FDA, USP, and the 503B Outsourcing Facilities

Scott Sutton, Ph.D.

Introduction

The past two years has seen dramatic change in the regulation of compounding pharmacies. As a result of demonstrated quality issues with medicines related to the growth of compounding pharmacies into national outsourcing suppliers, the Food, Drug and Cosmetic Act (FD&C Act) has been amended to separate these entities from the traditional pharmacy. Where before there was only the traditional pharmacy as described in section 503, this pre-existing text now appears as section 503A, and a completely new entity is described—the outsourcing facility—in section 503B. This "503B" entity falls under US Food and Drug Administration regulatory authority, and FDA has been aggressively encouraging registration (1, 2). At the time of writing, there were almost 40 companies (3) who registered as 503B entities (see Table I). They have taken advantage of the opportunity to:

- Manufacture large batches of compound sterile preparations (CSP) without:
  - Pre-registration (e.g., New Drug Application/Abbreviated New Drug Application)
  - Clinical studies
  - Specific prescriptions for individual patients.
- Ship across state lines.

This article will look at FDA expectations for the outsourcing facility in comparison to good compounding practice as described in *United States Pharmacopeia (USP)* <795>, <797>, and <1163>. These expectations are determined by a review of published 483 reports issued following inspections of pharmacies during the years 2013 and 2014 (4).

It should be noted that *USP* <797> "Pharmaceutical Compounding – Sterile Preparations" remains the primary source of guidance for the traditional pharmacy (503A) in the preparation of CSP. This article will consider requirements as described in *USP* chapter <797> only in relation to the demonstrated FDA expectations and the stated position that the 503B facility will be held to GMP manufacturing standards (5).

FDA and Recent Regulatory Activity

In response to the New England Compounding Center (NECC) situation (and its aftermath of congressional hearings), FDA embarked on an aggressive inspection schedule that focused on compounding pharmacies that either had issues in quality in the past or had a significant proportion of their business as outsourcing services that shipped preparations across the US. This effort resulted in multiple 483 reports (the inspection team reports their official observations on a government form numbered 483). Eighty-five 483 reports for compounding manufacturers producing sterile products were posted on the FDA website at the time of writing. There are many more listings on the site than these 85. One facility was audited a second time for non-sterile products; this non-sterile audit was not included in the analysis. Several compounding manufacturers responded to the 483 findings, and these responses, while posted, are not part of this analysis, and there is not one situation where a compounding manufacturer was audited twice in a very short period of time—this incident was treated as one report (however, several were audited twice over the course of about 14 months; these 483 reports are included). In addition, several different contract testing laboratories that service the compounding pharmacy industry were audited by FDA; their 483 reports are not included in this analysis. Finally, several of the 483 reports have been closed by FDA with referral of the issues to the relevant state boards of pharmacy. This referral is not a subject of this review.

Many of the FDA observations have a distinct Pharma-GMP flavor to them. This is understandable, given FDA's experience in the Pharma industry, and therefore, it is a fair indication of the type of scrutiny outsourcing facilities will be experiencing (5). While it might be argued that compounding pharmacies should not be held to Pharma GMP criteria, it must be remembered that many of these "pharmacies" were actually functioning as national outsourcing resources, andd furthermore, that the areas covered by Pharma GMP and the good compounding practices (GCP as described in *USP* <795>, <797>, and <1163>) are very similar (Table II).

FDA and Recent Regulatory Activity

In response to the New England Compounding Center (NECC) situation (and its aftermath of congressional hearings), FDA embarked on an aggressive inspection schedule that focused on compounding pharmacies that either had issues in quality in the past or had a significant proportion of their business as outsourcing services that shipped preparations across the US. This effort resulted in multiple 483 reports (the inspection team reports their

Table II: Major Quality Topics Covered in Pharma GMP and Good Compounding Practices Defined in USP.

