An Assessment for Implementation of the Endosafe Nexus Robotic Endotoxin Testing System

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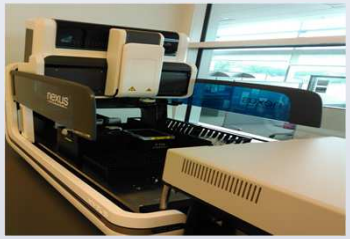
ABSTRACT

An evaluation of the Nexus Robotic System was conducted with the intent of comparing traditional microplate based endotoxin testing with that of the robotic system. This assessment explores the Nexus™ system, its components, advantages, process flow, applications and benefits as compared to traditional kinetic testing methodologies

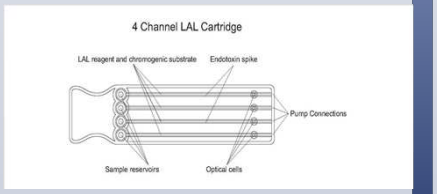
Nexus System

The Nexus System consists of an integrated Hamilton Microlab® NIMBUS automated liquid handler with air displacement pipette, robotic arm with custom jaws, MCS™ Cartridge Reader, and laptop computer with Endoscan-V software.



LAL Reagent Cartridges

- 4 channel single use
- Duplicate sample and positive product control
- All reagents required to perform a chromogenic LAL test are dried onto the cartridge
- Multiple cartridge sensitivity ranges available
  - 0.1-10 EU/mL, 0.05 -5.0 EU/mL, 0.01 - 1.0 EU/mL, 0.005 - 0.5 EU/mL



Nexus Process Flow

1. Analyst loads cartridges, pipette tips, and samples on the deck and initiates software
2. Analyst confirms number of samples and cartridges loaded
3. Analyst confirms cartridge lot and calibration code
4. NEXUS scans barcodes and Analyst initiates the run and **"walks away"**
5. Robot adds cartridges to MSC bays
6. Robot adds sample to cartridges
7. When assay is complete robot removes cartridge, adds new cartridge with sample then repeats until all samples have been tested

Conventional Kinetic LAL Testing

96 Well Plate Incubating Microplate Reader with desk top computer running Endoscan-V software.

Requires multiple reagents, equipment and consumables.

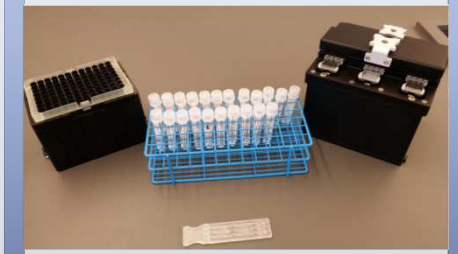
- LAL Reagent
- Control Standard Endotoxin
- Lysate Reagent Water (LRW)
- 96 Well plates
- Pipette tips including repeater pipette tips
- Depyrogented glass dilution tubes
- Depyrogenated glass pipettes for lysate reconstitution
- Multiple calibrated pipettes

Conventional Kinetic LAL Process Flow

1. Analyst gathers all reagents and consumables
2. Sample and assay information is entered into EndoScan-V
3. Standard curve is prepared
4. Negative control, standard curve, and samples are pipetted onto plate
5. Positive Product Control (PPC) are pipetted onto plate
6. Lysate is reconstituted
7. Lysate is pipetted onto plate
8. Plate is loaded into plate reader and assay is initiated

Kinetic LAL Samples, Reagents and Consumables

Nexus LAL Samples, Reagents and Consumables



Study Design

- Direct comparison of 300 samples tested using both the Nexus and conventional 96 well plate method
- To eliminate any possibility of sample interference LRW was used as the test article

Evaluation includes:

- Hands on Analyst time
- Time for assay completion
- Average % Recovery
- Average % PPC Spike Recovery
- % Difference
- Equivalency

Results

Time to get samples on test and evaluation of equivalence:

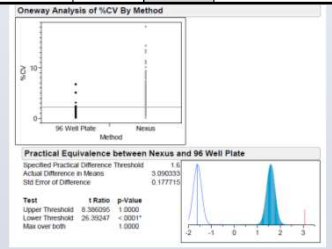
96 Well Plate:

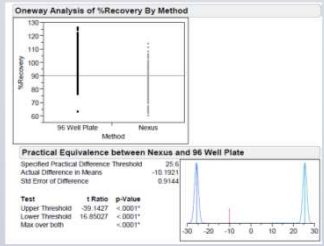
- 22 samples (Max Run)
- Approximately 31 minutes (hands on time)
- Time for assay completion - approx. 48 minutes

Nexus:

- 60 samples (Max Run)
- Approximately 10 minutes (hands on time)
- Time for assay completion - approx. 4.5 hours

Results	Nexus	96 Well Plate	Specified Practical Difference (2 x 96 well plate STDEV)
Average % Recovery	85	95	25.6
STDEV	10.5	12.8	
% Difference	11		
Average % CV	3.8	0.68	1.6
STDEV	2.9	0.8	
% Difference	459		





Conclusions

Performing LAL testing using the conventional 96 well format requires significant time by an experienced Analyst to get samples on test. Compared to the 96 well plate method the Nexus is capable of reducing Analyst time by as much as 300%.

Significant Analyst time is reduced by eliminating:

- Entry of sample information
- Standard curve preparation
- Loading of 96 well microplate

A means comparison of PPC recoveries using a two one-sided t -Test at a 0.05 significance level shows that both methods are practically equivalent . The same test however, does show a significant difference in %CV PPC recovery as compared to the 96 well plate method.

The 96 well plate method had an average %CV of 0.68 as compared to 3.8 with the Nexus. This being said, an average of 3.8% is well under the 25% acceptable range as recommended by the cartridge package insert. In addition, the Nexus showed a slightly lower standard deviation when comparing % PPC Recovery, 10.5 for the Nexus and 12.8 for the 96 well plate method.

The Genzyme Framingham site tests approximately 16000 water sample per year. Testing this amount of samples would require a minimum of 728 plates containing the maximum 22 samples per plate. Considering it takes an experienced Analyst 30 or more minutes to get a fully loaded plate on test, implementation of the Nexus System has the potential to save over 9 weeks of Analyst time per year.

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