Appeal of Revisions to General Chapters <797> and <795>

January 22, 2020
United States Pharmacopeia
12601 Twinbrook Pkwy., Rockville, MD 20852
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Introduction
The Coalition: Why We Are Here

• Alliance for Pharmacy Compounding
  Scott Brunner (CEO)
  Jennifer Burch (Chair, Executive Committee)
  Erik Tosh (Vice President, Compounding Support Services)

• Innovation Compounding
  Shawn Hodges (President and CEO)

• Wedgewood Village Pharmacy
  Barry Siegel (General Counsel)
  Anthony Grzib (Director of Pharmacy Compliance)
The Coalition: Why We Are Here

- The Coalition’s members, either directly or through their member organizations, are deeply involved with the development or dissemination of compounded sterile preparations (“CSPs”) or compounded nonsterile preparations (“CNSPs”).

- The Coalition is concerned that its patients and/or other constituents will be severely and adversely affected by USP’s worrisome and ill-considered revisions to USP General Chapter <797> Pharmaceutical Compounding—Sterile Preparations and to USP General Chapter <795> Pharmaceutical Compounding—Nonsterile Preparations.

- Among other things, those revisions would shorten the beyond-use dates (“BUDs”) assigned to CSPs or CNSPs which, in turn, will severely and negatively impact patient safety and care.

- The Coalition is appealing these changes and requesting that USP withdraw the proposed revisions to Chapters <795> and <797> and remand to a newly constituted Compounding Expert Committee (“CEC”) to start fresh.
• Chapter <797> previously assigned BUDs based on two factors: (i) a CSP’s nonsterility risk factor and (ii) its storage conditions.

• But now, under the revision, BUD assignment is based on five factors: (i) whether a CSP falls into “Category 1” or “Category 2”; (ii) whether it was aseptically processed or terminally sterilized; (iii) whether it was sterility tested; (iv) whether it was prepared from a sterile or nonsterile starting component; and (v) its storage conditions.

• Thus, under this new system, all CSPs, regardless of the conditions under which they are prepared, are presumed to have a high risk of nonsterility, and will therefore have drastically shorter BUDs; that, in turn, will force compounders to make smaller batch sizes, thereby increasing costs and effectively preventing many compounds from being made.

• In this respect, the Coalition determined that an estimated 91% of the CSPs it or its member organizations compound will be assigned shorter BUDs under the new regime—with the average BUD for certain categories of CSPs being shortened by five months.
One type of formulation that has been impacted by the new BUD table is fixed oil suspensions, which previously had a **180 day BUD**. In the revised chapter, fixed oil suspensions have a **90 day BUD**.

The practical effect of this BUD reduction is twofold: i) compounders will be forced to produce smaller CNSP batches more often to meet patient needs, **increasing the cost** to make each unit; and ii) compounders **will not be able to make adequate amounts** of CNSPs far enough in advance of receiving prescriptions to meet patient needs.
The Coalition appealed the revisions to Chapters <797> and <795>.

The Coalition's appeal raised four main substantive concerns:

1. Shortened BUDs are not based on science and conflict with scientifically sound information found elsewhere in USP’s standards.
2. The rationale for the revised BUDs is based on the premise that the previous Chapter <797> standards could not provide adequate assurance of sterility, thereby calling into question the value of the entire chapter.
3. Shortened BUDs will have a profoundly negative impact on patient safety due to a lack of availability of compounded pharmaceuticals and/or treatment interruptions.
4. Compounders will now face tremendous difficulties in trying to comply with the onerous, unprecedented demands imposed by the new standards, including by forcing them to produce smaller CSP and CNSP batches at a much higher cost.
The Coalition’s Concerns
Roadmap of the Coalition’s Appeal

1. Threshold Legal Concerns
2. Problems with USP’s Development of the Revised Chapters
3. Problems with the Adequacy of this Appeal Hearing
4. Remand to New, Fairly Informed CEC
1. **Threshold Legal Concerns**

2. Problems with USP’s Development of the Revised Chapters

3. Problems with the Adequacy of this Appeal Hearing

4. Remand to New, Fairly Informed CEC
USP’s Unique Status Under Federal Law

- USP is a *private, non-governmental organization* that, among other things, revises and drafts compendial standards, including the official USP-NF compendium.