Firm Name	Date of Registration	Last FDA Inspection Related to Compounding	Was a Form FDA-483 Issued?	Other FDA Action	Compounds Sterile Drugs From Bulk Drug Substances
Advanced Pharma, Inc., Houston, TX	1/22/2014	3/17/2014	Yes	Open	No
Allergy Laboratories, Inc., Oklahoma City, OK	12/30/2013	4/26/2013	Yes	Warning Letter - 9/4/2013	Yes
Avella of Deer Valley, Phoenix, AZ	2/24/2014	2/25/2013	Yes	Warning Letter - 1/17/2014	No
Banner Health, Chandler, AZ	12/26/2013	Not yet inspected	N/A	N/A	No
Cantrell Drug Company, Little Rock, AR	12/16/2013	11/4/2013	Yes	Open	Yes
Central Admixture Pharmacy Services, Inc., Allentown, PA	2/28/2014	Not yet inspected	N/A	N/A	Yes
Edge Pharmacy Services LLC, Colchester, VT	1/21/2014	Not yet inspected	N/A	N/A	Yes
Greer Laboratories, Inc., Lenoir, NC	2/24/2014	11/15/2013	Yes	Open	Yes
Healix Infusion Therapy, Inc., Sugar Land, TX	2/12/2014	Not yet inspected	N/A	N/A	Yes
Infusion Options INC., Brooklyn, NY	1/24/2014	Not yet inspected	N/A	N/A	No
Institutional Pharmacy Solutions, LLC, Irwindale, CA	3/6/2014	Not yet inspected	N/A	N/A	No
Institutional Pharmacy Solutions, LLC, Virginia Beach, VA	3/4/2014	Not yet inspected	N/A	N/A	No
IV Specialty Ltd, Austin, TX	2/26/2014	Not yet inspected	N/A	N/A	No
JCB Laboratories, North Wichita, KS	1/21/2014	2/27/2013	Yes	Open	Yes
Kings Park Slope, Inc., Brooklyn, NY	12/23/2013	3/14/2014	Yes	Open	Yes
KRS Global Biotechnology, Inc., Boca Raton, FL	12/15/2013	3/17/2014	Yes	Open	Yes
Leiter's Compounding, (Great Oaks Blvd), San Jose, CA	1/31/2014	Not yet inspected	N/A	N/A	Yes
Lowlite Investments, Inc. dba Olympia Pharmacy, Orlando, FL	3/17/2014	3/21/2013	Yes	Warning letter - 2/18/2014	Yes
Marlborough Hospital, Marlborough, MA	12/26/2013	Not yet inspected	N/A	N/A	Yes
Medi-Fare Drug & Home Health Center, Inc., Blacksburg SC	12/17/2013	1/18/2013	Yes	Warning Letter – 3/7/2013	Yes
Methodist Hospital, Omaha, NE	3/17/2014	Not yet inspected	N/A	N/A	Yes
OPS International, Inc. dba Olympia Pharmacy, Orlando, FL	3/10/2014	Not yet inspected	N/A	N/A	Yes
Pharmaceutic Labs, LLC, Albany, NY	3/10/2014	Not yet inspected	N/A	N/A	Yes
Pharmagen Laboratories Inc., Stamford, CT	1/21/2014	8/23/2013	Yes	Open	Yes
Pharmakon Pharmaceuticals, Noblesville, IN	1/23/2014	3/13/2014; 4/8/2014	Yes (3/13/2014) and (4/8/2014)	Open	No
PharMedium Services, LLC, Cleveland, MS	12/11/2013	2/22/2013	Yes	Open	No
PharMedium Services, LLC, Edison, NJ	12/11/2013	2/28/2013	Yes	Open	No
PharMedium Services, LLC, Memphis, TN	12/11/2013	3/22/2013	Yes	Open	No
PharMedium Services, LLC, Sugar Land, TX	12/11/2013	2/27/2013	Yes	Open	No
RC Compounding Services LLC, Poland, OH	2/12/2014	2/7/2013	Yes	Open	Yes
Region Care, Inc., Great Neck, NY	12/24/2013	3/20/2014	Yes	Open	Yes
SCA Pharmaceuticals, Little Rock, AR	12/13/2013	4/1/2014	Yes	Open	Yes
SSM St. Clare Health Center, Fenton, MO	2/18/2014	Not yet inspected	N/A	N/A	No
Triangle Compounding Pharmacy Inc., Cary, NC	1/24/2014	3/1/2013	Yes	Warning Letter - 1/14/2014	Yes
Unique Pharmaceuticals, Ltd., Temple TX	1/17/2014	4/2/2014	Yes	Open	Yes
US Compounding, Inc., Conway, AR	12/20/2013	3/27/2014	Yes	Open	Yes
US Specialty Formulations LLC, Bethlehem, PA	1/31/2014	Not yet inspected	N/A	N/A	Yes

