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ScanRDI System Performance Data as a Sterility Test Method for Pharmacy Compounded Preparations: A Ten Year Survey

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Abstract

Since 2007 Eagle Analytical Services has utilized the ScanRDI system to test for the sterility of pharmacy compounded products. During this time period, 40,000 tests were performed encompassing approximately 1500 different drug compounds for 500 different pharmacy compounding operations. This complex data indicated that of the products tested, 0.96% (383) were shown to be non-sterile, 96% sterile and 3.4% were found to be incompatible (no test) with the testing process. During this same time period traditional sterility testing outlined in USP 71 was also performed. During this time period over 45000 tests, using USP 71 requirements, were performed for approximately 1000 similar pharmacy operations encompassing over 1500 drug compounds. The USP 71 sterility positive rate was .63% (288). It was shown that no statistical difference exists between pharmacy operations, and drug product preparations compounded. In addition, there was no statistical difference between trained Eagle scientists performing either test. This data supports the conclusion that Eagle ScanRDI methods function as an effective, efficient, alternative to the USP 71 Sterility test method.

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Introduction

Proposed USP 797 revisions will dramatically reduce current BUD (beyond use dates) for sterile compounded product preparations. (REF 1) Finished product testing required to assign the maximum allowable BUD requires a final preparation sterility test to be performed. USP (United States Pharmacopeia) test for sterility, USP <71>, requires a minimum of 14 up to 18 days for completion which could severely affect the availability of compounded preparations. For example, without a sterility test room temperature stored sterile compounded drugs would have a labeled BUD of 4 to 6 days but after testing the BUD extends to 42 days. Even if these dates are ultimately extended it is apparent that it is critical to minimize the testing period so as to ensure the delivery/ dispensing of prescribed products to the patient within the required time of not only dispensing but patient use.

Since 2004 Eagle Analytical has studied and developed procedures for use within the ScanRDI analyzer for the sterility testing of compounded product preparations. The ScanRDI system is the subject of an FDA Type V Drug Master file (DMF 14621) which contains data to support the technology for the detection of bacteria, spores yeast and molds (REF 2). This master file also contains the validation data for process water microbial analysis which supported previously published data. (REF 3). This published data and data contained within the DMF, documents the requirements of USP 1225. Simply stated the robustness, ruggedness, precision and accuracy of the ScanRDI has been proven.

Using this process, a sterility test can be performed, reviewed and reported within one day.

Method

All samples were prepared and managed through the Eagle Analytical procedure system. This was, in the beginning, a research procedural system focused on the research associates documenting what was performed. As procedures were developed they were codified including a functional change control system for tracking effective dates for all procedures. The ScanRDI units were installed by the manufacturer who was also tasked with the performance of IQ, OQ, and PQ to include final reports. All recommended maintenance requirements are performed, and have always been, on contract by the manufacturer. All reagents and supporting material are supplied by the manufacturer. All personnel involved in the performance of tests are trained directly by the manufacturer. Only degreed scientists have been trained to use this system.

As a summary, the ScanRDI system can be described as follows. ScanRDI uses a combination of fluorescent labeling and solid phase laser cytometry to identify viable microorganisms from filterable samples. The system sensitivity can detect a single cell within 3 hours once presented with the product sample. Proprietary stains which consist of non – fluorescent membrane permeant substrates are used which are cleaved by non-specific esterase and retained in viable cells. This accumulated measurable chromophore is then detected during the laser scanning step in the ScanRDI analyzer. Within a 3 minute period results are displayed without operator interpretation. Some products are incompatible with this system due to the fact of auto fluorescence of the preparation. The unit will automatically indicate as such and it would not be reported as a sterility failure. A scan map display showing the precise location of each organism for visual confirmation is a system microscope option and was and is used by Eagle to confirm all results. The reader is referred to the manufacturer for a more detailed description of the operation. (REF 4).