- The idea for USP developed in early colonial America, as physicians and apothecaries largely relied on pharmacopeias published in London and Edinburgh for guidance.

- In 1818, Dr. Lyman Spalding invited medical societies and schools to send delegates to regional conferences, where delegates would draft versions of a pharmacopeia for submission to a national conference.
USP’s Unique Status Under Federal Law

• The first USP standards were published in December 1820.
• The USP standardized the ways in which patients obtained and used pharmaceuticals.
• The USP standards continued to be revised and republished every 10 years.
• By the early 1900s, the USP standards gained wide acceptance in the drug trade as an authoritative reference work.
• The USP standards were incorporated into federal law in 1906 in the Pure Food and Drug Act, and subsequently amended in 1937 by the Food, Drug, and Cosmetic Act (“FDCA”).
USP Standards Incorporated into Federal Law

- FDCA provides that when a drug is recognized by the USP, “it shall be subject to the requirements of the United States Pharmacopeia.” 21 U.S.C. § 351(b).
- FDCA incorporates all future revisions to USP’s standards. 21 U.S.C. § 351(b).
- FDCA defines when a drug is “misbranded” by reference to USP standards. 21 U.S.C. § 502(g).
- Because FDCA’s definition of “drug” incorporates USP standards, it enables the USP to fundamentally alter what items qualify as drugs under federal law.
Recently issued FDA Guidance expressly recognizes that failure to adhere to USP standards could lead to criminal prosecution:

**A. Compounding Pursuant to Patient-Specific Prescriptions for Nonfood-Producing Animals**

At this time and based on our current understanding of the risks of animal drugs compounded from bulk drug substances, FDA does not intend to take enforcement action against the compounding of animal drugs from bulk drug substances for any nonfood-producing animal for violations of the new animal drug approval requirements in sections 512 and 501(a)(5) of the FD&C Act, the adequate directions for use requirements in section 502(f)(1) of the FD&C Act, and the cGMP requirements in section 501(a)(2)(B) of the FD&C Act, provided:

1. The drug is compounded by or under the direct supervision of a veterinarian or a pharmacist in a State-licensed pharmacy or Federal facility;

2. The drug is compounded in accordance with the current United States Pharmacopeia and National Formulary (USP-NF) Chapters <795> “Pharmaceutical Compounding—Nonsterile Preparations” or <797> “Pharmaceutical Compounding-Sterile Preparations” and complies with the standards of all applicable USP-NF monographs (e.g., a monograph for a bulk drug substance or a monograph for a compounded finished product);
The Problem? USP’s Incorporation into Federal Law Is *Unconstitutional*

- Article I, Section I of the U.S. Constitution provides that “[a]ll legislative Powers herein granted shall be vested in a Congress of the United States[.]” U.S. CONST. art. 1, § 1.

- From Article I, Section I of the U.S. Constitution comes the *non-delegation doctrine*, which prevents Congress from farming its legislative power out to anyone outside of the Legislature.
The Non-Delegation Doctrine and Separation of Powers

The Non-Delegation Doctrine and the “Intelligible Principle”

Delegation to USP *Per Se* Unconstitutional?

**United States Court of Appeals**
**FOR THE DISTRICT OF COLUMBIA CIRCUIT**

Argued February 19, 2013  
Decided July 2, 2013

No. 12-5204

ASSOCIATION OF AMERICAN RAILROADS, APPPELLANT

v.

UNITED STATES DEPARTMENT OF TRANSPORTATION, ET AL., APPELLEES

Appeal from the United States District Court for the District of Columbia (No. 1:11-cv-01499)

Thomas H. Dupree, Jr. argued the cause for appellant. With him on the brief was Louis F. Worchot.

Michael S. Raab, Attorney, U.S. Department of Justice, argued the cause for appellees. With him on the brief were Stuart F. Delery, Acting Assistant Attorney General, Ronald C. Machen Jr., U.S. Attorney, Mark B. Stern and Daniel Tenney, Attorneys, Paul M. Geier, Assistant General Counsel for Litigation, U.S. Department of Transportation, Peter J. Plocki, Deputy Assistant General Counsel for Litigation, and Joy Park, Attorney.