official observations on a government form numbered 483). Eighty-five 483 reports for compounding manufacturers producing sterile products were posted on the FDA website at the time of writing. There are many more listings on the site than these 85. One facility was audited a second time for non-sterile products; this non-sterile audit was not included in the analysis. Several compounding manufacturers responded to the 483 findings, and these responses, while posted, are not part of this analysis, and there is not one situation where a compounding manufacturer was audited twice in a very short period of time—this incident was treated as one report (however, several were audited twice over the course of about 14 months; these 483 reports are included). In addition, several different contract testing laboratories that service the compounding pharmacy industry were audited by FDA; their 483 reports are not included in this analysis. Finally, several of the 483 reports have been closed by FDA with referral of the issues to the relevant state boards of pharmacy. This referral is not a subject of this review.

Many of the FDA observations have a distinct Pharma-GMP flavor to them. This is understandable, given FDA's ex-

Table I: 503B Registrations (3.)

GMP Topic	21 CFR 211	*USP* <795>	*USP* <797>	*USP* <1163>
Buildings and Facilities	X	X	X	--
Equipment	X	X	X	--
Personnel	X	X	X	X
QAU	X	X (Under QC)	X (Under QA)	X
Raw Materials	X	X	X	--
Control of Components	X	X	X	--
Production/Compounding Controls	X	X	X	--
Holding and Distribution	X	--	X	--
Records	X	X	X	--
Packaging & Labeling	X	X	X	--
Stability	X	X	X	--
Complaints	X	--	X (under Adverse Events)	--
QC Lab	X	--	X	X
Subcontractor QA	X (under subpart I)	--	--	X

perience in the Pharma industry, and therefore, it is a fair indication of the type of scrutiny outsourcing facilities will be experiencing (5). While it might be argued that compounding pharmacies should not be held to Pharma GMP criteria, it must be remembered that many of these "pharmacies" were actually functioning as national outsourcing resources, andd furthermore, that the areas covered by Pharma GMP and the good compounding practices (GCP as described in *USP* <795>, <797>, and <1163>) are very similar (Table II).

With this in mind, let's take a closer look at the information to be gleaned from the FDA 483 observations. The most common of these 483 topics are listed in Pareto format in the Figure, with a full listing presented in Table III. Explanations of some of these findings are below:

