Automated Extraction and Purification of DNA and RNA from Multiple Sample Matrices Using ClassiX™ DNA/RNA on the SwiftXtractor™ SL

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Summary

The ClassiX™ DNA/RNA kit (CXDR-96) is a universal magnetic-bead system for the extraction and purification of DNA and RNA from a broad range of biological samples in both manual and automated formats.

This application note describes validation of the automated protocol (CXDR-A) on the SwiftXtractor™ SL benchtop instrument across human and porcine whole blood, nasal swabs, urine and stool,

The findings were corroborated at independent external laboratories on authentic clinical specimens, fecal, rectal and vaginal swabs, whole blood and respiratory samples, where ClassiX DNA/RNA detected every expected target and, pooled across all 186 matched experiments performed to date, returned a lower Cq than the reference method in 68% of comparisons. The workflow uses a single combined lysis-and-binding step, requires no centrifugation, and delivers PCR-ready DNA and RNA in approximately 30 minutes.

These results confirm that the SwiftXtractor™ SL achieves performance equivalent to, or better than, that obtained by a skilled operator performing the ClassiX DNA/RNA protocol manually.

Manual and automated multi-matrix nucleic acid extraction. ClassiX™ DNA/RNA manual protocol and automated protocol on the SwiftXtractor™ SL.

Introduction

Nucleic acid extraction is the foundational step of virtually every molecular workflow. Automation reduces hands-on time, minimizes operator-to-operator variability, and improves run-to-run reproducibility, considerations that are critical for laboratories seeking standardized, higher-throughput workflows. A robust automated method should reproduce the performance of the validated manual procedure, so that a protocol developed manually can be transferred to the instrument with minimal re-optimization.

ClassiX™ DNA/RNA employs magnetic-particle technology that combines the speed and efficiency of silica-based purification with the simple handling of magnetic beads. Sample material is combined with Proteinase K and, in a single step, with a mix of the guanidinium lysis buffer (Buffer XL), the binding buffer (Buffer XB) and silica-coated magnetic particles (Beads D). Lysis and binding therefore proceed together at 65 °C, inactivating pathogens, arresting nuclease activity, releasing nucleic acids and capturing them on the beads in one operation. Three sequential washes (Buffer XW1, Buffer XW2 and an ethanol wash) remove protein, cell debris and matrix components; after a brief air-drying step, DNA and RNA are eluted in a detergent-free elution buffer (Buffer XE). The same chemistry underlies both the manual and the automated protocols.

The SwiftXtractor™ SL is a compact benchtop instrument that automates this workflow using passive liquid handling through magnetic rods. It processes up to four samples per run through programmable mixing, magnetic-rod separation and thermal incubation, requiring no centrifugation and minimal operator intervention. The automated workflow is summarized in Figure 1.

Experimental Methods

Sample material. 200 µL input was used for every extraction. Sample types comprised of human and porcine whole blood; porcine whole blood spiked with Gram-negative or Gram-positive organisms; nasal swabs, either unspiked (human genomic DNA) or spiked with Gram-negative, Gram-positive or fungal organisms; urine spiked with *Neisseria gonorrhoeae* and assessed for human DNA, human RNA, pathogen DNA and total nucleic acid; and stool, assessed for PMMoV, crAssphage and *Escherichia coli*. Where sample volume was below 200 µL, PBS was added to reach the input volume. Identical sample material was processed in parallel by the automated, manual and reference workflows to enable direct comparison.

Instrumentation. Automated extractions were performed on the SwiftXtractor™ SL (Cat. No. SXT-SL, Xpedite Diagnostics GmbH, Hallbergmoos, Germany), a compact benchtop instrument that processes up to four samples per run through magnetic rods, with programmable mixing, magnetic separation and thermal incubation. Manual extractions followed the ClassiX DNA/RNA Instructions for Use (IFU V1.1) using the combined lysis-and-binding protocol, with the accessories listed below. At the external sites, ClassiX was automated on the platform used at each site. The following instruments were used:

- SwiftXtractor™ SL automated extractor: Xpedite Diagnostics GmbH, Cat. No. SXT-SL;
- MagnetaPure 32 automated nucleic acid purification system: Dutscher, REF 74421.4.
- GeneXplorer automated extraction system: Chroma ATE Inc., Taoyuan, Taiwan.
- Maelstrom automated nucleic acid extractor: TANBead (Taiwan Advanced Nanotech Inc.).
- Magnetic separation rack: Xpedite Diagnostics GmbH, Cat. No. MAG-12 or MAG-4 (manual workflow).
- Vortexer: Xpedite Diagnostics GmbH, Cat. No. VOR-01 (manual workflow).
- Heating block: Xpedite Diagnostics GmbH, Cat. No. ACC-15 (manual workflow).
- Mini spin centrifuge: Xpedite Diagnostics GmbH, Cat. No. CEN-01 (manual workflow).