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1095, 1143 (D.C. Cir. 1984) (per curiam). 3 Even an intelligible principle cannot rescue a statute empowering private parties to wield regulatory authority. Such entities may, however, help a government agency make its regulatory decisions, for “[t]he Constitution has never been regarded as denying to the Congress the necessary resources of flexibility and practicality” that such schemes facilitate. Pan Raff Co. v. Ryan, 293 U.S. 388, 421 (1935). Yet precisely how much involvement may a private entity have in the administrative process still is an open question.

Pre-approval of private has a framework.

Sunshine Anthracite Coal Co. v. Adkins, 310 U.S. 381 (1940). In *Curtis* Congress circumscribed its delegations of

3 At least one commentator has suggested that the “doctrine forbidding delegation of public power to private groups is, in fact, rooted in a prohibition against self-interested regulation that sounds more in the Due Process Clause than in the separation of powers.” A. Michael Fromkin, *Wrong Turn in Cyberspace: Using ICANN To Route Around the APA and the Constitution*, 50 DUKE L.J. 17, 153 (2000). Carrier Coal offers some textual support for this position, describing the impermissible delegation there as “clearly a denial of rights safeguarded by the due process clause of the Fifth Amendment.” 294 U.S. at 311. While the distinction evokes scholarly interest, neither party before us makes this point, and our own precedent describes the problem as one of unconstitutional delegation. See *NARUC*, 737 F.2d at 1143 n.41. And, in any event, neither court nor scholar has suggested a change in the label would effect a change in the inquiry.
Delegation to USP Per Se Unconstitutional?

We open our discussion with a principle upon which both sides agree: Federal lawmakers cannot delegate regulatory authority to a private entity. To do so would be “legislative delegation in its most obnoxious form.” Carter v. Carter Coal Co., 298 U.S. 238, 311 (1936). This constitutional prohibition is the Supreme Court held that the United States Department of Transportation, United States, could not delegate its regulation of ‘common carriers’ to a private entity because such delegation is not consistent with the Constitution and to the U.S. 3d 2d. This constitutional prohibition applies to any delegation of regulatory authority to a private entity.

The Non-Delegation Doctrine and the “Intelligible Principle”

• When Congress wants to provide statutory authorization for an agency within the Executive Branch to regulate, Congress is constitutionally constrained to do so pursuant to an “intelligible principle”—that is, a clear prescription for how its delegated authority is to be used. See Whitman v. Am. Trucking Ass’ns, 531 U.S. 457, 472 (2001) (emphasis added).

• When Congress fails to provide any “guidance for the exercise of discretion,” it has failed to offer an “intelligible principle,” and any attempted delegation of legislative authority, even within the federal government, is unconstitutional. Id. at 474 (emphasis added).
FDCA’s sweeping delegation of power to the USP is not accompanied by any statutory language to guide or constrain its conduct.

FDCA does not allow FDA (or any other governmental entity) to modify or veto additions or revisions to the USP.

Any additional articles added to the USP standards are automatically incorporated in the definition of “drug,” and any changes to drug standards are automatically incorporated into law.
Non-Delegation Doctrine: *Not if...but when...*

• A majority of Supreme Court Justices have signaled an inclination to enforce the non-delegation doctrine.

Source Document: Mark Stern, *The Supreme Court's Conservatives Are Ready to Take a Wrecking Ball to the Entire Federal Bureaucracy*, Slate (June 20, 2019).
Non-Delegation Doctrine: Not if...but when...

If Congress could pass off its legislative power to the executive branch, the “[v]esting [c]lauses, and indeed the entire structure of the Constitution,” would “make no sense.”