- **Stability Program**
  This topic refers to the frequent FDA observations of a lack of data supporting the potency, sterility, or lack of pyrogenicity (or occasionally any data whatsoever) of the preparation that might be stored for over a year. Clearly, this is a GCP concern as well as a GMP concern for compounding manufacturers.
- **Validation of Sterilization—Media Fills**
  This observation referred to the common failing of terminally sterilized preparations being subjected to a validated sterilization cycle in an autoclave or for an aseptic fill operations to have performed a relevant media fill (simulated aseptic fill). *USP* <797> discusses this consideration in the section "Verification of Compounding Accuracy and Sterility – Sterilization Methods – Sterilization of High-Rick Level CSPs by Steam" where it is stated, "The description of steam sterilization conditions and duration for specific CSPs is included in written documentation in the compounding facility." The effectiveness of steam sterilization is verified using appropriate biological indicators (see "Biological Indicators" <1035>) or other confirmation methods (see "Sterilization and Sterility Assurance of Compendial Articles" <1211> or "Sterility Tests" <71>).
- **Inadequate/Improper Environmental Monitoring**
  This observation referred to a wide range of issues with environmental monitoring, including (EM) from insufficient frequency, failure to qualify sampling sites, failure to trend data, failure to respond to excursions, etc. This area is one of divergence between GCP (<795>, <797>, and <1163>) and GMP, as the expectations of GMP are designed to address manufacturing facilities, —not the compounding pharmacy. This increased emphasis on environmental monitoring and trend analysis will be expected of 503B outsourcing facilities although it is unlikely (at least at the time of this writing) that environmental monitoring will be expected at the same level and frequency of the outsourcing facility as of the Pharma aseptic manufacturer.
- **SOPs to Prevent Microbial Contamination Non-existent or Not Followed**
  This general topic covered a wide range of specific issues, such as failure to have a qualified sanitization (or in some cases any sanitization) program, failure to have cleaning/sanitization procedure, having procedures but ignoring them in practice, etc. This is clearly both a GCP and GMP issue as there are multiple references in both <795> and <797> to activities designed to control, monitor, and minimize microbial contamination.
- **Inadequate Gowning**
  Common issues under this topic included lack of critical pieces of gowns (hairnet, beard covers, foot covers, etc.), having gaps in gowns, poor gowning technique, and poor aseptic technique with gowns. This concern is covered in GCP in the *USP* <797> section "Additional Personnel Requirements – Personnel Cleansing and Garbing."
- **Laboratory Procedures: Testing/Contract Lab Control**
  This procedure included poor or non-compliant performance of required testing—most commonly potency testing or *USP* <71> "Sterility Testing." This issue, and the related issue of control over outsourced contract resources, is critically important to the overall quality documentation for the pharmacist. Sending CSP out for testing to a lab that asserts compliance with USP test methods has not proven adequate. The GCP requirements for testing according to compendial methods are spread throughout <797> and

are clearly established for manufacturers under GMP. The interested reader is referred to *USP* <117> for more information on best practices for the microbiology lab.

- **Batch Release**
  This topic dealt with the release of sterile product under improper conditions without either potency testing, sterility testing, or perhaps any testing whatsoever to confirm the preparation's strength, purity, quality, or safety. While this topic is a complicated one for the compounding pharmacy, the compounding manufacturers inspected by FDA in 2013 are clearly storing, selling, and shipping product for use well past beyond-use date (BUD). Some surety is required that the product batch meets release specification under GMP—this is normally not an issue for GCP when small batches are produced. It is also important to be able to unambiguously identify all units in a batch to allow tracking of their destinations in case a problem is discovered necessitating a recall of released vials.
- **Inadequate Cleaning/Disinfection**
