Annex A

Additional figures and explanation of the Minimum requirements

HrHPV analysis will be performed in three laboratories (screening sites), each using the BD Onclarity assay on two separate BD COR systems (Becton Dickinson). Therefore the QA-tool must be able to integrate the data from multiple systems and laboratory sites. For analysing and reporting purposes it is necessary to

1. be able to run analyses and reports on the site of the laboratories, using the data of that site, whether or not plotted/benchmarked in comparison to the total data of all sites,
2. as well as run analyses and reports on behalf of BVO-NL, using the data of all participating laboratories

Dashboard of the QA-tool

The display of the QA Tool must have a dashboard functionality in which the actual data are presented in a standard and clear way. The performers of the HPV screening should be able to use the QA Tool for a graphical and tabulated display of the results and see at a glance how the performance is.

To be able to signal that there are deviations, the QA Too will contain an automatic alert system (e.g. based on Westgard rules) in which deviations from a standard are calculated and indicated on the dashboard. deviations will be recognized quickly in this way. Upon discovering a deviation in one or more datapoints it is essential to be able to find out the possible cause of the deviation. Therefore it is essential that the QA-tool features a hoover functionality (e.g. down drill function).

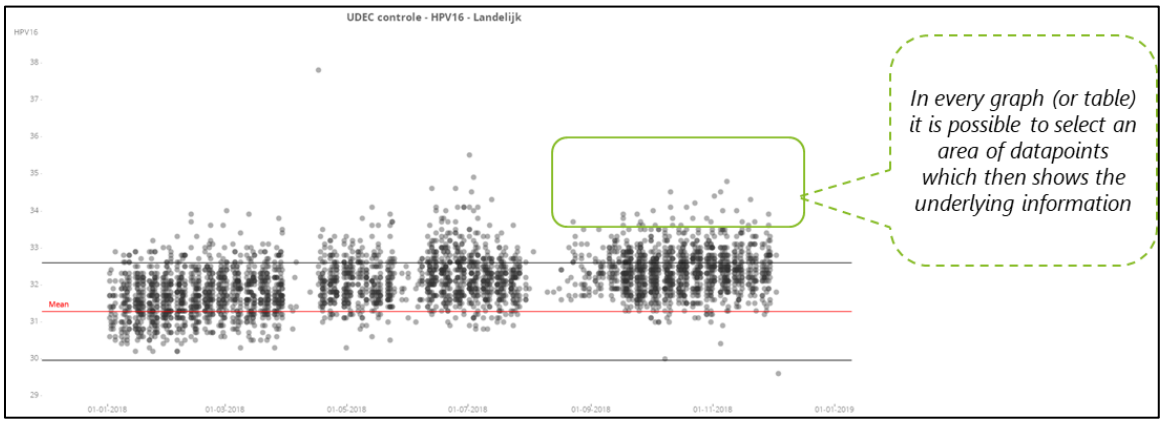


***Figure 1**: Example hoover functionality*

Queries and searches

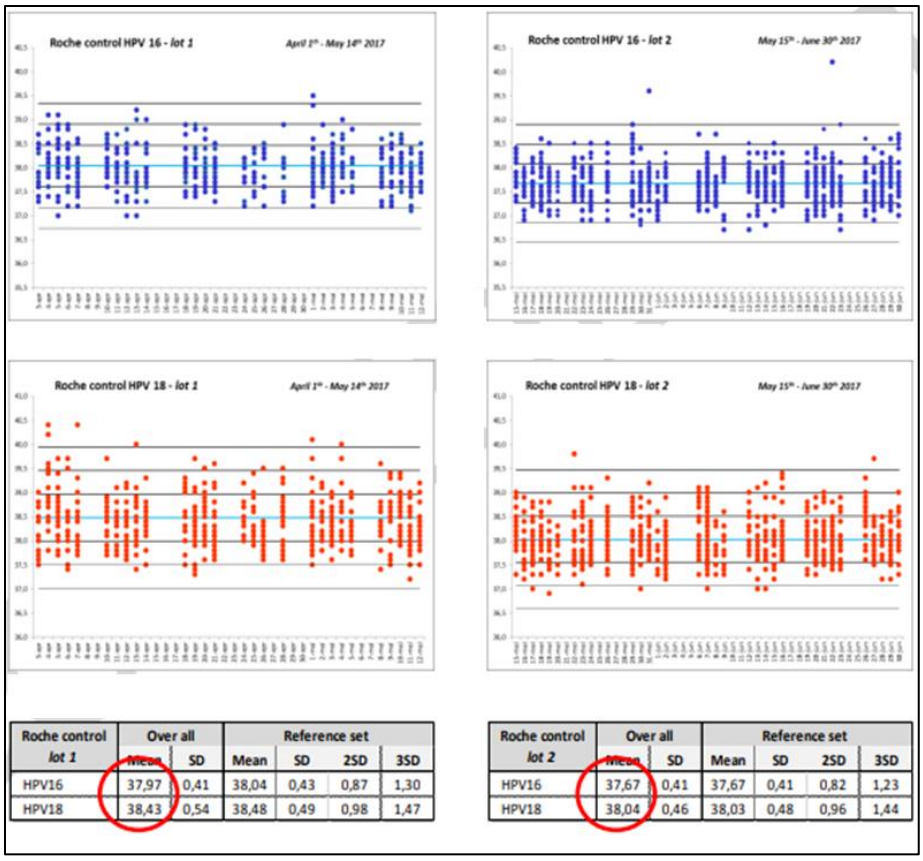
