An Inside Look at USP <71>

April 13, 2018

Thomas C. Kupiec, Ph.D.
kupiec@arlok.com

Objectives

• Review Sterility Tests - USP <71>
• Growth Promotion, Media and Test Organisms
• Examine Method Suitability and Sampling requirements
• Understand Interpretation and Limitations of the Sterility test
• Evaluate Environments: Sterility Testing and Pharmacy Operations

REVIEW STERILITY TESTS
USP <71>
USP <71> Sterility Tests

- Applies to substances, preparations, or articles which, according to the Pharmacopeia, are required to be sterile.
- Pharmacopeial procedures are not by themselves designed to ensure that a batch of product is sterile or has been sterilized. This is accomplished primarily by validation of the sterilization process or of the aseptic procedures.
- A satisfactory result only indicates that no contaminating microorganism has been found in the sample examined under the conditions of the test.

What does the USP <71> test tell you?

- USP <71> testing does not ensure a batch or lot is sterile.
- To ensure batches/ lots are sterile, a validated sterilization procedure combined with aseptic processing MUST be followed.
- Sterility Testing is a process control evaluation and a general indicator of microbiological quality of a product.
- For additional quality assurance, a USP <71> test can be run on products even if the test is not required by USP <797>.

USP <797> and USP <71>

- Must meet a sterility test before they are dispensed:
  - High-risk level CSPs prepared in groups of more than 25 identical individual single-dose packages (e.g., ampules, bags, syringes, vials)
  - Multiple-dose vials (MDVs) for administration to multiple patients
  - Exposed longer than 12 hours at 2°C to 8°C before sterilization
  - Exposed longer than 6 hours at warmer than 8°C before sterilization
- High-Risk Level CSPs of < 25 articles, and not fitting one of the other categories, do not need a USP <71> sterility test
- Requirements may also vary between states – check with the State Boards of Pharmacy
USP <797> and USP <71>  

- Limits to storage periods before administration without a passing sterility test:

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Ambient</th>
<th>Refrigerated</th>
<th>Freezer (&lt;-20°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>48 hours</td>
<td>14 days</td>
<td>45 days</td>
</tr>
<tr>
<td>Medium</td>
<td>30 hours</td>
<td>9 days</td>
<td>46 days</td>
</tr>
<tr>
<td>High</td>
<td>24 hours</td>
<td>3 days</td>
<td>45 days</td>
</tr>
</tbody>
</table>

- A method not described in the USP may be used if verification results demonstrate that the alternative is at least as effective and reliable as the USP method.
  - See USP <1223> Validation of Alternative Microbiological Methods
  - This is the framework Rapid Sterility Testing is operating under to find acceptance as an alternative method.

GROWTH PROMOTION, GROWTH MEDIA, AND TEST ORGANISMS  

Growth Promotion  

- For a valid sterility test, you must prove that the media used will grow bacteria and fungi.
- Growth promotion is not a test of a drug product.
- Each lot or batch of media must have a growth promotion performed.
- < 100 cfu of each of the 6 USP <71> organism into the media
- Short Incubation (3-5 days)
- Clearly visible, representative growth must be present by the conclusion of the incubation period.
Test Medias – 2 Types

- Fluid Thioglycollate Medium, referred to as FTM or FTG
  - Detects aerobic & anaerobic (won’t grow with oxygen) bacteria
  - Incubated at 30°C – 35°C

- Soybean-Casein Digest Medium, referred to as Trypticase Soy Broth, or TSB
  - Detects aerobic bacteria and fungi
  - Incubated at 20°C – 25°C

