ATCC

APPLICATION NOTE

DEVELOPMENT AND PERFORMANCE EVALUATION OF MICROQUANT™ – QUANTITATIVE, RAPIDLY REHYDRATING REFERENCE MATERIALS FOR STREAMLINED MICROBIAL QUALITY CONTROL TESTING

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ABSTRACT

Microbial quality control testing is a cornerstone of pharmaceutical product development and essential for the safety, efficacy, and purity of biological products. To ensure the accuracy of these tests, pharmaceutical manufacturers need full confidence that their microbial controls are authenticated, low passage, and precisely quantitated. Leveraging innovative preservation technologies, ATCC has developed our best-in-class microbial quality control strains in a rapidly rehydrating pelleted format that delivers consistent quantitation. In this study, we demonstrate the performance of this novel suite of products in streamlining microbial quality control testing.

INTRODUCTION

Microbial contamination of pharmaceutical products is one of the leading causes of product recalls in the pharmaceutical industry.[1,2] These recalls can lead to extensive financial losses, regulatory consequences, brand erosion, and reputational damage.[1,2] More importantly, microbial contamination can significantly affect patient health and safety, potentially resulting in permanent disabilities or life-threatening conditions. To ensure product safety and integrity, pharmaceutical manufacturers are required by their respective government agencies to perform robust quality control procedures that, when properly followed, can help identify microbial contamination prior to product release.

Pharmaceutical manufacturers in the United States perform tests such as antimicrobial effectiveness testing, environmental monitoring, growth promotion testing, bioburden testing, sterility testing, and suitability testing as recommended by the United States Pharmacopeia (USP).[3-7] To ensure the accuracy of these tests, the regulatory guidance recommends the use of test strains that are maintained by reputable culture collections like ATCC. While ATCC has consistently met the needs for microbial quality control testing by providing authenticated reference materials, the laboratories performing microbial quality control testing often face infrastructure and resource limitation challenges when preparing control strains for testing.

For instance, many testing laboratories choose to develop and maintain their own internal control banks of reference materials. Creation and maintenance of the control banks requires complex expansion protocols and extensive laboratory space and equipment. These processes can be error prone. Precise quantitation of the reference materials is also a challenge. Several quality control tests require reference materials to be prepared in either a low-titer or high-titer format. Meeting these specifications is traditionally obtained by preparing a culture of the required strain, which can require a significant investment in time and resources. Additionally, accurate quantification and passage of the microbial strains require highly skilled microbiologists to be involved. All these factors can make the process of microbial quality control testing a costly, time-intensive, and often inconvenient affair.

To address these challenges and to help streamline microbial quality control testing in pharmaceutical manufacturing, ATCC has developed MicroQuant™. This novel product suite leverages an innovative preservation technology to deliver precisely quantitated microbial reference materials in a single-use format that rapidly rehydrates and is convenient to store at 2-8°C. This product suite allows use of authenticated reference microbial strains from ATCC in an easy-to-use format. In this study, we demonstrate the precise quantitation and rapid rehydration of MicroQuant™ controls and showcase their performance against similar products on the market.

MATERIALS AND METHODS

DEVELOPMENT OF MICROQUANT™ CONTROLS

In this study, we targeted microbial strains listed in the microbial quality control tests as referenced in USP chapters <51> and <61> (Table 1);[3,5] each of these chapters details assays that require a specific quantity of microorganisms. The selected microorganisms were cultured in tightly controlled conditions using methods and media outlined in the specific product sheets for each strain. Following microbial culture, the strains were then processed using a proprietary preservation process to create a user-friendly microbial pellet format (Table 2).