Without the involvement of representatives from...
Non-Delegation Doctrine: *Not if...but when...*


Accepting, then, that we have an obligation to decide whether Congress has unconstitutionally divested itself of its legislative responsibilities, the question follows: What's the test? Madison acknowledged that “no skill in the

[Picture of Supreme Court Justices]
Non-Delegation Doctrine: *Not if... but when...*

Non-Delegation Doctrine: *Not if...but when...*

**Kavanaugh Joins Gorsuch in Fight To Revive Nondelegation Doctrine**

An important development in the legal wrangling over the separation of powers.

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**SUPREME COURT OF THE UNITED STATES**

RONALD W. PAUL v. UNITED STATES

ON PETITION FOR WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE SIXTH CIRCUIT

No. 17-6830. Decided November 25, 2019

The petition for a writ of certiorari is denied.

Statement of JUSTICE KAVANAUGH respecting the denial of certiorari.

I agree with the denial of certiorari because this case ultimately raises the same statutory interpretation issue that

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The U.S. Supreme Court narrowly upheld a law in June that, in the dissenting words of Justice Neil Gorsuch, "half-nation’s chief prosecutor the power to write his own criminal code." Today, Justice Brett Kavanaugh spoke up in support of Gorsuch.

The June ruling came in *Gundy v. United States*, a case that centered on a 2006 federal law known as the Sex Offender Registration and Notification Act (SORNA). Among other things, SORNA required convicted sex offenders to register, check in periodically in

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agency to exercise regulatory authority over a major policy question of great economic and political importance, Congress must either: (i) expressly and specifically decide the major policy question itself and delegate to the agency the authority to regulate and enforce; or (ii) expressly and specifically delegate to the agency the authority both to decide

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U. S. ____ (2019). I write separately because JUSTICE GORSUCH’s scholarly analysis of the Constitution’s nondelegation doctrine in his *Gundy* dissent may warrant further consideration in future cases. JUSTICE GORSUCH’s opinion

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By contrast with the tight restrictions placed on the Attorney General’s exercise of penal discretion in *Touby*, defendants point out (accurately) that the references to the USP in the FDCA are “patchy” and unsystematic, that no guidance is provided directly by Congress (or indirectly through the Food and Drug Administration (FDA)) to the USP’s Expert Committees, that the FDA has no discretion to accept or reject the revisions made in the USP by the USPC, and that the FDA has no oversight authority over the USPC, only permission from Congress to “cooperate” with it in the making of revisions to the USP. *See* 21 U.S.C. § 377. *Compare Sunshine Anthracite Coal Co. v.*

- Supreme Court likely to decide that USP’s standards violate the non-delegation doctrine.
- One lower court has essentially already decided as much.
Implications of *Cadden* and *Amtrak* for USP

- Threatens the entire USP system.
- System ripe for legal challenge.
- This would present a compelling test case.
- Renewed emphasis on the non-delegation doctrine from a majority of the Supreme Court.
“With Great Power Comes Great Responsibility”: Due Process Concerns
The Due Process Clause

• “No person shall be . . . deprived of life, liberty, or property, without due process of law.” U.S. CONST. amend. V.

• Due process protects against deprivations by state actors.

• Private entities, such as USP, qualify as a state actor if the government “participat[es]” in its activities, putting “its power, property and prestige behind” the entity, or when there is “interdependence” between the entity and the state. Burton v. Wilmington Parking Auth., 365 U.S. 715, 722, 725 (1961) (emphasis added).

• The relationship between USP and the FDA answers to both criteria.
USP, a State Actor, Is Bound by the Due Process Clause

• FDA’s relationship with USP is codified in federal law. See 21 U.S.C. § 377.

• The actual interdependence between FDA and USP confirms USP’s status as a state actor.
  – “Five FDA centers and the Office of the Commissioner have established delegates at USP’s Convention, the [USP’s] top leadership body” (United States Pharmacopeia, *USP and FDA Working Together To Protect Public Health* (2018));
  – “USP staff maintain executive-level contacts with FDA leadership and routine contacts with FDA’s Compendial Operations and Standards Branch through quarterly meetings” (*Id.*);
  – “More than 100 FDA staff participate as government liaisons on USP’s Expert Committees and Expert Panels, the scientific bodies that develop and revise USP’s written and physical standards” (*Id.*); and
  – “FDA and USP work together to identify areas for monograph or general chapter development . . . .” *Id.*