The dataset of the hrHPV test contains a lot of different parameters. Part of the parameters (e.g. lab name, date, HPV type or system number) will be used in standard searches, so the QA Tool must possess the possibility to define standard queries and searches. Besides it should also be possible to perform ad hoc queries on the same and or other parameters in the database. A search functionality that is easy to use (e.g. an intuitive user interface) and has the opportunity to display the results in tables or graphs, is essential to perform these searches.

Reports and export of results

To monitor the HPV screening process, the results are collected, presented in tables and graphs and put in a report at the end of every month. The preparation of this report is still done manually which is time consuming, so the QA Tool should be able to do this automatically. Besides the QA-tool should also be able to automatically generate graphical and tabulated representations of non-standardised

queries, which could be exported using various formats (XLS, XML for aggregated results, graphical formats for charts).

For clarification, some figures, both tables and graphs, of the current program are depicted and explained below.



Roche control lot 1	Over all		Reference set			
	Mean	SD	Mean	SD	2SD	3SD
HPV16	37,97	0,41	38,04	0,43	0,87	1,30
HPV18	38,43	0,54	38,48	0,49	0,98	1,47

Roche control lot 2	Over all		Reference set			
	Mean	SD	Mean	SD	2SD	3SD
HPV16	37,67	0,41	37,67	0,41	0,82	1,23
HPV18	38,04	0,46	38,03	0,48	0,96	1,44

***Figure 2**: Example of a lot change*

Before a new lot of critical reagents is accepted, the three screening laboratories perform a entrance check. Upon passing the pre-defined criteria the data from this entrance check is used to adapt the limit values to the new lot of critical reagents.