Table 1: ATCC® microbial strains used in the study

ATCC® No.	Species	Strain Designation	USP <51>	USP <61>
16404™	*Aspergillus brasiliensis*	WLRI 034(120)	✓	✓
6633™	*Bacillus spizizenii* (Formerly *Bacillus subtilis*)	NRS 231		✓
10231™	*Candida albicans*	3147	✓	✓
8739™	*Escherichia coli*	Crooks	✓	
9027™	*Pseudomonas paraeruginosa* (Formerly *Pseudomonas aeruginosa*)	R. Hugh 813	✓	✓
6538™	*Staphylococcus aureus* subsp. *aureus*	FDA 209	✓	✓

Table 2: ATCC® MicroQuant™ products

ATCC® No.	Description	Quantitation (CFU/vial)
16404-LQ-PACK™	MicroQuant™ *Aspergillus brasiliensis*, low CFU	100-1,000
16404-HQ-PACK™	MicroQuant™ *Aspergillus brasiliensis*, high CFU	10^7-10^8
6633-LQ-PACK™	MicroQuant™ *Bacillus spizizenii*, low CFU	100-1,000
6633-HQ-PACK™	MicroQuant™ *Bacillus spizizenii*, high CFU	10^7-10^8
10231-LQ-PACK™	MicroQuant™ *Candida albicans*, low CFU	100-1,000
10231-HQ-PACK™	MicroQuant™ *Candida albicans*, high CFU	10^7-10^8
8739-LQ-PACK™	MicroQuant™ *Escherichia coli*, low CFU	100-1,000
8739-HQ-PACK™	MicroQuant™ *Escherichia coli*, high CFU	10^7-10^8
9027-LQ-PACK™	MicroQuant™ *Pseudomonas paraeruginosa*, low CFU	100-1,000
9027-HQ-PACK™	MicroQuant™ *Pseudomonas paraeruginosa*, high CFU	10^7-10^8
6538-LQ-PACK™	MicroQuant™ *Staphylococcus aureus* subsp. *aureus*, low CFU	100-1,000
6538-HQ-PACK™	MicroQuant™ *Staphylococcus aureus* subsp. *aureus*, high CFU	10^7-10^8

EVALUATING THE PROCESSING TIME AND QUANTITATION OF MICROQUANT™ CONTROLS

MicroQuant™ controls were evaluated for their performance in the following two areas: the time required to process the pellet and the quantitation of the product following recovery of the material. Both attributes were also evaluated against comparable products from other vendors.

To evaluate preparation time, MicroQuant™ products and comparable vendor products were removed from the appropriate storage unit. Vendor products that were designed to be stored at -20°C were thawed according to instructions provided on the respective instructions for use (IFU). MicroQuant™ products and vendor products that were designed to be stored at 2-8°C were rehydrated according to instructions provided on the respective IFU. The processing time for each product was evaluated in units of minutes.

To evaluate quantitation following recovery, MicroQuant™ products and comparable vendor products were prepared as stated above and were plated on non-selective media. Following an appropriate growth period, CFUs were enumerated.

RESULTS

MICROQUANT™ PRODUCTS RAPIDLY REHYDRATE WITH CONSISTENT PROCESSING TIMES

The time required to process MicroQuant™ products was assessed and compared to that of other vendor products with similar applications. In this analysis, we followed ATCC's IFU for MicroQuant™ products and the respective IFUs for vendor supplied products to process the strains. Both the IFU-described processing time and maximum observed processing time required by users were reported (Figure 1). Here, MicroQuant™ products consistently rehydrated in approximately 1 minute with minor user-to-user variations. When compared to vendor products, the overall processing time for MicroQuant™ was much shorter than lyophilized products (Company A and B) and similar to frozen products (Company C and D).

