FIND Evaluation of Cepheid Xpert MPX

Version 1.1, Date: 2024-09-05

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Evaluation Process – private sector engagement

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FIND conducted an independent evaluation of Mpox point-of-care tests following an Expression of Interest (EOI) process that was available on FIND's webpage.

Document History

Document Version	Date	Comment
1.0	2024-09-04	Initial version
1.1	2024-09-05	Updated evaluation details

1.0 **Product info:**

Manufacturer name	Cepheid
Test name	Xpert MPX
Product code(s)	GXMPX-10
Pack size(s)	10 cartridges per kit
Kit content	• Cartridges • Disposable 300 µL Transfer Pipettes • Flyer • Quick Reference Instructions
Equipment and consumables required, but not provided	• GeneXpert Dx System • Nylon flocked swab (Copan P/N 502CS01, or equivalent) • Viral transport medium/Universal transport medium (VTM/UTM), 3 mL (Copan P/N 3C047N or equivalent) • Printer
Product storage (temperature range)	2–28 °C
Shelf-life (months)	6 months, up to 25°C
Manufacturing site (country)	United States of America

2.0 **Study Details**

Study design	Prospective and retrospective diagnostic evaluation study across multiple, independent sites to determine the accuracy of Mpox point-of-care tests, using consecutive enrolment. Presence
Index assays	Novel point-of-care tests (i.e. point-of-care molecular and rapid diagnostic tests) that detect monkeypox virus (MPXV) sequences or antigens.
Reference method	Results of the index tests are compared to RT-PCR result, which is the recommended test for mpox diagnosis.
Limit of detection	Analytical sensitivity, i.e., the Limit of detection (LOD), was performed at the University Hospital of Geneva, where standardized serial dilutions of cultured viral isolates were prepared. The kit's proprietary swabs were soaked in the viral dilution series. Dilutions were tested in triplicate, and LOD was defined as the last dilution where all repeats were interpreted as positive.
Clinical performance	Sensitivity was calculated as the proportion of true positive results detected by the INDEX TEST among all positives by the reference method and reported as a percentage. Specificity was calculated as the proportion of true negative specimens identified as negative by the INDEX TEST among all negatives by the reference method and reported as a percentage. The 95% confidence intervals were calculated to assess the level of uncertainty introduced by sample size using Wilson’s score method.

3.0 **Evaluation details**

Country of collaborator	Democratic Republic of the Congo (DRC)	United Kingdom (UK)	Switzerland (CH)
Location of clinical site(s) (city, town)	INRB - Goma	Liverpool School of Tropical Medicine	University Hospital of Geneva
Study Period	2023-2024	2023-2024	2023-2024
Study design	Prospective using lesion and oropharyngeal samples in VTM	Retrospective using frozen lesion and respiratory samples	Analytical study using viral cultures
Study cohort inclusion/exclusion	Inclusion: Individuals ≥ 2 years of age suspected to have mpox (and/or specimens collected from them), as per national or WHO case definitions Exclusion: individual with no visible rash or lesions	Inclusion: Individuals ≥ 2 years of age suspected to have mpox (and/or specimens collected from them), as per national or WHO case definitions. Exclusion: individual with no visible rash or lesions	Not applicable
MPXV clade present	Clade 1 (presumed)	Clade 2b (presumed)	Clade 1, Clade 2a, Clade 2b (virus culture)
Sample type, index test	Lesion swab in viral transport media (VTM), Oropharyngeal swab in VTM	Lesion swab in VTM, Oropharyngeal swab in VTM	Virus cultures in PBS
Reference PCR method	Monkeypox virus Nucleic Acid Diagnostic Kit (Sansure Biotech)	Monkeypox virus Nucleic Acid Diagnostic Kit (Sansure Biotech)	Lab-developed protocol[1]
Sample type, PCR test	Lesion swab in VTM, Oropharyngeal swab in VTM	Lesion swab in VTM, Oropharyngeal swab in VTM	Virus cultures in PBS

[1] https://www.hug.ch/sites/interhug/files/structures/laboratoire_de_virologie/documents/Monkeypox/protocol_for_the_detection_of_monkeypox_by_rt.pdf

4.0 Results

4.1 Study cohort

Table 1. Study Cohort – **Lesion Sample** Population.