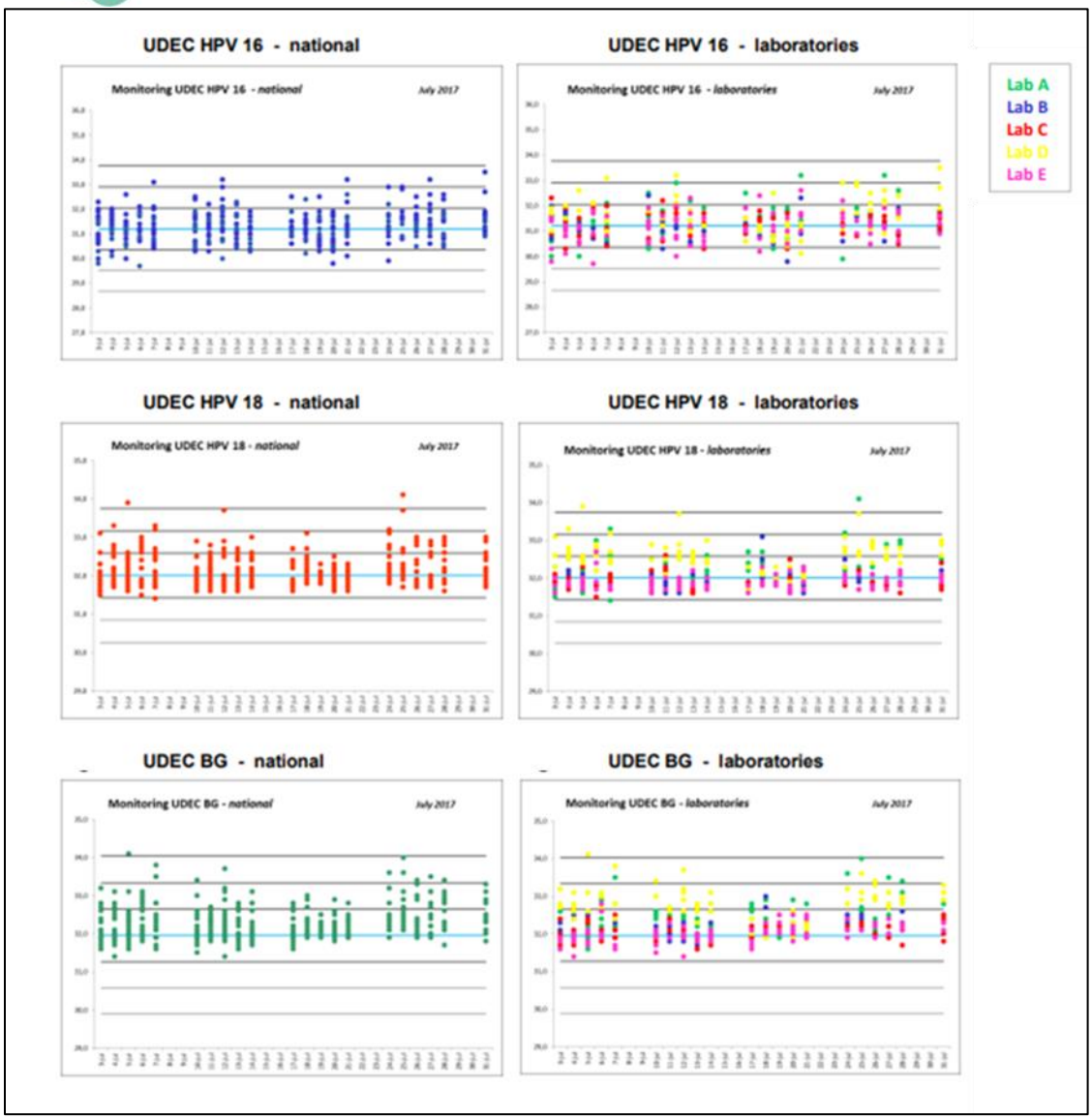


Figure 3 *Example of short term monitoring of UDEC using different colors for the different laboratories*

For the short term monitoring the Ct values of the UDEC as well as the assay controls are plotted as single data points in Levey-Jennings charts, using the mean and 1SD-3SD from the reference set. To make any differences between the laboratories visible, a colour scheme is used as depicted in Figure 3. Note in this Annex A only an example of the UDEC is displayed, the QA-tool must generate similar graphs for the other controls.

For the long term monitoring the Ct values of the UDEC are plotted as single data points in graphs with a trend line as depicted in figure 4.