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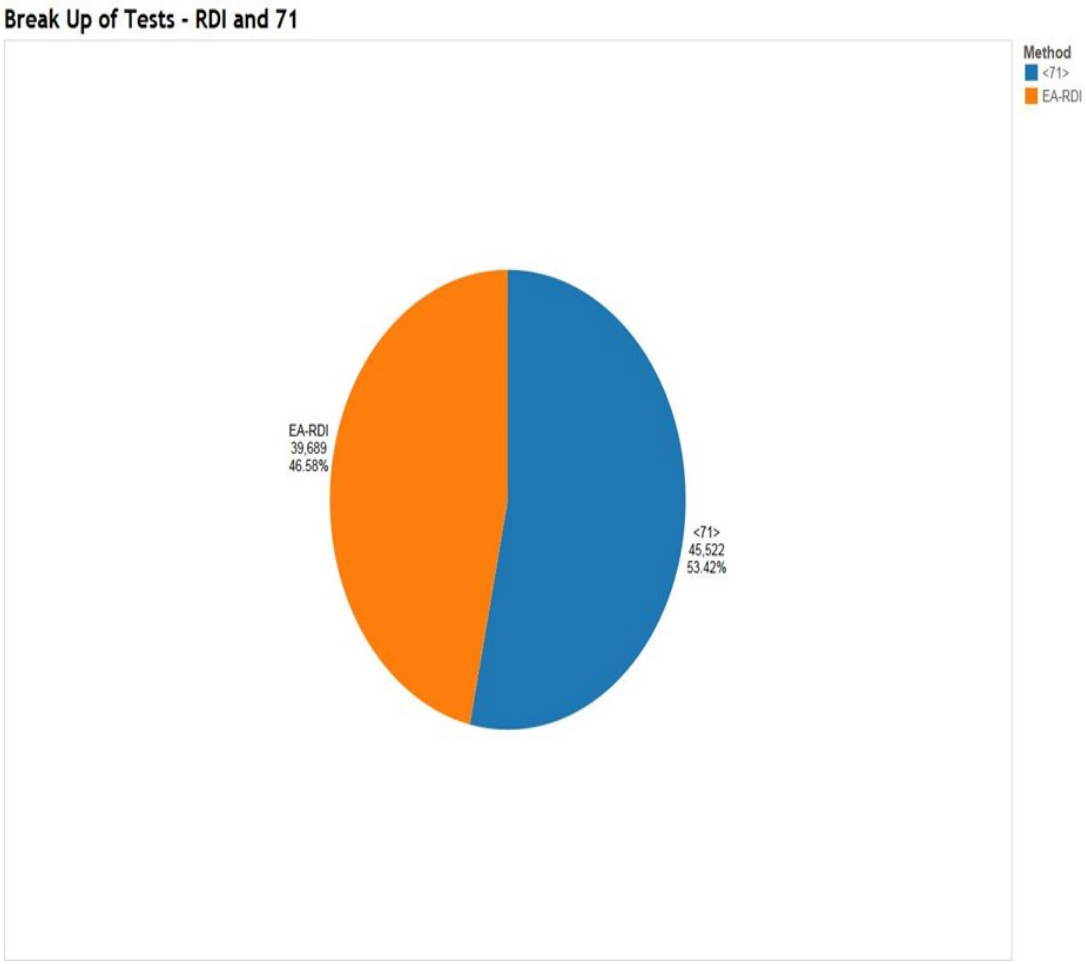
Survey

Eagle Analytical analyzed data compiled, using both the ScanRDI system and classical USP 71 testing, over a period of ten years. Research and analysis of sterility testing performed on unique patient specific sterile compounds prepared in multiple pharmacy locations was the focus of the study. From the approximately 85,000 data points 47% were ScanRDI processed and 53% were processed via methods described in USP 71.



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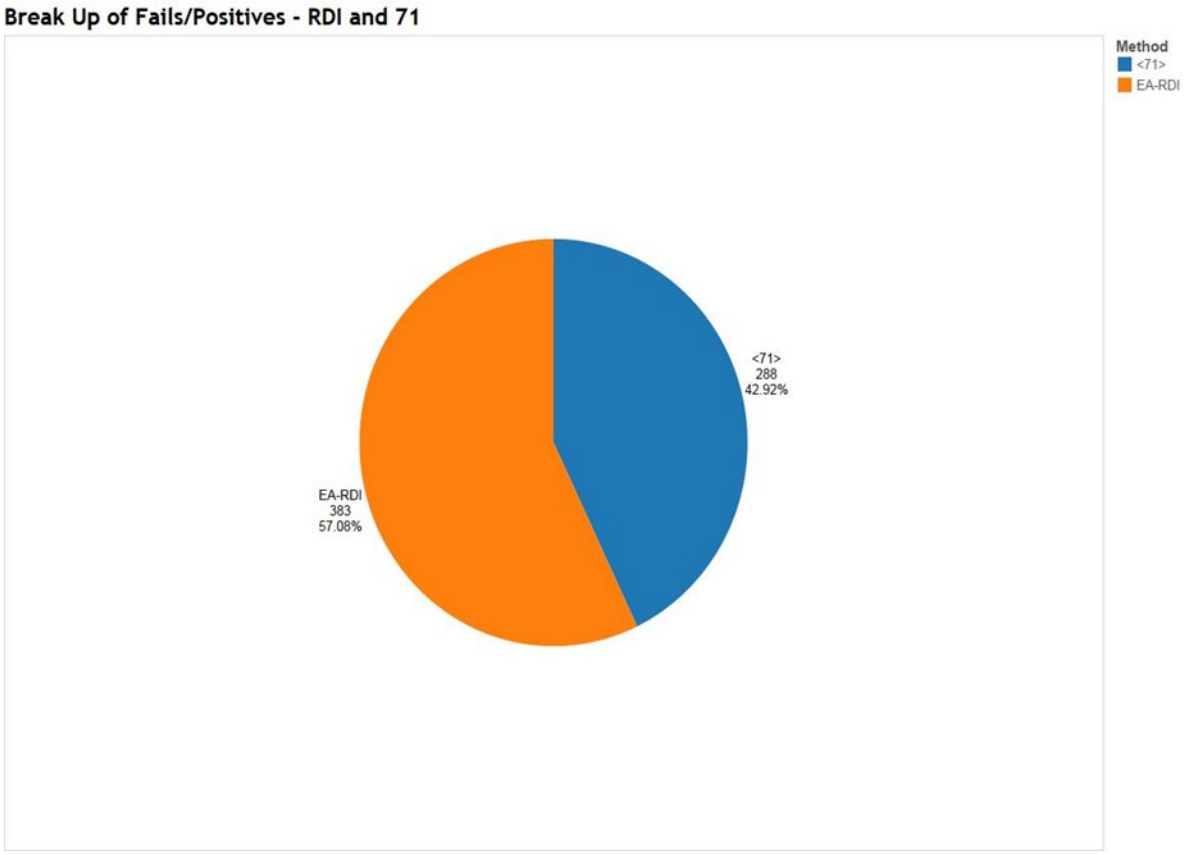
Survey