### Organism Type Properties Oxygen? Media

<table>
<thead>
<tr>
<th>Organism</th>
<th>Type</th>
<th>Properties</th>
<th>Oxygen?</th>
<th>Media</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>Bacteria</td>
<td>Gram-positive cocci (Spherical)</td>
<td>Aerobic</td>
<td>FTG 30°C – 35°C</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Bacteria</td>
<td>Gram-negative Rod</td>
<td>Aerobic</td>
<td>FTG 30°C – 35°C</td>
</tr>
<tr>
<td>Clostridium sporogenes</td>
<td>Bacteria</td>
<td>Gram-positive Rod, Spore forming</td>
<td>Anaerobic</td>
<td>FTG 30°C – 35°C</td>
</tr>
<tr>
<td>Bacillus subtilis</td>
<td>Bacteria</td>
<td>Gram-positive Rod, Spore forming</td>
<td>Aerobic</td>
<td>TSB 20°C – 25°C</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>Fungi</td>
<td>Budding yeast</td>
<td>Aerobic</td>
<td>TSB 20°C – 25°C</td>
</tr>
<tr>
<td>Aspergillus brasiliensis</td>
<td>Fungi</td>
<td>Spore forming filamentous mold</td>
<td>Aerobic</td>
<td>TSB 20°C – 25°C</td>
</tr>
</tbody>
</table>

EXAMINE METHOD SUITABILITY AND SAMPLING REQUIREMENTS
Sterility Test Methods

- Membrane Filtration – The preferred method
  - The sample is passed through a set of filters, the filters are rinsed, then each is placed in growth media, and incubated.
  - Easy to test large volumes
  - Low risk of contamination

- Direct Inoculation
  - The sample volume is deposited directly into each growth media and incubated.
  - Useful for testing non-filterable products (oils, suspensions, etc.)

- Emulsifying, neutralizing, and inactivating agents can be added, as long as they don’t affect the recovery of microorganisms.
  - Ex. B-Lactamase to deactivate Penicillin

Membrane Filtration

- Diluting and Rinsing Fluids - 3 Types
- Filters – Options for different sample types
- Sterile tubing and sterile pathways can be flushed with rinse, then the rinse filtered.
- There are limits to the sample and rinse that can be used per filter, a product may require several filters to test if it is a large volume.

Direct Inoculation

- The sample is aseptically transferred directly into each growth media.
- Oils, Suspensions, Pellets
- In addition to drug products, the direct inoculation method can be used to test gauze, dressings, and medical devices.
  - Gauze and dressings are tested either by weight if from a large package or the entire contents if the sample is an individually wrapped, single-use item.
  - Sterile devices can be tested either whole or disassembled, but must be made into small enough sections so as to be completely immersed in growth media.
USP <71> 
Sterility Tests - Method Suitability Test 

- Method suitability demonstrates the sterility test is valid, in that it eliminates the antimicrobial activity in the formulation, and establishes the contamination, if present, will be detected.

- Once method suitability has been demonstrated, it applies to that specific formulation and does not need to be repeated unless there is a change in formulation, production method, or test procedures.

Method Suitability – Membrane Filtration 

- Method suitability includes all 6 USP <71> organisms.

- The volume should meet or exceed the volume that will be tested on production batches.

- Method suitability may require significantly more volume than the actual sample test.

- Validate the volume needed to cover the largest batch that might be made. Filtration method suitability is volume sensitive, method suitability must be repeated if the required test volume increases.

Method Suitability Direct Inoculation 

- Compared to filtration methods, there are fewer variables in a direct inoculation test.

- The main variable in direct inoculation is the dilution ratio. 
  - Ex. 1:10, 1:40, 1:100

- The ratio can be very high if the sample to be tested has significant antimicrobial properties that cannot be overcome with neutralizing agents.

- Direct inoculation is used for unfilterable products, like suspensions, oils, etc.

- Method suitability for direct inoculation requires lower sample volumes than membrane filtration.
Method Suitability Evaluation

- Requirements of a passing method suitability
  - Clearly visible growth is observed after 5 days of incubation.
  - Growth is comparable to a control without product.

- If method suitability fails, the test method is modified and repeated.
  - Increased dilution, larger rinse volume, additional reagents, etc.

- A sample will have a specific combination of sample volume, rinse fluid, rinse fluid volume, filter type, and neutralizing agent that are standardized for testing a specific formulation.

- After passing method suitability, lots should be tested using the method.