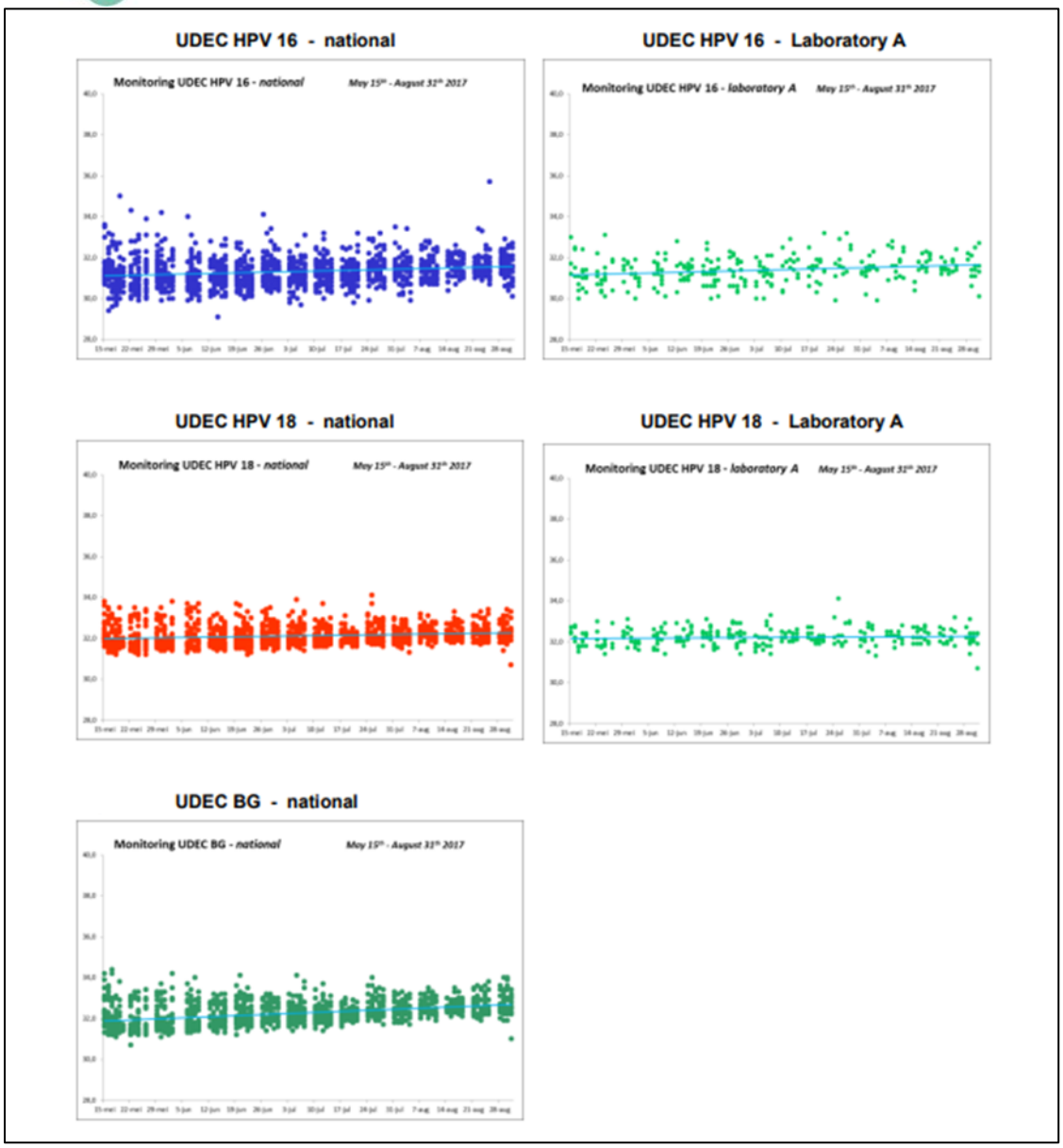


***Figure 4**: example of long term monitoring of UDEC using a trend line*

Note in this Annex A only examples of the UDEC are displayed, the QA-tool must generate similar graphs for the other controls.

Interlaboratory comparison

For interlaboratory comparison, the mean and the standard deviation of the assay control (control samples delivered by BD, which are used in every run and by which runs are approved) and the UDEC results (Ct-values) are calculated. The results of the 3 laboratories are compared with the national average. In addition, each laboratory will monitor its performance (e.g. variation between the 2 systems, operator effects etc).