Reagents and consumables. All ClassiX extractions were performed with the ClassiX™ DNA/RNA kit. Reference extractions were performed with the commercial kits listed below, each according to the manufacturer's instructions; at the external sites the reference kit in use at that site was used. Ethanol, isopropanol and PBS were supplied by the user. The following kits and reagents were used:

- ClassiX™ DNA/RNA kit, 96 extractions: Xpedite Diagnostics GmbH, Cat. No. CXDR-96; supplied with Proteinase K, Buffer XL, Buffer XB, Buffer XW1, Buffer XW2, Buffer XE and Beads D.
- QIAamp DNA Blood Mini Kit: Qiagen, Cat. No. 51104 (reference kit for whole blood).
- QIAamp UCP Pathogen Mini Kit: Qiagen, Cat. No. 50214 (reference kit for swabs and urine).
- NZY Mag Blood & Tissue DNA Isolation Kit, RUO: NZYTech, Cat. No. MD0834 (reference kit for whole blood).
- STARMag 96x4 Universal Plus Cartridge Kit: Seegene Inc., GUDID 08809240000069 (reference kit for stool).
- External-site automated platforms Singuway; Chroma ATE Inc.; TANBead.
- Ethanol, 96% (v/v) or absolute, non-denatured: user-supplied (wash step).
- Isopropanol: user-supplied (Buffer XB reconstitution).
- Phosphate-buffered saline (PBS): user-supplied (sample volume adjustment).

Automated protocol. The SwiftXtractor SL executes the ClassiX DNA/RNA chemistry as an automated, walk-away workflow (Figure 1). Proteinase K is added to the 200 µL sample, followed by a single combined mix of Buffer XL, Buffer XB and Beads D, so that lysis and binding take place together at 65 °C. Nucleic acids captured on the beads are then separated magnetically and washed three times, with Buffer XW1, Buffer XW2 and an ethanol wash, all of which are part of the standard instrument program, followed by air-drying and detergent-free elution in Buffer XE at 65 °C. All mixing, magnetic separation and incubation steps are performed by the instrument; no centrifugation is required at any point.

Analysis. Nucleic acid recovery was assessed by target-specific real-time PCR and reported as the quantification cycle (Cq); because Cq is inversely related to the amount of amplifiable target, a lower Cq indicates greater recovery. Values are presented as mean ± standard deviation (SD) with the number of

replicates (n) indicated for each condition (n = 2 to 11). Two comparisons are reported: the automated protocol against the manual protocol (Table 1), and the automated protocol against the corresponding commercial reference kit for each matrix (Table 2).