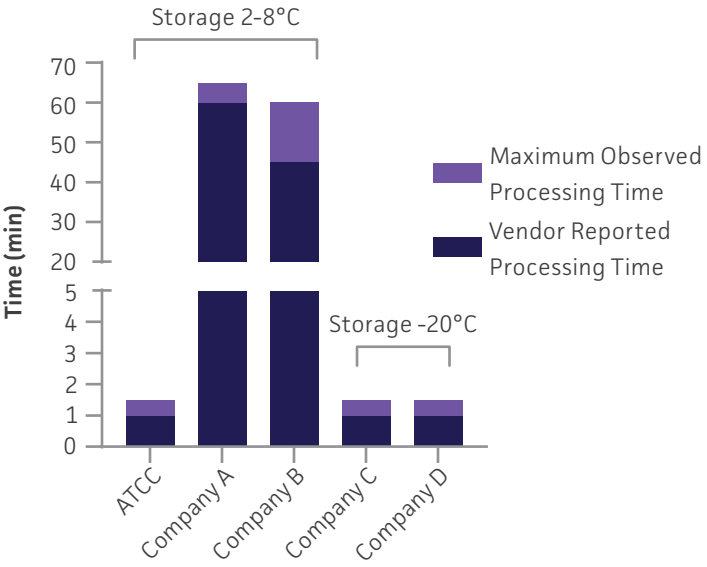

Figure 1: Evaluating the processing time of MicroQuant™ products in comparison to similar vendor products following removal from storage. This is a compilation of observations including a minimum of 6 units from each product for each vendor. No differences in processing time were seen between species or titer range.

MicroQuant™ delivers precise quantitation that is consistent for low and high CFU targets

We then assessed the recoverable CFU from both the low and high CFU preparations for each of the MicroQuant™ strains following rehydration with the respective proprietary buffers. Our data demonstrate that MicroQuant™ products can consistently achieve the indicated target ranges for all tested organisms (Figure 2).

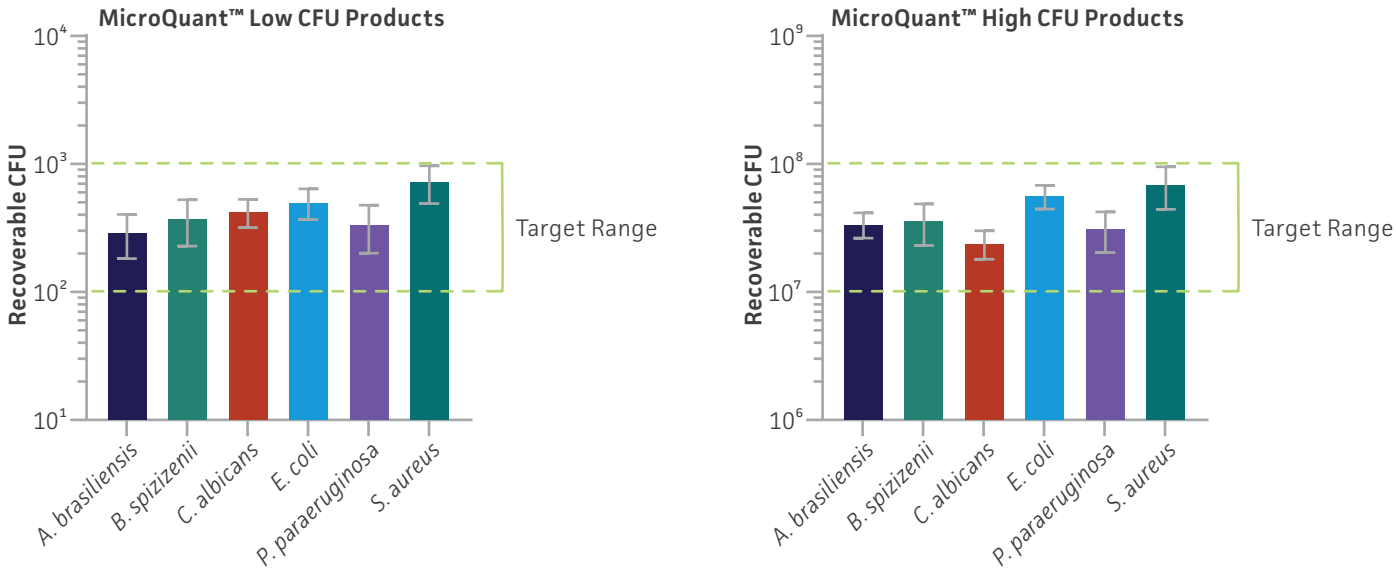

Figure 2: Evaluating MicroQuant™ quantitation following recovery. Recoverable CFU for low and high CFU MicroQuant™ products. The target range was 100-1,000 CFU for low CFU and 10^7-10^8 CFU for high CFU MicroQuant™. Each bar represents 60 data points collected by a minimum of three separate biologists. Error bars show standard deviation.