  This 483 topic dealt with either the manufacturing equipment or the facility cleanliness, the failure of the pharmacy to ensure that there was no carry-over of preparations from one batch to the next, or whether the disinfection of the aseptic area and primary engineering control (PEC) were actually working. The GCP requirements for this issue are discussed in *USP* <797> in the section "Cleaning and Disinfecting the Compounding Area." The interested reader is referred to *USP* chapter <1072> for further information.
- **Control of Equipment**
  This 483 topic commonly dealt with a failure of the pharmacy to ensure that the equipment used for compounding was fit for its intended use. This could include high-efficiency particulate air (HEPA) filtration in the heating, ventilation, and air conditioning (HVAC), autoclave operations, incubators, pH meters, balances, or any other critical piece of equipment. This GCP topic is discussed in the section "Elements of Quality Control – Equipment" where it is stated, "…equipment, apparatus, and devices used to compound a CSP be consistently capable of operating properly and within acceptable tolerance limits. Written procedures outlining required equipment calibration, annual maintenance, monitoring for proper function, and controlled procedures for use of the equipment and specified time frames for these activities are established and followed." The interested reader is referred to *USP* <1052> for more information on equipment qualification.
- **Inadequate Facility/Smoke Studies**
  These observations dealt with adequacy of design and qualification studies to ensure the facility is meeting expectations for air balance and airflow in aseptic areas. It should be noted that *USP* <797> does expect air pressure differentials of 0.02 to 0.05-inch water column between rooms providing physical separation in the aseptic core, and that "In situ air pattern analysis via smoke studies should be conducted at the critical area to demonstrate unidirectional airflow and sweeping action over and away from the product under dynamic conditions" (see section "Facility Design and Environmental Controls"). Examples of specific observations included:
  - Smoke studies not performed to demonstrate laminar air flow
  - Firm doesn't continuously monitor air pressure differentials during production
  - "…the firm lacks a system of continuous monitoring of positive pressure differential limits during aseptic processing of sterile drug products."
  - "The area designated as the clean room and identified by the firm as being classified with [International Organization for Standardization] (ISO) 5 and ISO 6 areas has been modified structurally and is not supported by continuous monitoring data to be considered a classified area for sterile drug production."
- **Investigations**
  This topic dealt with the general topic of response to problems or errors whether they occurred in process (for example environmental monitoring excursions), in finished product (failure of potency or sterility testing), or from products returned from the field. *USP* <797> states, "When action levels are exceeded, an investigation into the source of the contamination shall be conducted." (see section "Environmental Monitoring - Action Limits, Documentation, and Data Evaluation") and "Positive sterility test results should prompt a rapid and systematic investigation of aseptic technique, environmental control, and other sterility assurance controls to identify sources of contamination and correct problems in the methods or processes." (see section "Finished Preparation Release Checks and Tests – Sterility Tests"). The expectation is that failures, excursions, and returns are to be evaluated fully so that a root cause can be determined, corrections for this root cause determined and implemented, and then the effectiveness of this corrective action monitored.
- **Control of Pyrogenic Contamination**
  USP <797> addresses this specific topic in "Verification of Compounding Accuracy and Sterility – Depyrogenation by Dry Heat" where it is stated, "The description of the dry heat depyrogenation cycle and duration for specific load items shall be included in written documentation in the compounding facility." The effectiveness of the dry heat depyrogenation cycle shall be verified using endotoxin challenge vials (ECVs). The bacterial endotoxin test should be performed on the ECVs to verify the cycle is capable of achieving a 3-log reduction in endotoxin. This is addressed as a finished product specification in the <797> section "Finished Preparation Release Checks and Tests – Bacterial Endotoxin (Pyrogen) Testing." Examples of 483 observations directed at compounding manufacturers include:
  - "The firm does not test final units for the presence of bacterial endo-