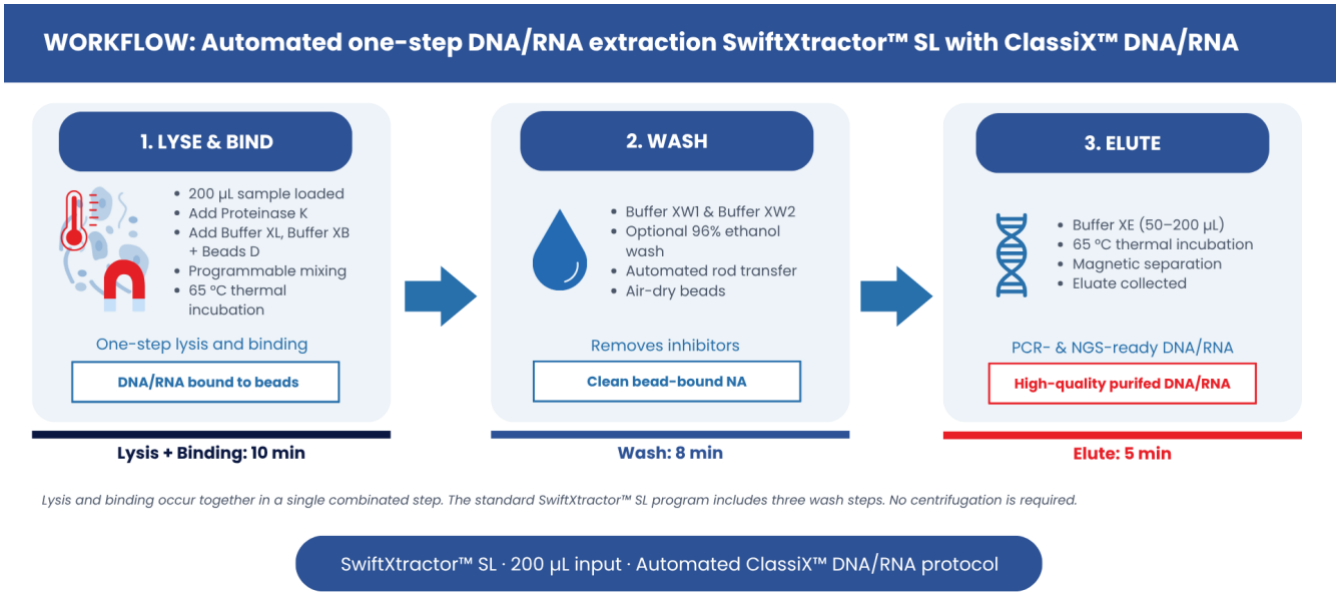

Figure 1 *Automated workflow for the extraction and purification of DNA and RNA from a 200 µL sample input on the SwiftXtractor™ SL using the ClassiX™ DNA/RNA kit (CXDR-96). Lysis and binding are performed together in a single combined step at 65 °C; the captured beads are then washed three times as part of the standard instrument program, air-dried, and the DNA and RNA eluted in a detergent-free buffer. The complete run is executed automatically through programmable mixing, magnetic-rod separation and thermal incubation, with up to four samples per walk-away run.*

Results

Automated versus manual performance. Across whole blood, nasal swabs and stool the two formats were closely concordant, with a mean absolute ΔCq of 0.42 and a maximum of 1.26 cycles. Urine was the exception: there the automated protocol recovered consistently more nucleic acid than the manual procedure, by 1.7 to 3.3 Cq for the RNA and pathogen targets, indicating that automated wash and elution handling benefits this low-biomass matrix (Table1).

Automated versus reference kits. The automated protocol matched or outperformed the reference methods in most matrices (Table 2). The clearest gains were in urine, where human RNA and *N. gonorrhoeae* DNA were detected at Cq values 5.0 and 4.2 cycles lower, respectively, than with the QIAamp UCP Pathogen Mini reference. In porcine whole blood the reference returned no detectable signal for any of the three targets, whereas the automated protocol recovered all three. In human whole blood it was equivalent to the QIAamp DNA Blood Mini reference and gave a Cq 2.5 cycles lower than NZY Mag, and in stool it was equivalent to the STARMag reference. For the Gram-positive and fungal spiked swabs the QIAamp UCP

Pathogen Mini reference produced lower Cq values than ClassiX DNA/RNA. This difference is most likely explained by the reference workflow's glass bead-beating step, which provides additional mechanical disruption during lysis; bead beating is well established to improve lysis efficiency for difficult-to-lyse organisms, particularly Gram-positive bacteria with thick peptidoglycan cell walls, and can also enhance recovery from fungal cells.

Table 1. *Automated versus manual recovery (mean Cq ± SD). ΔCq is calculated as automated minus manual; a negative value indicates that the automated protocol recovered more target. PMMoV (pepper mild mottle virus) is a plant virus used as a faecal process control to monitor extraction and amplification.*

Matrix	Target	n	CXDR-A (auto)	CXDR-M (manual)	ΔCq (A – M)
Whole blood	Human, non-coding DNA	4	17.62 ± 0.15	17.47 ± 0.04	**+0.15**
Porcine blood	Genomic DNA	8	20.21 ± 0.30	20.57 ± 0.23	**−0.36**
Porcine blood	Gram-negative	4	22.48 ± 0.17	22.11 ± 0.09	**+0.37**
Porcine blood	Gram-positive	4	21.77 ± 0.12	21.33 ± 0.03	**+0.44**
Nasal swab	Human genomic DNA	11	27.75 ± 1.97	27.66 ± 1.86	**+0.09**
Nasal swab	Gram-negative	6	24.17 ± 0.55	24.15 ± 0.56	**+0.02**
Nasal swab	Gram-positive	9	28.73 ± 2.67	27.97 ± 2.32	**+0.76**
Nasal swab	Fungal	5	34.43 ± 0.99	33.17 ± 0.82	**+1.26**
Urine	Human DNA	4	28.24 ± 2.44	28.67 ± 2.57	**−0.43**
Urine	Human RNA	4	24.42 ± 1.25	27.01 ± 1.20	**−2.59**
Urine	*N. gonorrhoeae* DNA	4	15.46 ± 0.51	17.18 ± 0.50	**−1.72**
Urine	*N. gonorrhoeae* total NA	4	14.20 ± 0.37	17.52 ± 0.55	**−3.32**
Stool	PMMoV	3	28.02 ± 3.76	28.25 ± 3.64	**−0.23**
Stool	crAssphage	2	21.67 ± 1.74	20.96 ± 2.00	**+0.71**
Stool	*E. coli*	3	30.12 ± 0.79	29.65 ± 0.92	**+0.47**