• USP has gone so far as specifying that FDA officials work with it in their official capacities: “*Government liaisons represent FDA opinions and viewpoints* (as opposed to other USP volunteers, who represent their own opinions rather than their employers’) at public USP meetings such as the Expert Committee Meetings, Expert Panels and Stakeholder Forums.” *Id.*
USP Has Violated Its Due Process Obligations

• The U.S. Supreme Court has emphasized that the “fundamental requirement of due process is the opportunity to be heard ‘at a meaningful time and in a meaningful manner.’” *Mathews v. Eldridge*, 424 U.S. 319, 333 (1976).

• Here, USP’s efforts to revise Chapters <795> and <797> failed to provide the Coalition’s members and the public with a fair opportunity to be heard in a meaningful manner, free from arbitrary decision-making or bias.
  – USP ignored scientific authority and reasoned comments and concerns submitted by Coalition-members.
  – USP’s crucial standard-setting operations and procedures are shrouded in secrecy.
  – Neither USP’s Bylaws nor its Rules and Procedures of the Council of Experts commit definitively to what procedures or standards USP must follow when revising its General Chapters.
• USP’s standard-setting procedures fail to satisfy important, well-established strictures of the APA.
• The APA governs how “agencies” of the United States are to develop and issue regulations, rules, and guidance, including through the notice-and-comment process that traditionally defines public rulemaking.
• Because USP is directly and uniquely shaping federal law and policy concerning the use, development, and distribution of pharmaceuticals—a role that is reserved for the government—it is subject to the same constraints imposed upon the government.
USP Has Violated the APA

- USP does not offer sufficient reasons why comments were adopted or rejected. 5 U.S.C. § 553(c).
- USP does not publish the comments that it receives from interested parties or otherwise make them readily available to the public or other interested stakeholders.
- USP’s standards are not based on a record demonstrating rational, evidence-based scientific justifications. 5 U.S.C. § 706(2)(A).
- USP has not publicly articulated its rationales for the revised standards. 5 U.S.C. § 552(a).
Conflicts of Interest and the APA

- Under the APA, an unmitigated conflict of interest will render resultant agency action “arbitrary and capricious” in violation of the APA.

- Courts routinely overturn agency action that is tainted by unmitigated conflicts: *Am. Safety Council, Inc. v. U.S.*, 122 Fed. Cl. 426, 443 (2015) (Department of Labor’s failure to consider conflicts of interest in taking official agency action was arbitrary and capricious under the APA); *Jacobs Tech. Inc. v. United States*, 100 Fed. Cl. 198, 210 (2011) (Department of Defense subsidiary’s failure to account for known conflict of interest issues rendered agency’s action arbitrary and capricious under the APA).

- This precise scenario happened recently within the FDA context, and FDA’s action was declared to be a violation of the APA.

  “FDA erred in determining that the three Challenged Members of the TPSAC did not have financial and appearance conflicts of interest, and second, that therefore the FDA’s appointment of those members was arbitrary and capricious, in violation of the APA, and fatally tainted the composition of the TPSAC and its work product, including the Menthol Report.” *Lorillard, Inc. v. United States Food & Drug Admin.*, 56 F. Supp. 3d 37, 40 (D.D.C. 2014), vacated sub nom. on other grounds *R.J. Reynolds Tobacco Co. v. U.S. Food & Drug Admin.*, 810 F.3d 827 (D.C. Cir. 2016).
USP Cannot Regulate as FDA’s Proxy

- FDA has dispatched USP to serve as its proxy, regulating on FDA’s behalf while circumventing the APA and requirements of notice-and-comment rulemaking that constrain FDA.

- FDA cannot deputize USP to effect what amount to seismic changes in the rules governing the compounding industry, without providing any reasoned justification for doing so or otherwise complying with the most basic and essential requirements of the APA, or adhering to basic principles of due process.