When evaluating the quantitation of MicroQuant™ products against comparable vendor products that target the same titer ranges, we found that MicroQuant™ is the only single-use control that is completely within the acceptable range for all six cultures for both the low (Figure 3) and high (Figure 4) CFU formats. At the time of our analysis, only two vendors had inventory to ship all six species at both high and low concentrations.

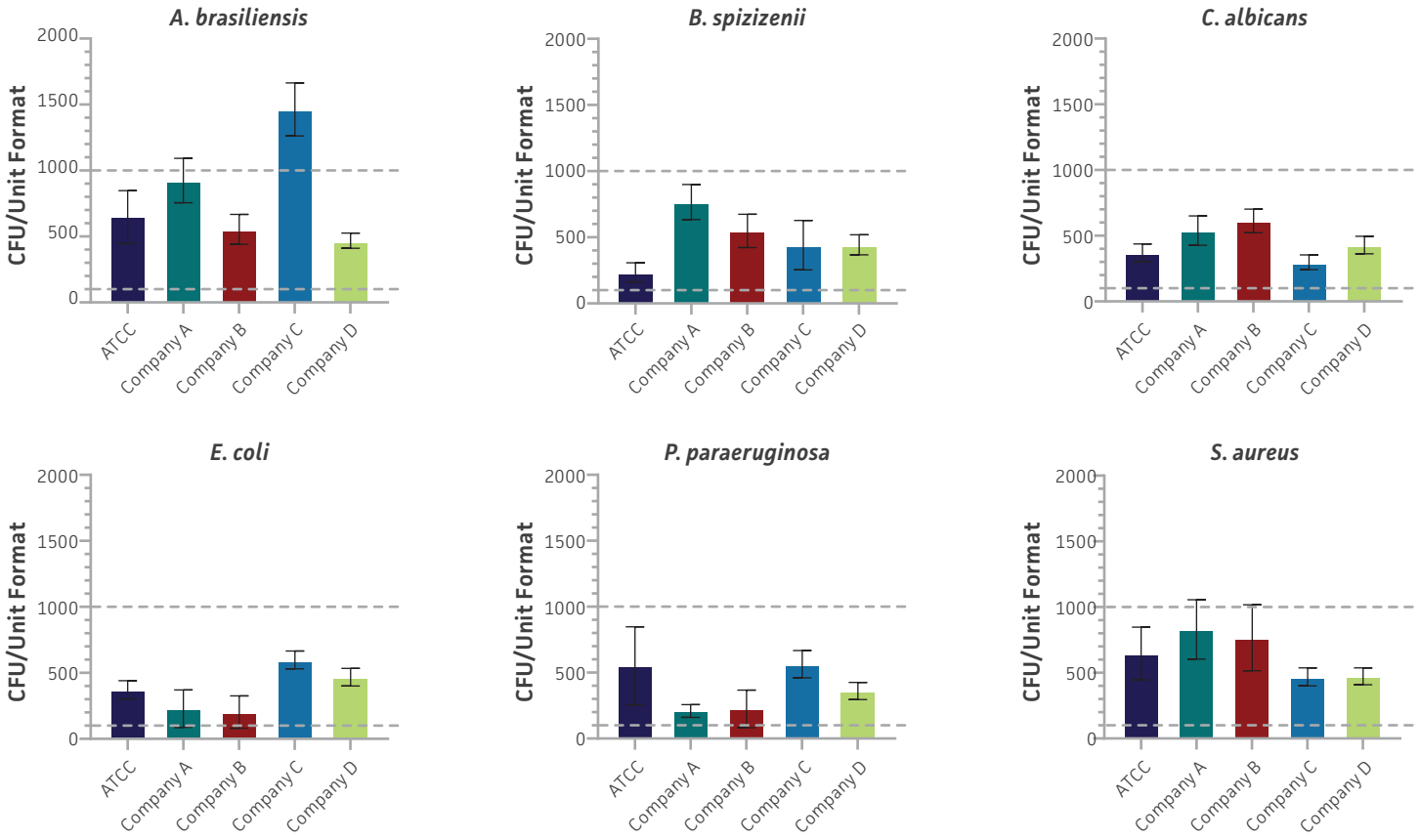

Figure 3: Comparison of low CFU product quantitation (100 to 1000 CFU per unit) of MicroQuant™ and comparable vendor products.
Each bar represents a minimum of 12 data points, error bars show standard deviation.