	Overall	DRC	UK
Total N (Valid PCR Results)	79	68 (86.1%)	11 (13.9%)
Age [mean (min-max), N]	19 (2-46), 79	17 (2-46), 68	34 (24-45), 11
Gender [%F, (n/N)]	43% (34/79)	50% (34/68)	0% (0/11)
Days from symptom onset [median (Q1-Q3); N]	Not applicable	4 (2.75-7), 68	Information not available
Days 0-3 (n, %)	Not applicable	32 (47.1%)	Information not available
Days 4-7 (n, %)	Not applicable	22 (32.4%)	Information not available
Days 8+ (n, %)	Not applicable	14 (20.6%)	Information not available
Positivity [% (n/N)]	36.7% (29/79)	27.9% (19/68)	90.9% (10/11)
PCR Ct [median (Q1-Q3); N]	26.6 (22.7-34.2), 29	26.7 (22.6-34.4), 19	26 (24.3-30.3), 10
Ct ≤ 25, n (%)	25, (86.2%)	16 (84.2%)	9 (90%)
Ct ≤ 30, n (%)	17, (58.6%)	11 (57.9%)	6 (60%)
Ct ≤ 35, n (%)	10, (34.5%)	7 (36.8%)	3 (30%)

Table 2. Study Cohort – **OP Sample** Population

	Overall	DRC	UK
Total N (Valid PCR Results)	82	68 (82.9%)	14 (17.1%)
Age [mean (min-max), N]	20 (2-58), 82	17 (2-46), 68	36 (24-58), 14
Gender [%F, (n/N)]	41.5% (34/82)	50% (34/68)	0% (0/14)
Days from symptom onset [median (Q1-Q3); N]	Not applicable	4 (2.75-7), 68	Information not available
Days 0-3 (n, %)	Not applicable	32 (47.1%)	Information not available
Days 4-7 (n, %)	Not applicable	22 (32.4%)	Information not available
Days 8+ (n, %)	Not applicable	14 (20.6%)	Information not available
Positivity [% (n/N)]	29.3% (24/82)	20.6% (14/68)	71.4% (10/14)

PCR Ct [median (Q1-Q3); N]	29.4 (25.9-35.8), 24	34.5 (27.7-36.8), 14	28.9 (25-30.2), 10
Ct ≤ 25, n (%)	16 (66.7%)	8 (57.1%)	8 (80%)
Ct ≤ 30, n (%)	13 (54.2%)	6 (42.9%)	7 (70%)
Ct ≤ 35, n (%)	5 (20.8%)	1 (7.1%)	4 (40%)

Table 3. Study Cohort – **population used for OP index test / Lesion reference test performance evaluation**.

Note. Only participants who had a lesion and oropharyngeal sample collected on the same day were eligible to be included in this analysis. This includes 68 participants from INRB and 5 participants from LSTM.

	Overall	**DRC**	**UK**
Total N (Valid PCR Results)	73	68 (93.2%)	5 (6.8%)
Age [mean (min-max), N]	18 (2-46), 73	17 (2-46), 68	32 (24-45), 5
Gender [%F, (n/N)]	46.6% (34/73)	50% (34/68)	0% (0/5)
Days from symptom onset [median (Q1-Q3); N]	Not applicable	4 (2.75-7), 68	Information not available
Days 0-3 (n, %)	Not applicable	32 (47.1%)	Information not available
Days 4-7 (n, %)	Not applicable	22 (32.4%)	Information not available
Days 8+ (n, %)	Not applicable	14 (20.6%)	Information not available
Positivity [% (n/N)]	32.9% (24/73)	27.9% (19/68)	100% (5/5)
PCR Ct [median (Q1-Q3); N]	27.3 (22.9-34.4), 24	26.7 (22.6-34.4), 19	30.2 (25.3-33.6), 5
Ct ≤ 25, n (%)	20 (83.3%)	16 (84.2%)	4 (80%)
Ct ≤ 30, n (%)	13 (54.2%)	11 (57.9%)	2 (40%)
Ct ≤ 35, n (%)	8 (33.3%)	7 (36.8%)	1 (20%)

4.2 Estimation of clinical performance

Table 4. Performance evaluation on **lesion sample** (Reference sample is lesion).

	Overall	**DRC**	**UK**
Clinical Sensitivity [95% CI], N[1]	**79.31 [61.61-90.15], 29**	**68.42 [46.01-84.64], 19**	**100 [72.25-100.0], 10**
Sensitivity, CT ≤ 35, N	80 [60.87-91.14], 25	68.75 [44.4-85.84], 16	100 [70.09-100.0], 9