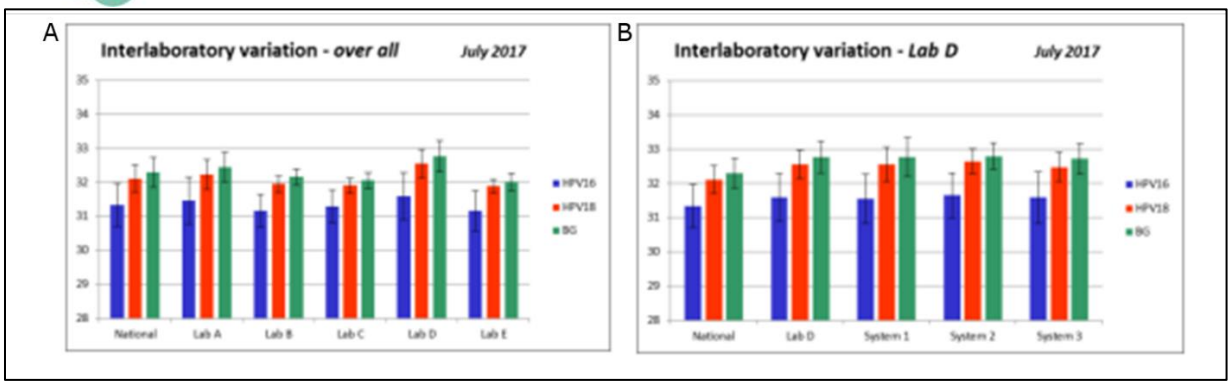


***Figure 5 A**; interlaboratory variation compared with the national average and **B**; variation between systems in 1 laboratory*

Equipment monitoring program

Equipment monitoring measures the technical performance of the HPV -systems. Errors are recorded and used for graphical and or tabulated display. Equipment monitoring needs to be provided both at laboratory and national level. In the equipment monitoring of the HPV-systems a distinction will be made in failed/invalid results at both run and sample level and errors like failed barcode reading.

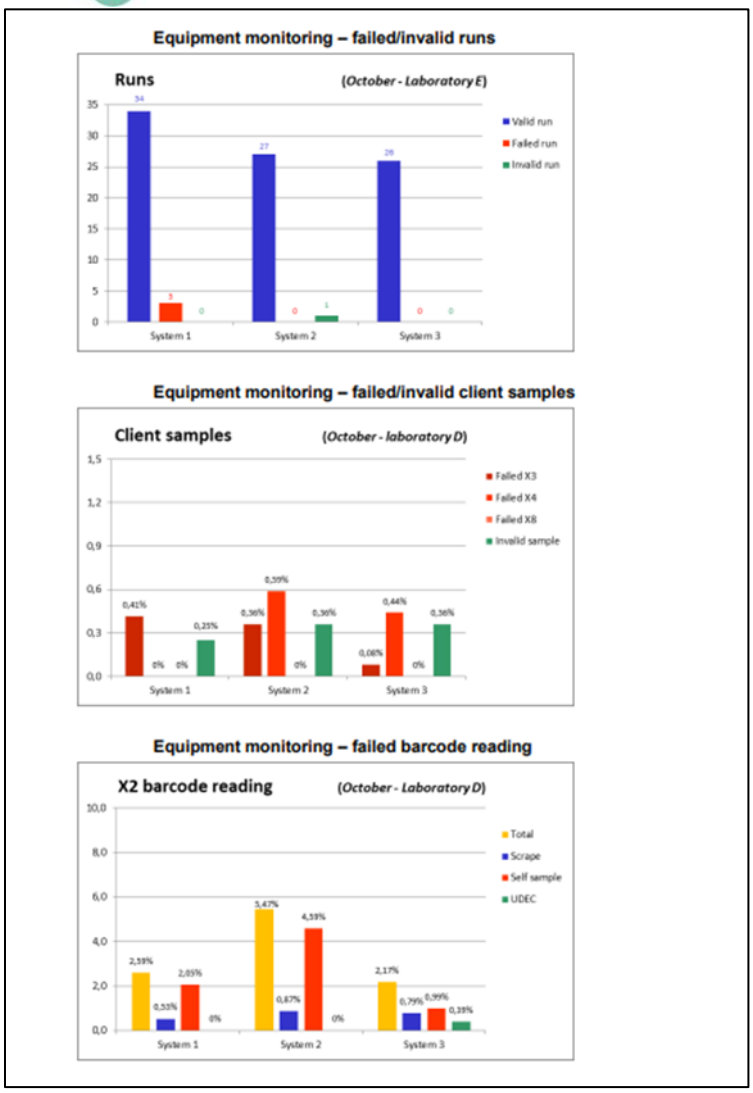


***Figure 6**: Example of equipment monitoring*