**Supplementary File 1. Sensitivity and s­pecificity of variant detection**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Copy | Variant | Original Pipelineb | | Current Pipelinec | |
| Numbera | Frequency | Sensitivity | Specificity | Sensitivity | Specificity |
|  |  |  |  |  |  |
| >105 | 0.05 | 1 | >0.9999 | 0.85 | 1.000 |
|  | 0.02 | 0.85 | 0.9999 | 0.15 | 1.000 |
|  | 0.01 | 0.95 | 0.9995 | - | - |
|  | 0.005 | 0.35 | 0.9999 | - | - |
|  |  |  |  |  |  |
| 104-105 | 0.05 | 0.95 | 0.9999 | 0.85 | 1.000 |
|  | 0.02 | 0.9 | 0.9999 | 0.15 | 1.000 |
|  | 0.01 | 0.8 | 0.9998 | - | - |
|  | 0.005 | 0.4 | 0.9999 | - | - |
|  |  |  |  |  |  |
| 103-104 | 0.05 | 0.8 | >0.9999 | 0.70 | 1.000 |
|  | 0.02 | 0.45 | 0.9999 | 0.15 | 1.000 |
|  | 0.01 | 0.2 | 0.9997 | - | - |
|  | 0.005 | 0.1 | 0.9999 | - | - |

a Per µl transport media

b As described in McCrone JT and Lauring AS, J. Virol. 90(15):6884, 2016.

c As described in Methods, benchmarked for frequencies 0.02-0.98 only