- Congress decides what the law is; FDA cannot use USP to back-channel changes in the law so as to circumvent statutory constraints, as well as public and judicial scrutiny.
Roadmap of the Coalition’s Appeal

1. Threshold Legal Concerns

2. Problems with USP’s Development of the Revised Chapters

3. Problems with the Adequacy of this Appeal Hearing

4. Remand to New, Fairly Informed CEC
Problems with USP’s Process: *USP Allowed FDA to Pull its Strings in Arriving at the Revised Chapters*
FDA Is Actively Involved in USP Standard-Setting

6. GOVERNMENT LIAISONS

6.01 Role in Standards-Setting Process

Government Liaisons (GLs) are representatives from the United States (U.S.) Food and Drug Administration or other federal or state governmental agencies in the U.S., or from government agencies in other countries. GLs participate in the setting of USP compendial standards of a USP Expert Committee or Expert Panel to which they are assigned and may offer opinions on all facets of the standards including content and implementation. GLs also may be tasked with seeking information or opinions from the agency they represent, and with identifying other representatives of their agency who may have specific subject matter expertise that might be helpful to the Expert Committee or Expert Panel.

- FDA Government Liaisons have a **guaranteed seat at the table** in the standard-setting process.
- FDA Government Liaisons’ role is to “offer **opinions on all facets of the standards** including content and implementation.”
FDA Operates Behind Closed Doors with USP

6. GOVERNMENT LIAISONS

6.01 Role in Standards-Setting Process

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6.02 Responsibilities and Confidentiality

GLs generally receive briefing materials and are allowed to participate in confidential discussions during an Expert Committee or Expert Panel meeting, but they do not vote on USP standards. GLs are required to sign confidentiality agreements allowing them to share information only within their agency as necessary to fulfill their GL responsibilities. Some information provided by USP to GLs may be proprietary, commercial, trade secret and confidential and not subject to public disclosure unless such information is already publicly available. The chair of an Expert Committee or Expert Panel may ask a GL to excuse him or herself during any discussion or deliberation in which the chairperson believes such GL’s participation would not be appropriate due to confidentiality, conflict, or other reasons.

- Tellingly, while USP closes certain meetings to the public, it nonetheless allows representatives of FDA “to participate in confidential discussions during an Expert Committee or Expert Panel meeting.”
10. MEETINGS

10.01 Expert Committee and Expert Panel Meetings

(b) **Closed Meetings.** If the determination is made to close an official meeting, such determination and the reason for closure shall be announced at the beginning of the meeting or during the meeting and noted in the meeting minutes. Any non-member participants (observers, invited guests, etc. described in section 10.03 (a) and (b) below) attending such meeting shall be excused from the meeting. Government Liaisons may participate in closed meetings unless excused by the chairperson for the reasons described in section 6.02 above. All ballot teleconferences held by an Expert Committee, Expert Panel or Joint Standard Setting Subcommittee are considered to be closed meetings to maintain the confidentiality of the information discussed. Meetings of the Council of Experts shall be closed unless otherwise indicated.
Document Disclosure

USP provides disclosure of information and records regarding USP standards-setting activities consistent with:

- The rights of individuals to privacy
- USP’s need to protect the confidentiality of trade secrets and other proprietary commercial or financial information
- USP’s need to promote frank internal deliberations and to pursue standards-setting activities without disruption

* * *

In addition, communications between USP and third parties relating to standards-setting activities will be made available upon specific written request, including copies of written correspondence to and from third parties and memoranda of telephone conversations and meetings with third parties. Such third-party communications do not include communications of any kind among or between USP staff and members of the Board of Trustees, Council of Experts, or Expert Committees. Furthermore, unless required by law, USP will not disclose documents containing any trade secrets or confidential commercial information.