toxin in finished sterile drug product lots after aseptic manual filling operations."

- "There are no written standards or specifications, methods of testing, methods of cleaning, and methods of sterilization to remove pyrogenic properties."
- "Specifically, the firm fails to ensure that each batch of aseptically processed injectable drug products, which it distributes, passes sterility and endotoxin testing before distribution. The last sterility testing was conducted on the product XXXXX on Jul 25, 2008. No endotoxin testing has ever been conducted."

FDA's concerns over these topics have not arisen in a vacuum. Fundamentally reactive in nature, the Pharma GMPs have grown over time in response to significant problems in the safety of the nation's medicines. This expansion of FDA authority over the outsourcing facility is just the latest example of this evolution.

A Short History of USP and Compounding Pharmacies

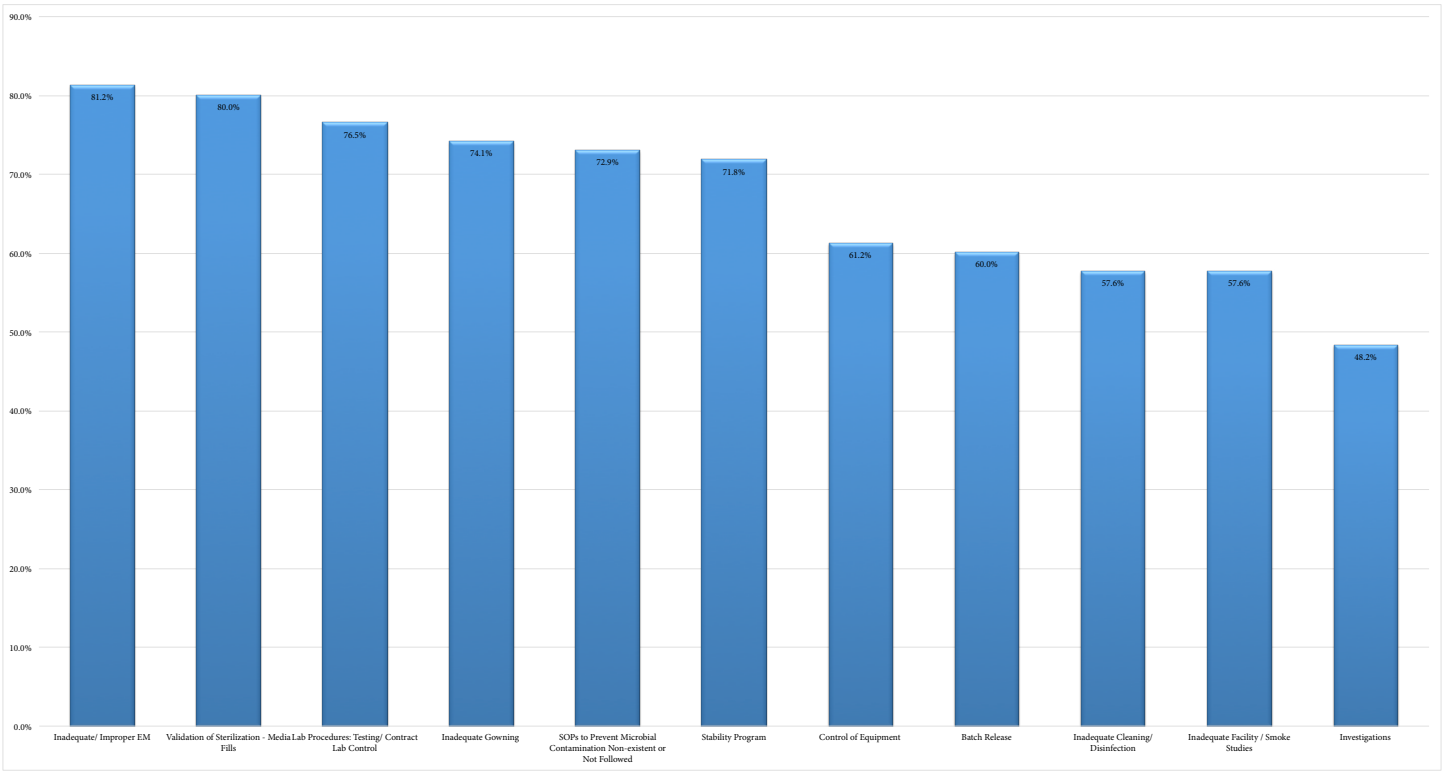
Early efforts during the period of 1790–

Table III: Frequency of FDA 483 Observation Topic.

483 Topic Issue	Frequency
Inadequate/ Improper Environmental Monitoring	81.2%
Validation of Sterilization - Media Fills	80.0%
Lab Procedures: Testing/ Contract Lab Control	76.5%
Inadequate Gowning	74.1%
SOPs to Prevent Microbial Contamination Non-existent or Not Followed	72.9%
Stability Program	71.8%
Control of Equipment	61.2%
Batch Release	60.0%
Inadequate Cleaning/ Disinfection	57.6%
Inadequate Facility / Smoke Studies	57.6%
Investigations	48.2%
Control of Pyrogenic Contamination	43.5%
QAU Not Effective/ Production SOPs not followed/effective	38.8%
Separation of Clean and Dirty Operations/Storage of Materials	28.2%
Inadequate raw material control	25.9%
Container Preparation	21.2%
SOP/Control of Production	15.3%
Safeguard Against Penicillin/ Cephalosporine Cross Contamination	14.1%
Labelling Issues	14.1%
Records not Available	11.8%
Personnel not Trained/ Inadequate	9.4%
Obvious Product Contamination (Micro/Particulate)	3.5%
Change Control	3.5%

Frequency is the percentage of pharmacy 483 reports that reference this topic of the 85 present on the FDA Website. Interpretation of the 483 findings and assignation to a particular topic were performed solely by the author and some variations are possible in this admittedly subjective analysis.

Figure: Pareto Chart of 483 Observations.