USP <71> SAMPLE REQUIREMENTS: TABLES 2 AND 3

Minimum Quantity to be Used for each Medium

<table>
<thead>
<tr>
<th>Table 2.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity per Container</td>
</tr>
<tr>
<td>Liquefied</td>
</tr>
<tr>
<td>Liquid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
<tr>
<td>Solid</td>
</tr>
</tbody>
</table>
Minimum Number of Articles to be Tested in Relation to the Number of Articles in the Batch Table 3.

**Sampling Across the Batch – Beginning, Middle and End**

<table>
<thead>
<tr>
<th>Number of Items in the Batch</th>
<th>Minimum Quantity of Sample to Be Tested For Each Package, Bottles, or Vials</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 to 1000</td>
<td>More than 10 but not more than 100 containers, whichever is greater</td>
</tr>
<tr>
<td>&gt; 1000</td>
<td>20 containers</td>
</tr>
<tr>
<td>&gt; 5000</td>
<td>50 containers</td>
</tr>
<tr>
<td>&gt; 10000</td>
<td>100 containers</td>
</tr>
<tr>
<td>&gt; 100000</td>
<td>500 containers</td>
</tr>
<tr>
<td>&gt; 1000000</td>
<td>1000 containers</td>
</tr>
</tbody>
</table>

Sample Requirements

- Both tables must be taken into consideration to sample correctly.
- Articles should be taken from across the batch – beginning, middle, and end of run.
- Always round up for article requirements.
- If an article contains < 2 mL, the articles tested must be doubled to meet sampling requirements.

Sample Requirements – Example Calculations

- A pharmacy makes 400 article batches of a filterable parenteral in 30 mL vials:
  - From Table 3:
    - More than 10 but not more than 100 containers
      - Submit 10 vials
  - From Table 2:
    - 8-40 mL
      - Submit contents of each container, but not less than 1 mL
  - The entire contents of all 10 is used for testing; 300 mL (30 mL x 10) total test volume.
Sample Requirements – Example Calculations

• A pharmacy makes 2000 article batches of a filterable parenteral in 10 mL vials:
  – From Table 3:
    
    | More than 100 containers | 2% or 20 containers, whichever is less |
    |--------------------------|---------------------------------------|
    | 2000 x 2% = 40          | 40 > 20, Submit 20 vials |
  – From Table 2:
    
    | 1-50 mL | Half the contents of each container, but not less than 1 mL |
    1-50 mL | Half the contents of each container, but not less than 1 mL |
  – The entire contents of all 20 is used for testing; 200 mL (10 mL x 20) total test volume.

Sample Requirements – Example Calculations

• A pharmacy makes 780 articles of a filterable parenteral in 20 mL vials.
  – From Table 3:
    
    | More than 100 containers | 2% or 20 containers, whichever is less |
    |--------------------------|---------------------------------------|
    | 780 x 2% = 15.6, Round up to 16 |
    | 16 < 20, Submit 16 vials |
  – From Table 2:
    
    | 1-50 mL | Half the contents of each container, but not less than 1 mL |
    1-50 mL | Half the contents of each container, but not less than 1 mL |
  – The entire contents of all 16 is used for testing; 320 mL (20 mL x 16) total test volume.

Sample Requirements – Example Calculations

• A pharmacy makes 800 article batches of a filterable parenteral in 50 mL vials:
  – From Table 3:
    
    | More than 100 containers | 2% or 20 containers, whichever is less |
    |--------------------------|---------------------------------------|
    | 800 x 2% = 16           | 16 < 20, submit 16 vials |
  – From Table 2:
    
    | Greater than 40 mL, not greater than 100 mL | 20 mL |
    40 mL, not greater than 100 mL, 20 mL |
  – 40 mL is used out of each vial (20 mL into each media); 640 mL (40 mL x 16) total test volume.
Sample Requirements – Example Calculations

- A pharmacy makes 400 article batches of an antibiotic parenteral in 250 mL IV bags:
  - From Table 3:
    - >100 mL = Large Volume, 400 x 2% = 8
    - 8 < 10, Submit 8.
  - From Table 2:
    - Antibiotic seques
    - 1 mL
  - 2 mL is used out of each (1 mL/ media); 16 mL (2 mL x 8) total test volume.

