
- Trends in the performance of participants contributing to the EQA programmes, including qualitative and quantitative results were analysed over time
- The EQA performance indicators investigated were: ability to detect CMV, quantitative variation and false positivity

RESULTS

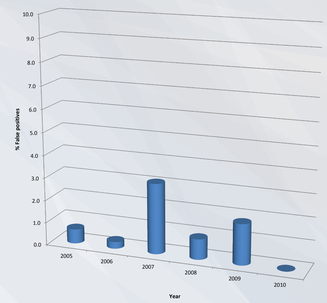
- From 2005 to 2010 the percentage of participating laboratories worldwide increased by 73%
- The majority of assays used by laboratories showed a high degree of sensitivity, reliably detecting down to 10^2 Copies/ml of CMV (Figure 1)
- The percentage of false positive results ranged from a high of 3.1% in 2007 to 0% in 2010 (Figure 2)
- Over 70% of the datasets received by QCMD contained both qualitative and quantitative data
- The vast majority of participants reported quantitative data in Copies/ml (Figure 3)
- The variation in the quantitative data, as measured by the standard deviation values, showed no improvement across the years, when the median standard deviation values across the whole panels were assessed (Figure 4)

Figure 1: Qualitative performance of participants in the 2010 QCMD CMV EQA programme



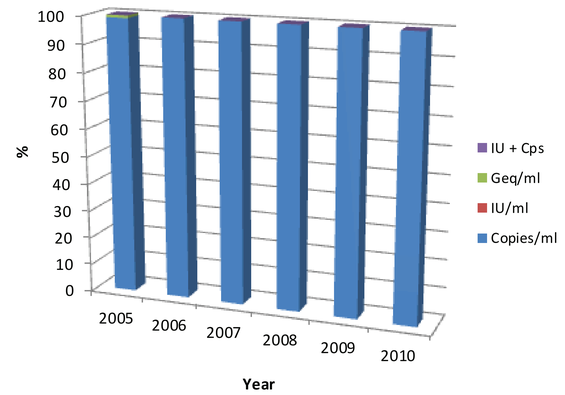
Key: The percentage of positive results reported for each panel sample in the QCMD CMV EQA panel in 2010. The panel contained a dilution series of CMV AD169.

Figure 2: Percentage of false positive results in the QCMD CMV EQA programmes



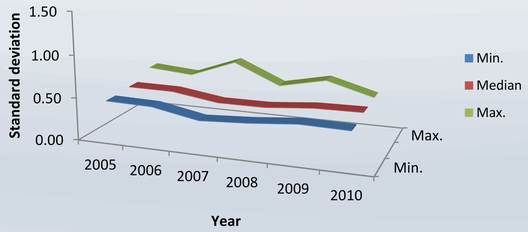
Key: The percentage of false positive results reported for each QCMD CMV distribution from 2005 to 2010.

Figure 3: Units of reporting in the QCMD CMV EQA programmes



Key: The percentage of quantitative units reported for each QCMD CMV distribution from 2005 to 2010.

Figure 4: Variation in quantitative results in the QCMD CMV EQA programmes



Key: Summary of the standard deviation values (median and range) reported for the QCMD CMV EQA programmes from 2005 to 2010. Participants results were reported in Copies/ml. All data were transformed to $\log_{10}$ prior to analysis.

CONCLUSIONS

- The majority of assays used by laboratories showed a high degree of sensitivity, reliably detecting down to 10^2 Copies/ml of CMV
- The rate of false positives has decreased overall but remains a concern
- The vast majority of laboratories report quantitative results in Copies/ml
- Quantitative inter-laboratory variation remains a concern for CMV testing and there is a need for further standardisation
- The first international standard for CMV was introduced in 2010 and this may well assist in reducing variation between laboratories, but only if laboratories and commercial manufacturers support its use