Sensitivity, CT ≤ 30, N	100 [81.57-100.0], 17	100 [74.12-100.0], 11	100 [60.97-100.0], 6
Sensitivity, CT ≤ 25, N	100 [72.25-100.0], 10	100 [64.57-100.0], 7	100 [43.85-100.0], 3
Sensitivity, Symptom Onset 0-3 days [95%CI], N	Not applicable	50 [18.76-81.24], 6	Information not available
Sensitivity, Symptom Onset 4-7 days [95%CI], N	Not applicable	100 [60.97-100.0], 6	Information not available
Sensitivity, Symptom Onset > 7 days [95%CI], N	Not applicable	57.14 [25.05-84.18], 7	Information not available
Clinical Specificity [95% CI], N[2]	**85.42 [72.83-92.75], 48**	**87.23 [74.83-94.02], 47**	**0 [0.0-79.35], 1**
Invalid rate (%, n/N)	2.53% (2/79)	2.94% (2/68)	0% (0/11)

1. For sensitivity columns, N represents the total number of positives included in the performance evaluation i.e., TP + FN.
2. For specificity columns, N represents the total number of negatives included in the performance evaluation i.e., TN + FP.

Table 5. Performance evaluation on **oropharyngeal samples** (Reference sample is lesion).

Note. Only participants who had a lesion and oropharyngeal sample collected on the same day were eligible to be included in this analysis. This includes 68 participants from INRB and 5 participants from LSTM.

	Overall	DRC	UK
Clinical Sensitivity [95% CI], N[1]	**68.18 [47.32-83.64], 22**	**66.67 [43.75-83.72], 18**	**75 [30.06-95.44], 4**
Sensitivity, CT ≤ 35, N	73.68 [51.21-88.19], 19	73.33 [48.05-89.1], 15	75 [30.06-95.44], 4
Sensitivity, CT ≤ 30, N	92.31 [66.69-98.63], 13	100 [74.12-100.0], 11	50 [9.45-90.55], 2
Sensitivity, CT ≤ 25, N	100 [67.56-100.0], 8	100 [64.57-100.0], 7	100 [20.65-100.0], 1
Sensitivity, Symptom Onset 0-3 days [95%CI], N	Not applicable	60 [23.07-88.24], 5	Information not available
Sensitivity, Symptom Onset 4-7 days [95%CI], N	Not applicable	83.33 [43.65-96.99], 6	Information not available
Sensitivity, Symptom Onset > 7 days [95%CI], N	Not applicable	57.14 [25.05-84.18], 7	Information not available
Clinical Specificity [95% CI], N[2]	**97.78 [88.43-99.61], 45**	**97.78 [88.43-99.61], 45**	**NaN [NaN-NaN], 0**
Invalid rate (%, n/N)	8.22% (6/73)	7.35% (5/68)	20% (1/5)

1. For sensitivity columns, N represents the total number of positives included in the performance evaluation i.e., TP + FN.
2. For specificity columns, N represents the total number of negatives included in the performance evaluation i.e., TN + FP.

Table 6. Performance evaluation on **oropharyngeal samples** (Reference sample is oropharyngeal)

	Overall	DRC	UK
Clinical Sensitivity [95% CI], N[1]	**87.5 [69.0-95.66], 24**	**78.57 [52.41-92.43], 14**	**100 [72.25-100.0], 10**
Sensitivity, CT ≤ 35, N	87.5 [63.98-96.5], 16	75 [40.93-92.85], 8	100 [67.56-100.0], 8
Sensitivity, CT ≤ 30, N	100 [77.19-100.0], 13	100 [60.97-100.0], 6	100 [64.57-100.0], 7
Sensitivity, CT ≤ 25, N	100 [56.55-100.0], 5	100 [20.65-100.0], 1	100 [51.01-100.0], 4
Sensitivity, Symptom Onset 0-3 days [95%CI], N	Not applicable	60 [23.07-88.24], 5	Information not available
Sensitivity, Symptom Onset 4-7 days [95%CI], N	Not applicable	100 [60.97-100.0], 6	Information not available
Sensitivity, Symptom Onset > 7 days [95%CI], N	Not applicable	66.67 [20.77-93.85], 3	Information not available
Clinical Specificity [95% CI], N[2]	**86.54 [74.73-93.32], 52**	**91.84 [80.81-96.78], 49**	**0 [0.0-56.15], 3**
Invalid rate (%, n/N)	7.32% (6/82)	7.35% (5/68)	7.14% (1/14)

1. For sensitivity columns, N represents the total number of positives included in the performance evaluation i.e., TP + FN.
2. For specificity columns, N represents the total number of negatives included in the performance evaluation i.e., TN + FP.

4.3 Estimation of analytical performance

Verified LOD

MPXV clade	Lowest dilution detected	Verified LOD concentration	Viral copy equivalent
Clade 1	To be determined	To be determined	To be determined
Clade 2a	To be determined	To be determined	To be determined
Clade 2b	To be determined	To be determined	To be determined