Matched-pair overview. Plotting every internal comparison as a matched Cq pair gives the same picture across all 16 target/matrix combinations: of 69 paired experiments, ClassiX returned a lower Cq than the reference in 44 cases (64%). The points clustering around the line of equivalence (Figure 2).

Additional manual data. Two RNA viruses were evaluated with the manual protocol only: SARS-CoV-2 in PBS (22.57 ± 4.07 Cq, n = 3) and Dengue virus in whole blood (36.06 ± 1.11 Cq, n = 2), both comparable to

the QIAamp DNA Blood Mini reference (23.11 ± 4.41 and 35.84 ± 0.38 Cq, respectively). These targets confirm the RNA-virus capability of the chemistry but were not run on the automated protocol.

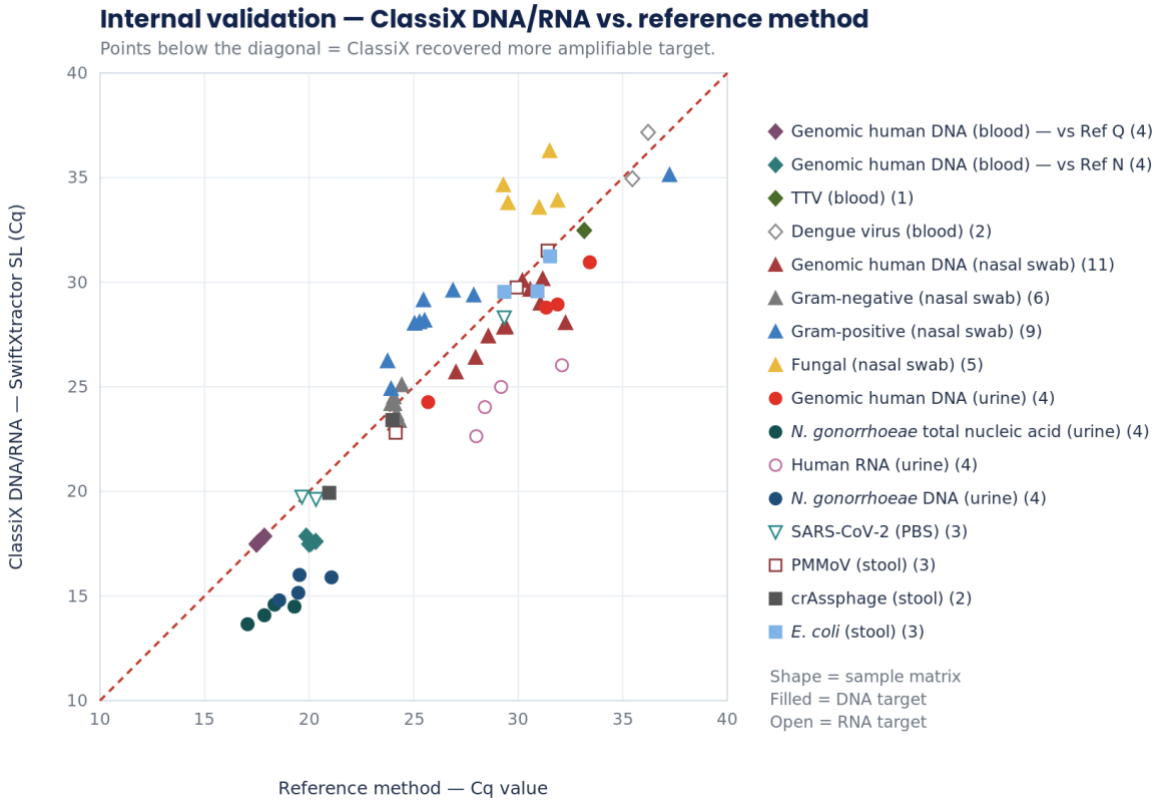

Figure 2 *Internal validation: ClassiX DNA/RNA on the SwiftXtractor™ SL versus the corresponding reference method for every internal matrix and target (n = 69 matched experiments, 16 target/matrix combinations). Nucleic acids were quantified by qPCR for a specific target from the same sample after extraction with ClassiX (Cq on the y axis) and with a reference method appropriate for that matrix (Cq on the x axis). The dashed line is the line of equivalence; points below it indicate that ClassiX recovered more amplifiable target. Marker shape denotes the sample matrix; filled markers are DNA targets and open markers RNA targets.*

