Abstract # C-281

High Throughput Testing of the APTIMA COMBO 2® Assay for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* on the Fully-Automated TIGRIS® DTS™ System

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ABSTRACT

Background: The APTIMA COMBO 2® (AC2) Assay (Gen-Probe Incorporated, San Diego, CA) is a nucleic acid amplification test (NAAT) utilizing Transcription-Mediated Amplification (TMA) for the detection of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (GC) in male urethral and endocervical swab specimens, male and female urine specimens, and more recently in patient- and clinician-collected vaginal swab specimens. This assay is currently FDA-cleared for marketing on the semi-automated Direct Tube Sampling 1600 instrument system (DTS 1600 System). The purpose of this study was to determine equivalent performance of the AC2 Assay on the DTS 1600 System versus the new, fully-automated TIGRIS® DTS™ System in a high throughput laboratory. The FDA-cleared TIGRIS DTS System can test up to 1,000 tests/day.
Methods: Swab and urine specimens were collected and tested in the AC2 Assay on the DTS 1600 System. Remnant samples were briefly centrifuged at low speed to bring all sample to the bottom of the tube, re-capped, and tested in the AC2 Assay on the TIGRIS DTS System. Discordant specimens were tested with alternate TMA assays targeting different CT or GC sequences.
Results: Results from over 8,000 specimens were compared between the DTS 1600 System and TIGRIS DTS System. CT percent positive agreements for swab and urine were 99.3% (285/287) and 98.8% (81/82) respectively. GC percent positive agreements for swab and urine were both 100% (53/53 and 32/32, respectively). Percent negative agreements for swab and urine were 99.9% (8639/8647) and 100% (2065/2065), respectively, for CT, and 99.99% (8936/8937) and 100% (2148/2148), respectively, for GC. Results from alternate target TMA testing using the APTIMA® CT (ACT) and APTIMA® GC (AGC) Assays indicated that TIGRIS DTS System gave the correct result for the majority of discordant specimens [CT: 91% (10/11); GC: 100% (1/1)].
Conclusion: This study shows excellent agreement between the AC2 Assay run on the DTS 1600 and TIGRIS DTS Systems and demonstrates the ability of the TIGRIS DTS System to efficiently run up to 1,000 samples per day with high accuracy.

BACKGROUND

- The APTIMA COMBO 2® (AC2) Assay (Gen-Probe Incorporated, San Diego, CA) is a nucleic acid amplification test (NAAT) that:
  - Utilizes Transcription-Mediated Amplification (TMA) and target capture for the *in vitro* qualitative detection and differentiation of rRNA from *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (GC)
  - Is FDA-cleared for marketing on the semi-automated Direct Tube Sampling 1600 instrument system (DTS 1600 System) in male urethral and endocervical swab specimens, plus male and female first-catch urine (FCU) specimens, and more recently in patient- and clinician-collected vaginal swab specimens
- The currently cleared DTS 1600 System encompasses manual and semi-automated methods for *in vitro* diagnostic analysis of biological samples
- The Kaiser Permanente Regional Reference Laboratories in southern California processes ~1100 specimens per day
  - Needs full automation to provide cost-effective, quality CT/GC testing to 3.2 million members
- The TIGRIS® DTS™ System is a fully-automated systemused for *in vitro diagnostic* analysis of biological samples and can test up to 1,000 tests/day

PURPOSE

The purpose of this study was to determine equivalent performance of the AC2 Assay on the new, fully-automated TIGRIS DTS System with that of the semi-automated DTS 1600 System in a high throughput laboratory.

METHODS

- Female endocervical swab and FCU specimens and male urethral swab and FCU specimens were collected from subjects throughout southern California and processed according to the Gen-Probe's package insert
  - Collected using the Gen-Probe AC2 transporters and transported to the Southern California Permanente Medical Group - Regional Reference Laboratories at ambient temperature
  - Tested per routine departmental protocol in the AC2 Assay on the DTS 1600 System
- After specimens were tested, they were re-capped, stored at room temperature, and held until testing in the AC2 Assay on the TIGRIS DTS System per routine departmental protocol
  - AC2 transporters extend the shelf life and stability of specimens
- Specimens were tested in the AC2 Assay on the TIGRIS DTS System
- Equivalent AC2 Assay performance was determined between the TIGRIS DTS and DTS 1600 Systems by calculating percent positive and negative agreement
- Discordant samples were re-tested using either the APTIMA® CT (ACT) or APTIMA® GC (AGC) Assay
  - These assays are specific for an alternative target for either CT or GC and are used as the confirmatory assay for amplified CT/GC testing