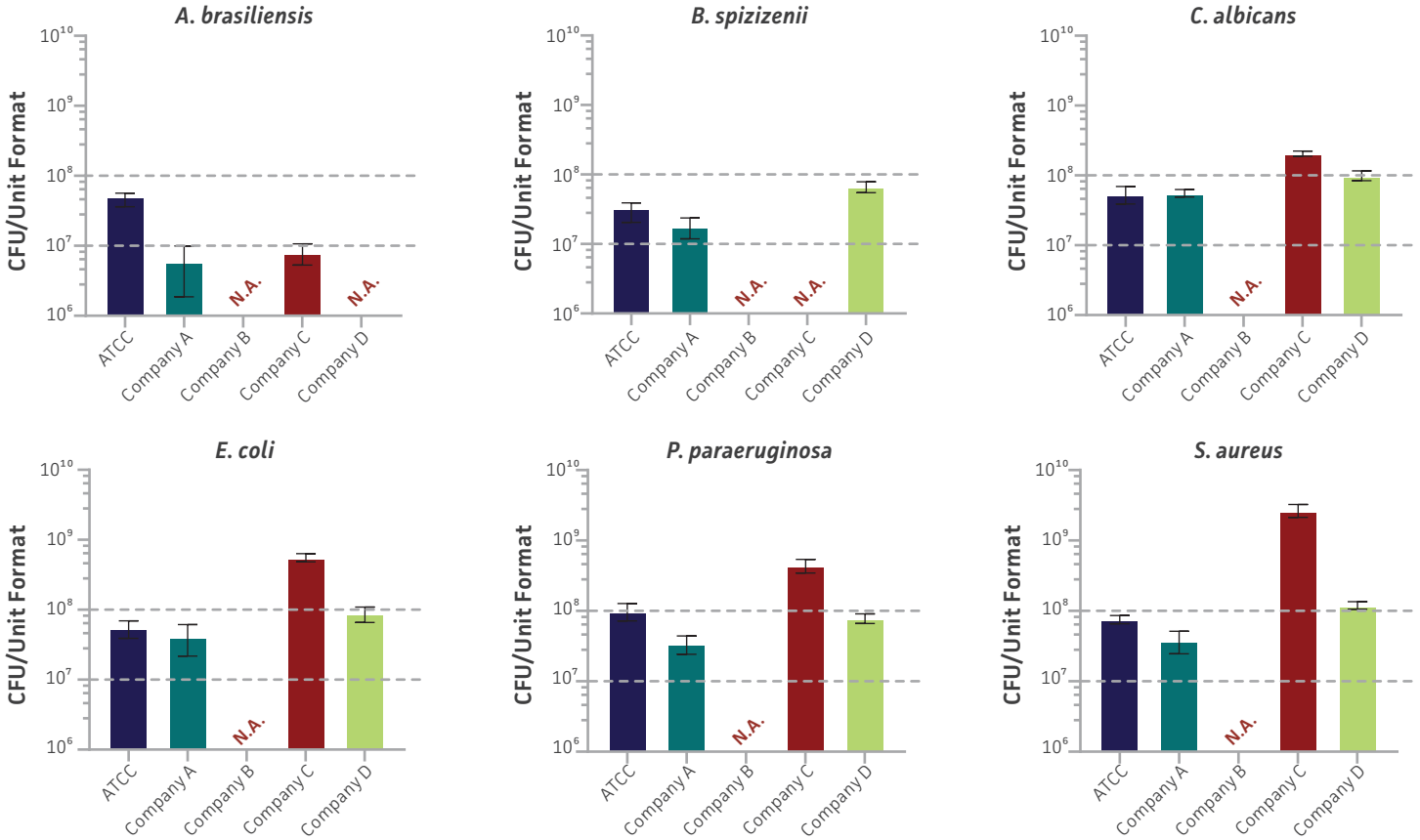

Figure 4: Comparison of high CFU product quantitation (10^7 to 10^8 CFU per unit) of MicroQuant™ and comparable vendor products.
Each bar represents a minimum of 12 data points, error bars show standard deviation. N.A. = Not Available.