Table 2. *Automated versus reference recovery (mean Cq ± SD). ΔCq is calculated as ClassiX (automated) minus reference; a negative value indicates that ClassiX recovered more target. [a]QIAamp DNA Blood Mini (Qiagen); [b]NZY Mag Blood & Tissue (NZYTech); [c]QIAamp UCP Pathogen Mini (Qiagen); [d] STARMag 96x4 Universal Plus Cartridge Kit.*

Matrix	Target	n	CXDR-A (auto)	Reference	ΔCq (A – Ref)
Whole blood	Human, non-coding DNA	4	17.62 ± 0.15	17.34 ± 0.17 [a]	**+0.28**
Porcine blood	Genomic DNA	8	20.21 ± 0.30	Not detected [a]	**n/a**
Porcine blood	Gram-negative	4	22.48 ± 0.17	Not detected [a]	**n/a**
Porcine blood	Gram-positive	4	21.77 ± 0.12	Not detected [a]	**n/a**
Nasal swab	Human genomic DNA	11	27.75 ± 1.97	29.24 ± 2.18 [c]	**–1.49**

Matrix	Target	n	CXDR-A (auto)	Reference	ΔCq (A – Ref)
Nasal swab	Gram-negative	6	24.17 ± 0.55	24.16 ± 0.17 [c]	**+0.01**
Nasal swab	Gram-positive	9	28.73 ± 2.67	26.77 ± 3.90 [c]	**+1.96**
Nasal swab	Fungal	5	34.43 ± 0.99	30.64 ± 1.05 [c]	**+3.79**
Urine	Human DNA	4	28.24 ± 2.44	30.58 ± 2.93 [c]	**−2.34**
Urine	Human RNA	4	24.42 ± 1.25	29.42 ± 1.60 [c]	**−5.00**
Urine	*N. gonorrhoeae* DNA	4	15.46 ± 0.51	19.66 ± 0.90 [c]	**−4.20**
Urine	*N. gonorrhoeae* total NA	4	14.20 ± 0.37	18.14 ± 0.81 [c]	**−3.94**
Stool	PMMoV	3	28.02 ± 3.76	28.49 ± 3.14 [d]	**−0.47**
Stool	crAssphage	2	21.67 ± 1.74	22.47 ± 1.51 [d]	**−0.80**
Stool	*E. coli*	3	30.12 ± 0.79	30.59 ± 0.92 [d]	**−0.47**

Evaluation of Clinical Specimens at External Sites

Beyond the spiked and contrived panels above, ClassiX DNA/RNA was evaluated at independent external laboratories on authentic clinical specimens. Each site processed the samples on its own automated platform and compared ClassiX against the reference extraction method in use at that site, using its established downstream PCR assays. These specimens spanned fecal, rectal and vaginal swabs, EDTA whole blood, respiratory specimens and serum.

Of the 117 matched comparisons generated at these partner sites, ClassiX returned the lower Cq in 82 cases (70%). The points cluster tightly around the line of equivalence (Figure 3). Together with the internal data this gives 186 matched comparisons overall, with ClassiX giving the lower Cq in 126 cases (68%).

Study-by-study outcomes. In clinical fecal swabs processed on the MagnetaPure 32, both workflows detected every target present in the samples, and ClassiX produced the lower Cq in six of the seven pathogen comparisons (Figure 4A). In clinical rectal swabs processed on the GeneXplorer, the expected STI target was detected in all six positive patients with both workflows, with closely aligned Cq values (Figure 4B). In clinical malaria samples, ClassiX produced a lower mean Cq for *Plasmodium falciparum* in all three patients, by 0.68 to 2.10 cycles, with internal controls unchanged (Figure 4C). Finally, in clinical respiratory specimens the manual and automated ClassiX formats detected the same targets in all five patients, on the Maelstrom, and the automated format returned a lower Cq in every one of the ten target and control measurements, by a mean of 1.16 cycles (Figure 4D), an independent, clinical confirmation of the manual-to-automated relationship reported in Table 1. Two *N. gonorrhoeae*-positive vaginal swabs gave the same result, with both workflows detecting the target and Cq values within 0.5 cycles. Larger matched series for

SARS-CoV-2 (48 specimens) and Dengue virus-positive serum (40 specimens) are included in Figure 2 and showed close agreement with the reference method throughout.