1818 to create a pharmacopeia included the pharmacopeias of the College of Physicians (Philadelphia) and the Massachusetts pharmacopeia. However, not all of the newly formed States adopted either of these pharmacopeias, which led to an effort to create a new pharmacopeia that enjoyed the support of all major medical societies and could serve as a "national" pharmacopeia. The first edition of this pharmacopeia was published in 1820. Throughout the 1800s, the compendia was periodically revised with the participation of pharmacists. The 1906 *Pure Food and Drug Act* specifically cited USP and the National Formulary (NF) as enforceable standards. The 1938 amendment to the FD&C Act established FDA as the empowered enforcement agency and again cited USP and NF for standards (10).

USP <797> is the recognized standard of practice for compounding pharmacies manufacturing sterile products in the US. While this standard is a huge improvement over the previous "best practice," it is far less stringent than the pharmaceutical GMP as described in *Code of Federal Regulations Title 21 Part 210 and 211*. This is point that must be remembered clearly—*USP* <797> is clearly best practice among the top compounding pharmacies (11), but it far less rigorous than the expectations of cGMP. Even when we add in the quality information present in <1163> "Quality Assurance in Compounding Pharmacy," the USP information may not be sufficient for large-scale production of pharmaceutical batches. The assumptions inherent in *USP* <797> are that the CSP produced will be very limited in number (in response to a specific script) and will have an extremely restricted BUD to prevent any potential microbial proliferation in a contaminated CSP. It is not intended to be a guide to manufacturing.

USP first published information on sterile compounding in 1995 in chapter <1206> "Sterile Products for Home Use" in *USP* <23> (12). This was a general informational chapter on compounding pharmacy and not as effective as was originally hoped (13). In response, USP changed the informational chapter <1206> to the mandatory chapter <797> with the expectation that this change in status would allow enforcement of the provisions. It was also at this point that different levels of "sterile" were incorporated into the chapter (reviewed in Newton and Trissel 2004). These levels of sterility included low, medium, and high-risk products based on compounding process, product characteristics, and storage conditions (14).

This effort met with limited success. Voluntary compliance with USP and American Society of Hospital Pharmacies (ASHP) was low—estimated at 5.2% in a 2003 industry survey (reviewed in Newton and Trissel 2004).

There were several "GMP"-like requirements that were new to the compounding pharmacy in 2005. Examples include the requirement for robust ISO Class 5 fill conditions as well as the contamination control, facility, environmental monitoring, personnel gowning, and training requirements.

However, these changes were not sufficient to address the continuing problems with compounding pharmacy quality issues. In one case, for example, a "for cause" type of inspection ran into difficulty as the inspector objected to the lack of any written procedures. In reply, the pharmacist challenged the inspector to show any such requirement. This, and similar, experiences led to the revision of *USP* <797> in 2009 to incorporate several additional quality controls (15).

It is interesting to note that, at the time of this writing, there remain no uniform expectations for observance of *USP*<797> requirements by the state boards of pharmacy; in fact, the best estimate is that only 23 states required compliance with *USP* <797> last year (16). A recent review article also highlighted the uneven training of pharmacists in the expectations of *USP* <797> (17).

It is clear that the traditional pharmacy, as previously described under the FD&C Act section 503, will continue unchanged under the amended FD&C Act section 503A. What may be a significant change for the traditional pharmacist, particularly one compounding CSP, will be the enforcement of expectations that the pharmacy not behave as an outsourcing facility and that the pharmacy adheres to *USP* <797> in practice as well as in theory.

Conclusion

The creation by law of the category "Outsourcing Facility" in section 503 of the FD&C Act also creates regulatory confusion in the industry. Pharmacies that adhere to the traditional practice of pharmacy will remain as before, described under Section 503A of the revised act. Pharmacies who wish to sell across state lines, manufacture large batches of CSP, etc. will be expected to register as 503B outsourcing facilities or face penalties. The operational expectations of FDA under GMP regulations compared to the customary practice of pharmacy can be determined by an analysis of the now large number of 483 observations available on the FDA website. This analysis shows significant areas of change available to the pharmacist operating as an outsourcing facility. Those pharmacies able to adapt to these expectations may prosper. Those who are unable or unwilling to change to meet the new regulatory realities will have a much more difficult road over the coming years.

Acknowledgements

I want to thank Dennis Guilfoyle, Radhakrishna Tirumalai, Eric Kastango and others for their helpful review and commentary on this manuscript.