The distribution of failures by test methods indicated that 57% of all failures were registered using the ScanRDI method.



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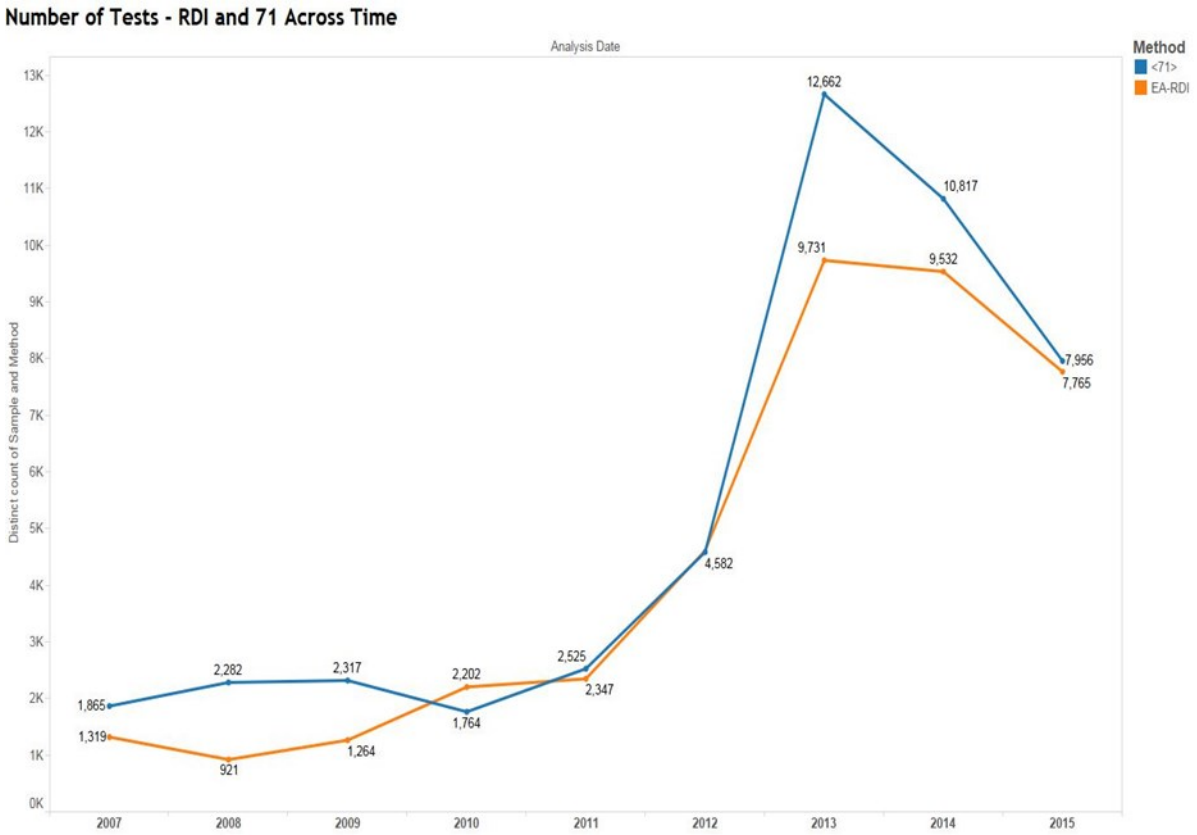
When studied further it was shown that the ScanRDI system detected a higher rate of positives than the USP 71 method, 0.97% v. 0.63% respectively. This increased level of sensitivity had been predicted by the manufacturers and others but this data set is unique to compounded products.