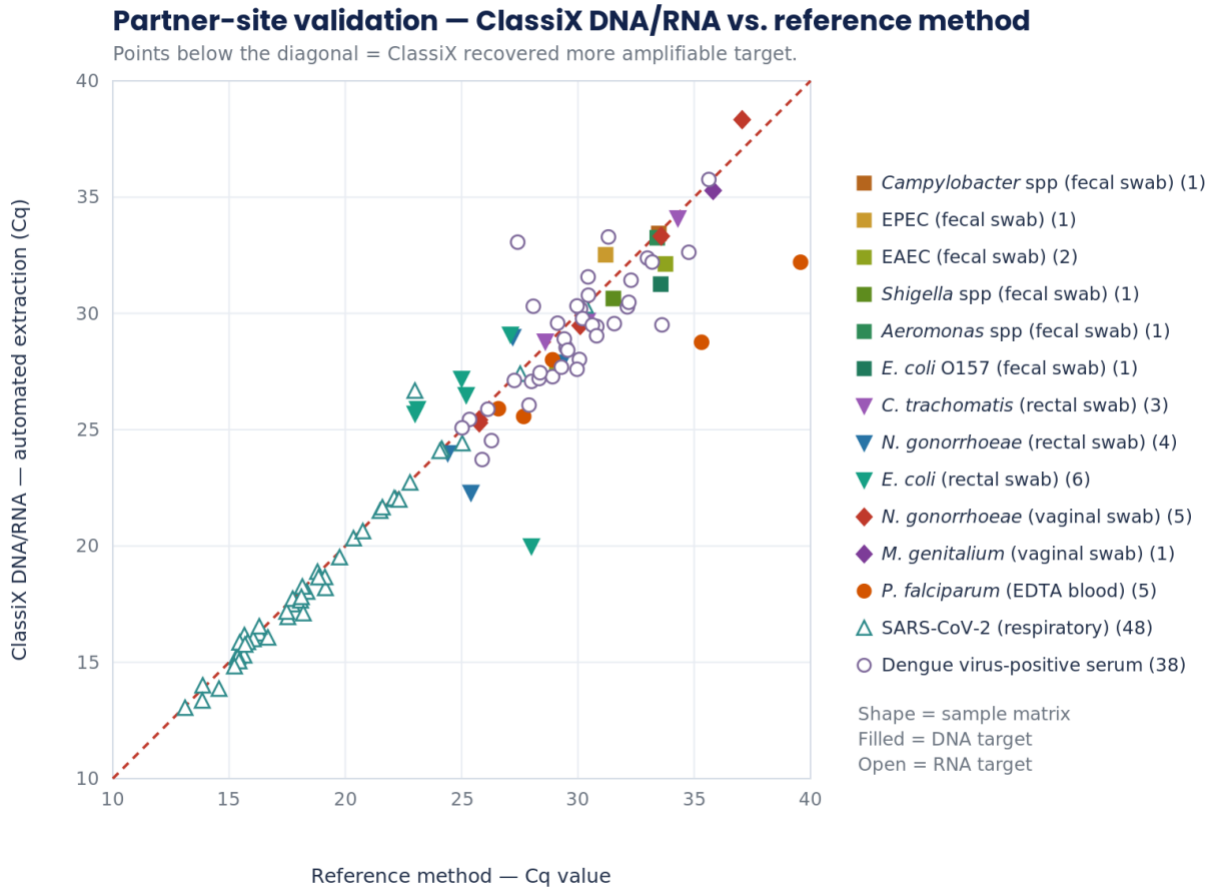

Figure 3 *Partner-site validation: ClassiX DNA/RNA versus each laboratory's own routine reference method on authentic clinical specimens (n = 117 matched experiments, 14 target/matrix combinations). ClassiX was automated on the platform used at each site. Axes, line of equivalence and interpretation as in Figure 2.*

Table 3. *Evaluation of clinical specimens at external sites. ΔCq is calculated as ClassiX minus reference a negative value indicates that ClassiX recovered more target. n is the number of matched target comparisons. [e] For this study ΔCq is calculated as ClassiX automated minus ClassiX manual, so a negative value indicates that the automated format recovered more target.*