References

1. FDA "Letter to State Officials," 2014, available here.
2. FDA, "FDA Letter to Hospitals, 2014, available here.
3. FDA, "Registerd Outsourcing Facilities," 2014, available here.
4. FDA, "2013 Pharmacy Inspections and Related Reports," and "2014 Pharmacy Inspections and Related Reports," *Electronic Reading Room,* available here and here.
5. FDA, *Guidance for Industry: Interim Product Reporting for Human Drug Compounding Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act* (Rockville, MD, December 2003), available here.
6. J. Wechsler, *FDA Marks 100 Years of Drug Manufacturing Oversight*, *Pharmaceutical Technology* **30** (9), 26–31, 2006.
7. B. Immel, "A Brief History of the GMPs," *Pharmaceutical Technology* **25** (9), 44–52, 2000.
8. J.P. Swann, "The 1941 Sulfathiazole Disaster and the Birth of Good Manufacturing Practices," *PDA Journal of Pharmaceutical Science Technology* 53(3), 148–153, 1999.
9. P.A. Offit, *The Cutter Incident: How America's First Polio Vaccine Led to the Growing Vaccine Crisis*, Yale University Press, ISBN 0-300-10864-8, 2005.

10. L. Anderson and G.J. Higby, *The Spirit of Voluntarism A Legacy of Commitment and Contribution – The United States Pharmacopeia 1820-1995*, United States Pharmacopeial Convention, ISBN 0-913595-88-8, 1995.
11. D.W. Newton and L.A. Trissel, "A Primer on USP Chapter <797> "Pharmaceutical Compounding – Sterile Preparations" and USP Process for Drug and Practice Standards," *International Journal of Pharmaceutical Compounding* **8** (4), 251–263, 2004.
12. *USP* <1206> "Sterile Products for Home Use" *USP 23/NF18*, 1963–1975. 1995.
13. ASHP, "ASHP Discussion Guide for Compounding Sterile Preparations: Summary and Implementation of USP Chapter <797>," 2008, available here.
14. *USP* <797> "Pharmaceutical Compounding – Sterile Preparations," *USP 27/NF22*, 2350–2370, 2004
15. *USP* <797> "Pharmaceutical Compounding – Sterile Preparations" *USP 32/NF27 Volume*,318–354, 2009.
16. NABP, "State Boards and NABP Take Action to Clarify Regulations and Bolster State Regulatory Systems Specific to Compounding Pharmacies Newsletter," *National Association of Boards of Pharmacy February* **42**(2), 25–30, 2013, available here.
17. L.F. McElhiney, " Misinterpretation of United States Pharmacopeia Chapter <797>," *International Journal of Pharmaceutical Compounding* **16** (1), 6–10, 2012.

About the Author

Dr. Scott Sutton earned his B.S. in Genetics from the University of California at Davis, and his Masters and Ph.D. in Microbiology from the University of Rochester (Rochester, NY). After an NIH postdoctoral fellowship at the Medical College of Virginia (Richmond, VA), he went to work for Bausch and Lomb (Rochester, NY) until 1994 when he accepted a position at Alcon Laboratories (Fort Worth, TX). Dr. Sutton left Alcon Laboratories in 2004 as a Director in the R&D division to accept a position as Pharma Consultant (Microbiology) with Vectech Pharmaceutical Consultants, Inc which he left in 2009 as Sr. Director, Microbiology Services. Scott Sutton is the Principal of Microbiology Network, Inc a company he started in 1996 as a means to encourage training and communications within the microbiological community. The Microbiology Network now provides webinars, training, conferences and Email discussion groups to the regulated industries with a wide range of experienced consultants. With over 70 publications and hundreds of presentations, he is a recognized consultant and trainer with emphasis in GMP, investigations, Environmental Monitoring and contamination control (both Aseptic manufacturing and non-sterile production facilities) as well as microbiology laboratory audits and operations. Dr. Sutton is an active author and speaker for the industry, supports ASM, PCPC and PDA, and has served with the USP Analytical Microbiology Committee of Experts since 1993.

Originally Published at: http://www.ivtnetwork.com/article/fda-usp-and-503b-outsourcing-facilities