The following depicts the number of tests performed over time for each method used.



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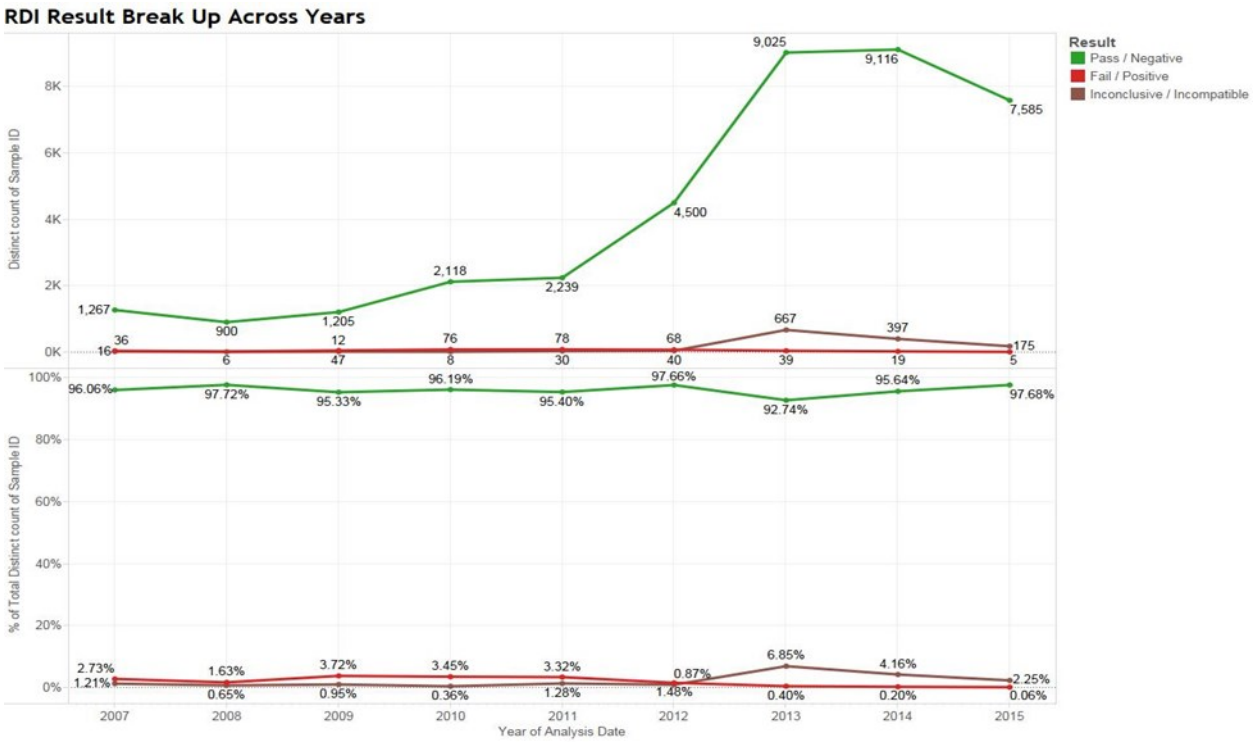
The following data indicates that frequency of positives was not impacted by the number of tests being performed. The increased rate of incompatibility as shown in years 2014 and 2015 may well be due to the expanding use of the method beyond its capability at that time. The rates of sterility test positives however appear consistent.



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Conclusion

As described by Smith "…the ScanRDI method is appropriate for use as a rapid alternative to the growth-based sterility test method." (REF 5) Eagle is not aware of any other system which has been evaluated as extensively with such a large data base of actual specific use to evaluate end product sterility of compounded preparations.

The data show that ScanRDI performance was as or more sensitive than the USP 71 method therefore supporting the utilization of this method for the sterility testing of compounded preparations.

Reference

1. USP General Chapter <797>, Revision in process

2. FDA Type V Drug Master File #14621

3. Jones DL, et.al Solid Phase, Laser- Scanning Cytometry: A new two hour method for the enumeration of Microorganisms in Pharmaceutical water. *Pharmaceutical Forum, Vol 25:1 pp7626-7645.*

4. www.Biomeriux-industry.com

5. Smith R. et.al. Evaluation of the ScanRDI as a rapid alternative to the Pharmacopeia Sterility Test Method: Comparison of the limit of detection. PDA Journal of Pharmaceutical Science and Technology **64** (4), 356-363, 2010.