Sample Requirements – Example Calculations

- A pharmacy makes 900 article batches of a filterable parenteral in 1 mL vials with a 0.8 mL fill:
  - From Table 3:
    - 900 x 2% = 18
    - 18 < 20, normal test = 18
  - Also consider Table 2 for # of articles calculation, since the fill is < 1 mL:
    - Less than 1 mL, The entire contents of each container
  - To meet the requirements of both Table 3, # of articles per media, and Table 2, quantity per article, Double original number.
    - 18 x 2 = 36
  - The whole contents of each container will be put into each media (since the volume is < 1 mL); 14.4 mL/ media, 28.8 mL total volume tested.

Sample Requirements – Example Calculations

- A pharmacy makes 1400 article batches of a subcutaneous pellet:
  - From Table 3:
    - 1400 x 2% = 28
    - 28 > 20, normal test = 20
  - From Table 2:
    - The entire contents of each container
  - The normal requirement for a batch of 1400 is 20, but pellets cannot split, so double it to 40. (Think of it the same way as a vial with < 1 mL)
  - Submit 40 pellets, 20 will be put into each media; 40 pellets tested.
Examination and Interpretation

- At intervals during the incubation period and at its conclusion (14-18 days), the test media is examined for evidence of microbial growth.
- If no evidence of microbial growth is found, the product meets the test requirements for sterility.
- A “Sterile” result is released which indicates that the product tested meets the test requirements for sterility.

Subcultures

- Drugs that cloud, distort, color, settle, crystalize, or precipitate in the growth media make it difficult to be certain the product is sterile.
- This generally happens with direct inoculation tests.
- If there is any doubt, a subculture is conducted.
  - 1 mL of sample from the original test is transferred to a fresh container of the same media.
  - The original and subculture are incubated at the original temperature.
  - After a 4 day incubation period, the original and subculture are examined for growth.
- Subcultured sterility tests require an 18 day turnaround time.
Subcultures
Examples of drug products frequently requiring subcultures:

1. Betamethasone: Clouds the media, settles on the bottom
2. Testosterone in Oils: Forms globules, the oil in water effect
3. Methylcobalamin: Can color the media very dark red
4. Pellets: Can dissolve and leave solids/ cloud the media
5. Ointments & Creams: Can form films, blobs in the media
6. Papaverine: Crystallizes out of the media

NON-STERILE TEST RESULTS
What happens if a test shows microbial growth?

- If evidence of microbial growth is found, the product to be examined does not meet the test requirements for sterility.
- A sterility test may be invalidated if it can be clearly demonstrated that the non-sterile result occurred for causes unrelated to the product examined.
- Possible reasons for invalidation:
  - The data of microbiological monitoring of the sterility testing facility show a fault.
  - A review of the testing procedure used during the test in question reveals a fault.
  - Microbial growth is found in the negative controls.
  - Once the contaminating organisms have been identified, the organism may be ascribed unequivocally to faults in the sterility test procedure.

Retesting an Invalidated Sterility Test

- If the test is invalidated, it is repeated with the same number of units as in the original test on the same lot of product.
- If no evidence of microbial growth is found in the repeat test, the product examined meets the test requirements for sterility.
- If microbial growth is found in the repeat test, the product examined does not meet the test requirements for sterility.

INTERPRETING CERTIFICATES OF ANALYSIS
Certificates of Analysis

• In-Progress Sterility Test Report

Certificates of Analysis

• Final Sterility Test Report

USP <71>
Sterility Tests

Limitation of the Sterility Test with Respect to Sample Size

Table 2. The Relationship between the Probability of Passing a Bulk Sterility test and the Microbial Cell Density

<table>
<thead>
<tr>
<th>Sample Size (mL)</th>
<th>Microbial Cell Density (cfu per mL)</th>
<th>Probability of Passing the Test</th>
<th>Probability of Failing the Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>0.001</td>
<td>0.99</td>
<td>0.01</td>
</tr>
<tr>
<td>10</td>
<td>0.01</td>
<td>0.91</td>
<td>0.09</td>
</tr>
<tr>
<td>10</td>
<td>0.1</td>
<td>0.37</td>
<td>0.63</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>0.00</td>
<td>100</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>0.00</td>
<td>100</td>
</tr>
</tbody>
</table>

What are the chances a USP <71> test will actually “catch” a contaminated sample?