CONCLUSION

Our data show that we have successfully created a convenient, quantitative microbial product format that can consistently provide a precise range of CFU for a suite of organisms in accordance with the specifications described in the USP <51> and <61> compendial assays. When assessed against comparable vendor products on the market, MicroQuant™ was the only single-use control that demonstrated a precise level of quantitation that was completely within both the low and high CFU target ranges for all six cultures. We also demonstrated that this product format can be rapidly processed in approximately a minute, minimizing the amount of hands-on time required to prepare materials for quality control testing. When compared to similar single-use products that are also stored at 2-8°C, the processing time for MicroQuant™ was considerably shorter. Overall, this novel suite of products provides best-in-class, original source strains from ATCC in a ready-to-use, rapidly rehydrating format that delivers consistent quantitation, enabling testing labs to minimize handling and streamline microbial quality control testing.

PRECISION IN EVERY PELLET, TRUST IN EVERY TEST

- **Sourced from reference strain:** Products were created from the authenticated ATCC strains mentioned in regulatory guidelines
- **Precisely quantitated:** Products are available in high-titer (10^7 to 10^8 CFU per vial) and low-titer (100 to 1,000 CFU per vial; 10 assays) formats to meet USP General Chapter requirements. Our precise quantitation across batches ensures lot-to-lot consistency.
- **Single-use format:** Our highly convenient ready-to-use format enables fast assay setup while minimizing handling. Reduces the need for special handling knowledge and the maintenance of expansive microbial cultures.
- **Immediate rehydration at room temperature:** With a processing time of a minute, you can reduce your hands-on time while improving efficiency.
- **Convenient storage at 2-8°C:** MicroQuant™ products are stable in refrigerator temperatures for 6-12 months (see individual products for expiry), making them easy to store and ready to use anytime—no need to thaw.
- **Reliable:** Each product is manufactured by ATCC under ISO 17034, so you can trust that you are receiving high-quality original source material.

REFERENCES

1. Hock SC, et al. Contamination Trends & Proposed Solutions. Pharmaceutical Engineering April 2023. Accessed online: https://ispe.org/pharmaceutical-engineering/march-april-2023/contamination-trends-proposed-solutions
2. atel R, et al. A retrospective regulatory analysis of FDA recalls carried out by pharmaceutical companies from 2012 to 2023. Drug Discov Today 29(6): 103993, 2024.
3. USP General Chapters. <51> Antimicrobial Effectiveness Testing. In: USP-NF. Rockville, MD: United States Pharmacopeia. DOI: https://doi.usp.org/USPNF/USPNF_M98790_03_01.html
4. USP General Chapters. <60> Microbiological Examination of Nonsterile Products Tests for *Burkholderia* Cepacia Complex. In: USP-NF. Rockville, MD: United States Pharmacopeia. DOI: >https://doi.usp.org/USPNF/USPNF_M12455_02_01.html
5. USP General Chapters. <61> Microbial Examination of Nonsterile Products: Microbial Enumeration Tests. In: USP-NF. Rockville, MD: United States Pharmacopeia. DOI: https://doi.usp.org/USPNF/USPNF_M98800_01_01.html
6. USP General Chapters. <62> Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms. In: USP-NF. Rockville, MD: United States Pharmacopeia. DOI: https://doi.usp.org/USPNF/USPNF_M98802_01_01.html
7. USP General Chapters. <71> Sterility Tests. In: USP-NF. Rockville, MD: United States Pharmacopeia. DOI: https://doi.usp.org/USPNF/USPNF_M98810_01_01.html

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AP-082025-v03

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