FDA Secretly Scripted USP’s Changes to the Revised Chapters
As a result of the 2012 New England Compounding Center ("NECC") fungal meningitis outbreak, **FDA expanded its participation on the CEC, specifically on the Subcommittee working on General Chapter <797>.**
FDA Secretly Scripted USP’s Changes to the Revised Chapters

**Compounding—Sterile Preparations Subcommittee.** *(797)* is critically important for the safe compounding of sterile preparations as regulated by the federal government and the states. FDA is making the CMP EC a priority in this cycle and is expanding its

- According to FDA’s then-lead on compounding, Jane Axelrad, *(797)* is critically important for the safe compounding of sterile preparations as regulated by the federal government and the states.*
Ms. Susan de Mars summarized USP’s dialog with the U.S. Food and Drug Administration (FDA) regarding General Chapter <797> revisions. She noted the following:

- Section 503A in the Drug Quality and Security Act (DQSA) heightened the importance of <797> at the federal and state level.
- FDA and USP want to ensure that the revised General Chapter is as clear as possible.
- FDA has offered an experienced medical writer to assist in revising General Chapter <797>. The FDA medical writer and the USP scientific writer will support the <797> Subcommittee in organizing and drafting the chapter.

In April 2014, “FDA . . . offered an experienced medical writer to assist in revising General Chapter <797>. The FDA medical writer and the USP scientific writer will support the <797> Subcommittee in organizing and drafting the chapter.”

- That writer would ultimately hold a pen in helping draft the final language of Chapter <797>.
• Feedback from stakeholders (e.g., industry, regulators, etc.)
  o Public comments on <800> were in excess of 3000 for the initial publication in PF and continue to stream in following the second publication in PF 41(2).
  o The CEC also received requests from professional organizations to exempt their stakeholders from standard practices established in <797> and <800>.
  o FDA expressed appreciation for the weekly meetings with USP and collegial working relationship in setting compounding standards.

• Beginning in the 2010-2015 cycle, FDA and USP started having undisclosed **private weekly meetings** to discuss “setting compounding standards.”
During the 2010-2015 cycle, USP’s and FDA’s relationship started out “rough,” but ultimately “evolved to a very strong and collaborative partnership.”

By January 2015, CEC members and FDA Government Liaisons had already “reach[ed] consensus on proposed revisions and new standards prior to the public comment period.”
• Thus, long before the standards for <797> were even released to the public for comment, FDA and USP had already come to an agreement, after years of weekly meetings, on what those precise standards should be.
c. U.S. Food and Drug Administration (FDA) Introduction

Ms. Jane Axelrad, the FDA lead on compounding, explained that 90 FDA liaisons serve on 24 USP ECs. As a result of the 2012 New England Compounding Center (NECC) fungal meningitis outbreak, FDA expanded its participation on the CMP EC, specifically on the subcommittee working on General Chapter <797> Pharmaceutical Compounding—Sterile Preparations Subcommittee. <797> is critically important for the safe compounding of sterile preparations as regulated by the federal government and the states. FDA is making the CMP EC a priority in this cycle and is expanding its participation by adding two FDA liaisons to identify cross-cutting policy issues that affect multiple subcommittees. Ms. Edisa Gozun will be the CMP EC’s central point of contact.

• By September 2015, FDA had “expanded its participation” on the CEC and announced that it was unilaterally “adding two FDA liaisons” to the committee, bringing the total number of FDA Government Liaisons to eight.
FDA Secretly Scripted USP’s Changes to the Revised Chapters

b. Creation of Subcommittees
Dr. Sun reported that EC members and FDA liaisons volunteered to serve on EC Subcommittees as follows:

1) <797> Pharmaceutical Compounding—Nonsterile Preparations
   Chair: Bob Shrewsbury
   EC Members: Gus Bassani, Gigi Davidson, John Musil, David Newton, Alan Parr, Brenda Yuzdepski
   FDA Liaisons: Jane Axelrad, Jonathan Bray, Ian Deveau, Susan Homire, John Metcalfe, Erika Pfeiler

2) <795> Pharmaceutical Compounding—Sterile Preparations
   Chair: Gigi Davidson
   EC Members: Deb Houston, Patti Kienle, Bill Mixon, Dave Newton, Abby Roth, Connie Sullivan, Jim Wagner
   FDA Liaisons: Jane Axelrad, Jonathan Bray, Ian Deveau, Susan Homire, John Metcalfe, Erika Pfeiler

• In September 2015, USP created the <797> and <795> Subcommittees for 2015-2020 cycle—both of which were overrun by FDA Government Liaisons.
Responding to Public Comments

USP staff clarified the following:

- Due to the high volume of comments expected, USP staff will distribute the comments to EC members and government liaisons throughout the comment period.
- USP staff will compile all comments received in a spreadsheet to facilitate EC review after the comment period closes.
- USP staff will ask commenters who do not provide line numbers to provide the line numbers relevant to their comments.