- If only a few articles are contaminated, it is unlikely a sterility test will detect them.
- There is a statistical limitation to the likelihood of finding a contaminated article.

<table>
<thead>
<tr>
<th>Contamination level</th>
<th>Probability of passing 100% of samples</th>
<th>Probability of passing 99% of samples</th>
<th>Probability of passing 95% of samples</th>
<th>Probability of passing 80% of samples</th>
<th>Probability of passing 50% of samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>0.91</td>
<td>0.31</td>
<td>0.13</td>
<td>0.01</td>
<td>0.001</td>
</tr>
<tr>
<td>1</td>
<td>0.62</td>
<td>0.24</td>
<td>0.08</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.30</td>
<td>0.14</td>
<td>0.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0.13</td>
<td>0.05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>0.01</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data from the United States Pharmacopeia. *
The Sterility Testing Environment

• The test area must be maintained to minimize the possibility of contamination from the test.
• Any measures taken to prevent contamination from the test must not affect microorganisms in the test sample.
• The test area should be adapted to create stable, easily monitored and controlled conditions conducive to aseptic processing.
• Testing laboratories should perform environmental monitoring to demonstrate control of the test area, and provide indications of failures in control.
• Sterility testing should be carried out by a trained individual.

Environmental Monitoring

• The purpose of an environmental monitoring program is to provide bioburden data of the compounding or manufacturing environment and confirm the effectiveness of microbial controls present in the compounding or manufacturing and testing areas.
• Some examples of microbiological controls are:
  • Sanitization procedures
  • HEPA filtration and air flow
  • Gowning procedures
  • Aseptic technique
Environmental Monitoring

- This is critical for areas where sterile products are made.
- This should include establishing a robust monitoring program, sampling of critical zones and high traffic areas, and trending of microbial counts and recoveries.
- The isolates should be identified for trending related to the type of microorganism, the level of control in the compounding environment, and the potential source of the microorganism.
- Nonsterile product manufacturers can monitor the environment with reduced frequency and with expectations of higher recovery.

Investigations and Microbial Identification

USP <1113> Microbial Characterization, Identification and Strain Typing

- Provides information regarding the level of identification that is appropriate for microorganisms that have been isolated during different phases of manufacturing and quality testing.
- Investigations are a major part of compounding or manufacturing and finished product testing.
- **Internal Investigations**
  - Any unexpected event
  - Process test falling out of specification
  - Environmental excursion does not meet quality specifications
  - Finished product does not meet quality specifications
Investigations and Microbial Identification
USP <1113> Microbial Characterization, Identification and Strain Typing

- Microorganisms, if detected in drug substances, water for pharmaceutical use, the manufacturing environment, intermediates, or finished drug products, typically undergo characterization and identification.

- Microbial identification can be especially useful during an investigation of product contamination, environmental excursion, and for determining potential sources of the contamination.
ALTERNATIVE STERILITY TEST METHODS

Rapid Sterility Testing

- **Cell Labeling – Ex. ScanRDI**
  - Extremely rapid testing (As little as 90 min)
  - Potential drawbacks:
    - Cannot test all sample types (Filterables only)
    - Viability of the treated cells is uncertain (Investigations?)
    - Testable sample volumes

- **Growth Based Methods – Ex. Celsis**
  - ATP, Headspace Measurement
  - Potential drawbacks:
    - Requires an incubation period (4-5 days)
    - Slow growing organisms
    - Only recognize organisms able to grow under the conditions of the test
    - Non-microbial ATP is also detected (false positives)
    - Testable sample volumes

Rapid Sterility Testing

**USP <1223> Validation of Alternative Microbiological Methods**

- **USP Perspective on Alternative Methods or Procedures**
  - General Notices and Requirements in the USP states, "Alternative methods and/or procedures may be used if they provide advantages in terms of accuracy, sensitivity, precision, selectivity, or adaptability to automation or computerized data reduction, or in other special circumstances."
  - USP allows alternative methods, as long as they provide an advantage over the existing methods AND appropriate measures are taken to evaluate the method technically and scientifically.
  - USP does not give specifics on how to accomplish this.
  - Requirements may also vary between states – check with the State Boards of Pharmacy.
Rapid Sterility Testing