RESULTS

Percent Positive and Negative Agreement

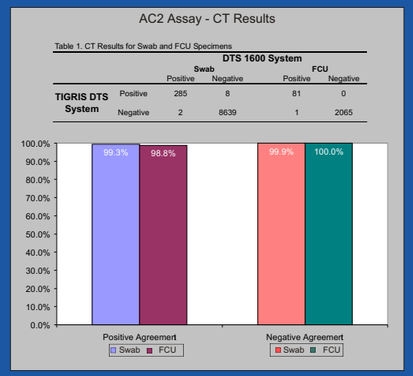


Table 1. CT Results for Swab and FCU Specimens

		DTS 1600 System			
		Swab		FCU	
		Positive	Negative	Positive	Negative
TIGRIS DTS System	Positive	285	8	81	0
	Negative	2	8639	1	2065

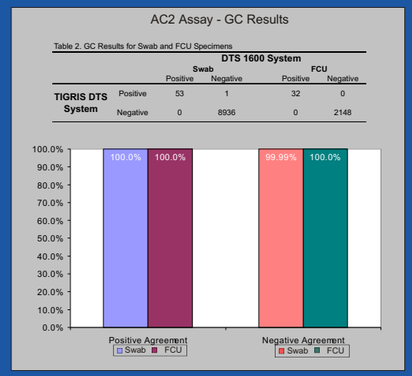


Table 2. GC Results for Swab and FCU Specimens

		DTS 1600 System			
		Swab		FCU	
		Positive	Negative	Positive	Negative
TIGRIS DTS System	Positive	53	1	32	0
	Negative	0	8936	0	2148

Discordant Results

Table 3. Discordant CT Results and Alternate TMA Testing

	Initial Results		Alternate TMA Results - ACT			
Specimen	DTS	TIGRIS	# Tested	Positive	Negative	% Agrmt TIGRIS
All	P	N	3	1	2	67.0%
	N	P	8	8	0	100.0%
Swab	P	N	2	1	1	50.0%
	N	P	8	8	0	100.0%
Urine	P	N	1	0	1	100.0%
	N	P	0	n/a	n/a	n/a

P = Positive, N = Negative, % Agrmt TIGRIS = Percent agreement with TIGRIS DTS System, n/a = not applicable

- ACT results agreed with TIGRIS DTS System results for 91% (10/11) of the discordant specimens

Table 4. Discordant GC Results and Alternate TMA Testing

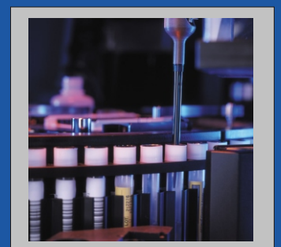
	Initial Results		Alternate TMA Results - AGC			
Specimen	DTS	TIGRIS	# Tested	Positive	Negative	% Agrmt TIGRIS
All	P	N	0	n/a	n/a	n/a
	N	P	1	1	0	100.0%
Swab	P	N	0	n/a	n/a	n/a
	N	P	1	1	0	100.0%
Urine	P	N	0	n/a	n/a	n/a
	N	P	0	n/a	n/a	n/a

P = Positive, N = Negative, % Agrmt TIGRIS = Percent agreement with TIGRIS DTS System, n/a = not applicable

- AGC results agreed with TIGRIS DTS System results for 100% (1/1) of the discordant specimens

DISCUSSION

- Nucleic acid amplification testing for CT/GC has come into widespread use in the clinical microbiology laboratory
  - The challenge for most high volume laboratories is the unavailability of full automation
  - The Kaiser Permanente Regional Reference Laboratories process ~1100 specimens per day and need full automation to provide cost-effective, quality CT/GC testing to 3.2 million members
  - The FDA-approved TIGRIS DTS system automates all phases of molecular diagnostics testing in one integrated system, increasing operator walk-away time
  - In addition, the cap piercing technology for specimen collection for the AC2 Assay is evolutionary and provides high quality specimen transport
  - The cap piercing technology also saves time during the pre-analytical phase of specimen processing since caps do not need to be removed
  - Not having to remove caps will undoubtedly decrease ergonomic injuries associated with that task and decrease cross-contamination of specimens that might have occurred during the pre-analytical processing steps, thereby reducing operator error



- Discordant test results were more common with CT tests than for GC
  - Using the alternate TMA assays (ACT and AGC Assays), more than 90% of the discordant results were resolved in favor of the TIGRIS DTS System
- The fully-automated TIGRIS DTS System compared favorably to the semi-automated DTS 1600 System with percent agreements ranging from 98.8% to 100%

CONCLUSIONS

The AC2 Assay performance on the fully-automated TIGRIS DTS System was equivalent to performance using the currently approved semi-automated DTS 1600 System. The ability of the TIGRIS DTS System to test more samples, increase operator walk-away time, and correctly report specimen results speaks to the value of using fully-automated NAAT systems. Although further testing is needed, these data suggest the TIGRIS DTS System combined with the APTIMA Combo 2 assay is a reliable, cost effective method for CT/GC testing in a high volume clinical laboratory.