Study / matrix	Platform	n	Detection concordance	Mean ΔCq	Range
Bacteria, clinical fecal swabs	MagnetaPure 32	7	All targets detected by both	**−0.72**	−2.30 to +1.33
STI targets, clinical rectal swabs	GeneXplorer	6	Target detected in all patients	**−0.12**	−1.40 to +1.80
N. gonorrhoeae, vaginal swabs	MagnetaPure 32	2	Detected in both by both	**−0.41**	−0.47 to −0.34

Study / matrix	Platform	n	Detection concordance	Mean ΔCq	Range
P. falciparum, clinical whole blood	MagnetaPure 32	3	Detected in all patients by both	**−1.23**	−2.10 to −0.68
Respiratory targets, clinical specimens [c]	Maelstrom	10	Same targets detected in both formats	**−1.16**	−2.34 to −0.17

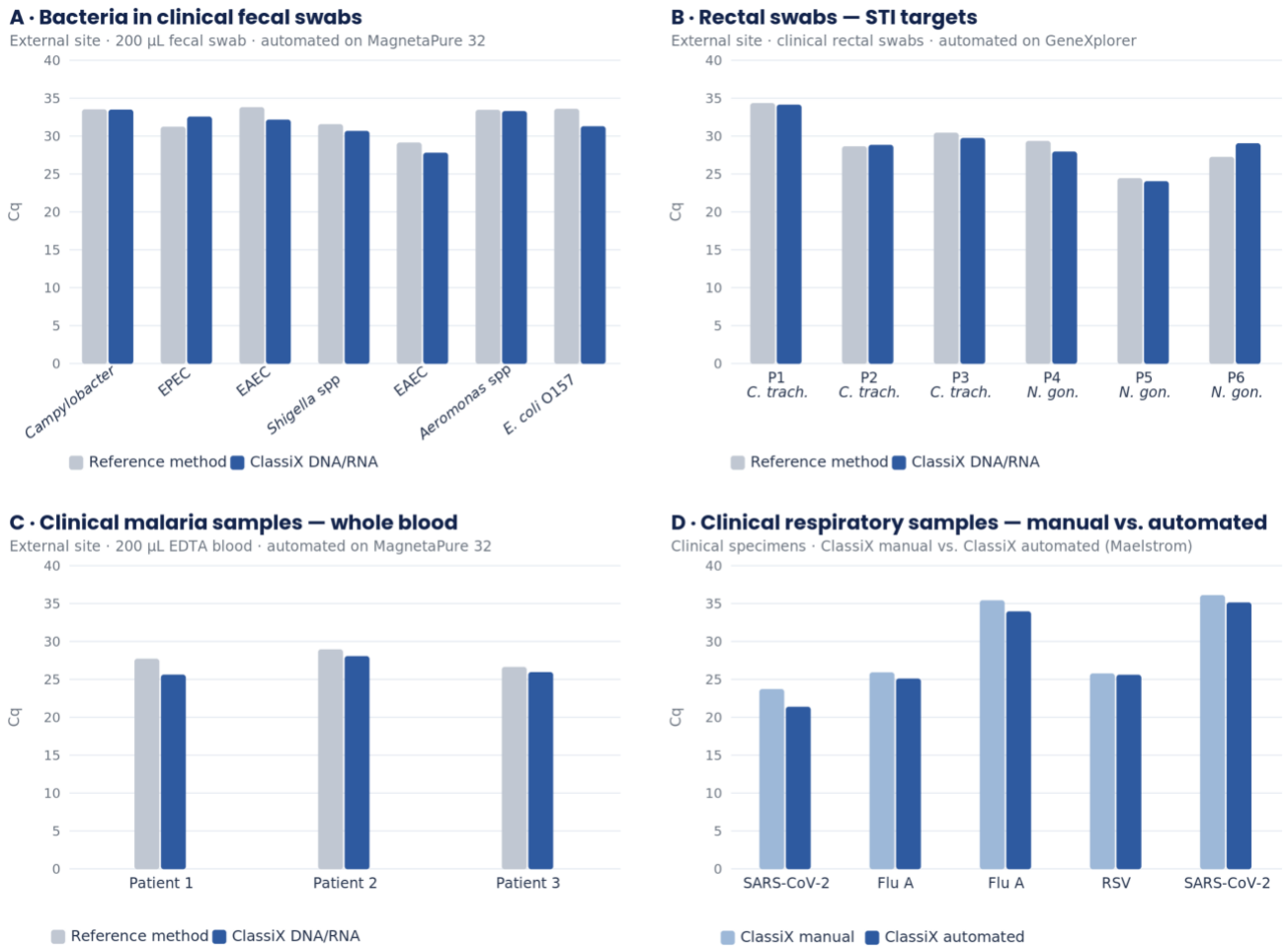

Figure 4 *Evaluation of clinical specimens at external sites. (A) Bacterial targets in clinical fecal swabs. (B) STI targets in clinical rectal swabs from positive patients. (C) Plasmodium falciparum in clinical whole blood. (D) Respiratory targets in clinical specimens, ClassiX manual versus ClassiX automated on the SwiftXtractor SL. All inputs were 200 µL. Internal and positive controls are omitted for clarity; in (D) each bar pair represents one clinical specimen.*

Discussion

This validation shows that the automated ClassiX DNA/RNA protocol on the SwiftXtractor SL reproduces the manual procedure across a broad matrix panel while removing hands-on liquid handling. For whole blood, nasal swabs and stool the two formats differed by no more than 1.3 Cq, so a protocol validated manually can be transferred to the instrument with minimal re-optimization. In urine, the automated protocol improved recovery relative to both the manual procedure and the commercial reference. Urine is a low-biomass matrix in which the target nucleic acid is present at low concentration and is therefore particularly sensitive to losses during washing and elution; the more reproducible, instrument-controlled handling of these steps is the most plausible explanation for the gain.

The evaluations of clinical specimens at external sites extend this conclusion from contrived panels to authentic clinical material. Four independent studies were performed on three different automation platforms, each against the reference method in use at that site. In every study ClassiX detected all expected targets and its Cq values tracked the reference closely. The clinical respiratory study is particularly informative: run manually and automatically on the same specimens, the automated format returned a lower Cq in all ten measurements, independently reproducing the manual-to-automated relationship seen in the internal panels.