USP Methods as Referee Tests

- Referee Test – The method used to evaluate whether a product conforms to specifications.
- USP chapters below 1000 are intended to be referee tests for any product legally marketed in the United States.
- If a dispute should occur for any reason, only the result obtained using the method or procedure published in USP is conclusive.
- Alternative methods implemented and qualified by a user will not serve as a legal replacement for the official USP method.

Rapid Sterility Testing

FDA – The Use of Alternative Methods

- In the U.S. Food and Drug Administration (FDA) cGMP 21 CFR Part 211.194 describes requirements for test methods utilized to assess the compliance of pharmaceutical articles with approved specifications.
- The regulations state that test methods must have suitable capability regarding accuracy and reliability.
- This subsection of the regulations also recognizes the legal basis of USP and the National Formulary (NF) standards and makes it clear that it is the responsibility of the user to validate methods or procedures that differ from those standardized in the compendia.

Rapid Sterility Testing

FDA – Rapid Methods on Biologics

- In February 2008, the FDA published draft guidance on the validation of growth-based RMMs for sterility testing of cellular and gene therapy products.
- The guidance was not intended for other pharmaceutical products that would normally be regulated by the Center for Drug Evaluation and Research (CDER).
- The validation described in the draft guidance applied only to growth-based techniques.
- In June 2011, for biologics the FDA amended the sterility test requirements to provide manufacturers greater flexibility, certain requirements and specifics were removed.
- Novel methods and any methods that deviate from the USP compendial sterility test methods would require a detailed validation.
- The 2008 guidance was subsequently withdrawn in 2015.
Rapid Sterility Testing
FDA – Rapid Methods on Drug Products

- Using a ScanRDI system, Alcon Laboratories developed the first rapid method approved by the CDER of the FDA.
- They were later cited by the FDA for the use of rapid methodology. Not specifically for using the technology, but for the completeness of validations.
- The rapid method was being conducted and claimed to meet requirements of USP.
- Equivalence to USP <71> needed to be conducted for each formulation.
- Method suitability similar to USP <71> should be conducted on each formulation.
- Rapid methods require equipment validation, adding another layer of complexity not found in the compendial sterility test.

Rapid Sterility Testing
In-Use and Regulatory Status

- Not well defined as to what specifically constitutes a proper validation/method suitability of a rapid sterility method.
- The burden of designing and executing an adequate method suitability that demonstrates the required equivalence to the USP <71> methodology is on the pharmacy/testing laboratory.
- The FDA reviews sterility testing using rapid sterility methods on a case-by-case basis when encountered.
- Due to fundamental differences between the USP <71> test method and Rapid Sterility methods, citing USP <71> as the test method while using a rapid method is inaccurate.
- Phrases such as “USP <71> compliant” and “Meets the requirements of USP <71>,” without citing USP <71> as the test method should be carefully evaluated to determine if they are sufficient for a pharmacy’s needs.

References and Resources

- United States Pharmacopoeia (USP)
- General Chapters and Monographs
- International Journal of Pharmaceutical Compounding (IPC)
- Remington’s Pharmaceutical Sciences
- California State Board of Pharmacy Regulations
- PCAB Standards and Compliance Indicators
- Ansell’s Pharmaceutical Dosage Forms and Drug Delivery Systems The Art, Science and Technology of Pharmaceutical Compounding
- Your Testing Laboratory (ARL, Eagle, Dynalabs and others)
- Repackagers (PCCA, MEDISCA, LETCO, Freedom Pharmaceuticals, Fagron and others)
- Laura Gillikin, cGMP Validation
- PDA and the Microbiology Network
- Andy Gunn, iKemance
- CompoundingToday.com
Thank You!

Contact Information:

Thomas C. Kupiec, PhD
Phone: (405) 271-1144
Email: tkupiec@arlok.com