The automated workflow retained the capability to retrieve both DNA and RNA and its multi-matrix reach, recovering human, bacterial and fungal targets and, notably, amplifiable DNA from porcine whole blood where the spin-column reference produced no detectable signal. The instrument adds walk-away operation of up to four samples per run and a centrifugation-free process, making the SwiftXtractor SL a practical automation route for laboratories standardizing their extraction workflows. The ClassiX chemistry itself contributes room-temperature reagent storage and a detergent-free elution.

Not every matrix favored ClassiX. For the Gram-positive and fungal spiked swabs the reference kit returned lower Cq values, which is consistent with the additional mechanical disruption provided by its glass bead-beating step. These observations are reported in full for transparency and define the current performance envelope of the automated protocol; they do not affect the overall conclusion of manual-equivalent, reference-competitive multi-matrix performance.

Recovery was assessed by real-time PCR and reported as Cq value rather than by absolute nucleic acid quantification; Cq values are inversely related to the amount of amplifiable, PCR-ready material, the parameter most relevant to downstream molecular testing. Replicate numbers varied by matrix (n = 2 to 11), with the porcine-blood and stool conditions in particular evaluated on small replicate sets; users working with these matrices should expect comparable performance but are advised to confirm this with matrix-specific verification. This study characterized automation on the SwiftXtractor SL; the ClassiX DNA/RNA chemistry is additionally compatible with other magnetic-bead automation platforms, which may be validated separately.

Conclusion

The automated ClassiX™ DNA/RNA protocol on the SwiftXtractor™ SL provides a validated, centrifugation-free, walk-away workflow for the extraction and purification of DNA and RNA from a wide range of sample matrices, based on a single combined lysis-and-binding step. Across whole blood, nasal swabs, urine and stool, automated recovery reproduced the manual procedure and was comparable to or better than established commercial reference kits, with a clear advantage in urine. With room-temperature-stable reagents, up to four samples per run and demonstrated recovery of both DNA and RNA, the SwiftXtractor SL is well suited to routine and research molecular laboratories seeking to automate a single, universal extraction method.

Ordering Information

- ClassiX™ DNA/RNA Kit — Cat. No. CXDR-96 (96 extractions)
- SwiftXtractor™ SL Instrument — contact Xpedite Diagnostics for pricing
- Rod sleeves and consumables for the SwiftXtractor™ SL — contact Xpedite Diagnostics
- Magnetic separation rack (manual workflow) — Cat. No. MAG-12 / MAG-4

The full Instructions for Use (IFU) and the SwiftXtractor™ SL program are available on request: info@xpedite-dx.com.

ClassiX™ DNA/RNA and SwiftXtractor™ SL are for Research Use Only (RUO). Not for use in diagnostic procedures.

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