- During the 2015-2020 cycle, the FDA Government Liaisons’ core role on the Chapter <797> Subcommittee was seemingly to push the 2010-2015 Subcommittee’s revisions through to completion, including by reviewing public comments.

Source Document: Compounding Expert Committee Meeting Minutes (Sept. 9, 2015), at p.5.
a. Overview of Revision Process Timeline
The Chair explained that she and the Vice Chair were in the process of reviewing the over 8,000 public comments received on <797>, and they have taken a first pass at incorporating the comments by section. EC members and Government Liaisons are reviewing the comments and proposed responses, section by section, in weekly teleconferences. USP will convene roundtables with allergists and radiopharmacists in 2017 to address their unique concerns. The EC has not discussed whether the general chapter will be republished in PF.

- By September 2016, the Chapter <797> Chair, Vice-Chair, <797> Subcommittee members, and FDA Government Liaisons were having weekly teleconferences to determine which comments to incorporate, how to incorporate them, and how to respond to commenters.
b. New Revision Process Instituted
A new process for revision was adopted to improve efficiency which involved the EC leadership (i.e., Chair, Vice Chair, and USP staff) incorporating public comment suggestions into a redline draft, which is sent to EC members for review and comment. EC members were given 2 weeks to provide comments and feedback on the redline draft to EC leadership. EC member feedback and comments are incorporated into the draft and sent to the Scientific Writer for cleanup and editing.

- Although the weekly conference calls were seemingly abandoned by September 2017, the FDA Government Liaisons apparently still had the opportunity to review and comment on the public comments received.
• The FDA Government Liaisons’ involvement in the comment review process for Chapter <797> continued into the second round of comments, when USP clarified that “the entire [Expert Committee]”—including, ostensibly, the FDA Government Liaisons—would “discuss specific topics” raised in the comments.
**FDA Secretly Scripted USP’s Changes to the Revised Chapters**

**Sterility Testing of Aqueous Solutions**

FDA Liaisons noted the following:

- A nonsterile drug could have a microbial contamination in the short term. If the microbial load is capable of growth, it could become dangerous the longer the drug is held.
- If a preservative is used and <51> testing is not conducted, the compounder would not know if the preservative will be effective for the stability period.
- To extend the BUD of an FDA-approved aqueous solution, a preservative or self-preserving API and <51> testing would be needed.
- The 14-day BUD for non-preserved aqueous dosage forms should be retained.

- FDA Government Liaisons were also heavily involved in the revisions to Chapter <795>, most of which came during the 2015-2020 cycle.
- For example, in an August 2018 CEC meeting, **FDA Government Liaisons provided extensive input on the sterility testing of aqueous solutions**—one of the key issues in this appeal.

USP Broke Its Purported Commitment to “Independence”

USP Publishes Notice of Intent to Revise Compounding Standards

Rockville, Md., September 23, 2019 – USP published a Notice of Intent To Revise (NITR) for the new and revised compounding standards released on June 1, 2019. [https://www.usp.org/notices/compounding-chapters-postponement]

About USP

USP is an independent scientific organization that collaborates with the world’s top experts in health and science to develop quality standards for medicines, dietary supplements, and food ingredients. Through our standards, advocacy and education, USP helps increase the availability of quality medicines, supplements and food for billions of people worldwide. For more information about USP, visit www.usp.org
USP Broke Its Purported Commitment to “Independence”

Avoid conflicts of interest

USP’s reputation depends on our independence. As an organization, we must avoid conflicts of interest that interfere or appear to interfere with our impartiality and objectivity. As individuals, we must avoid conflicts of interest that affect or appear to affect our ability to make objective decisions on behalf of USP. Additionally, we must also avoid conflicts that undermine USP’s role as an independent standards-setting organization. Conflicts of interest are situations in which an employee’s personal interest is competing with USP’s interests.

It is important to be open and disclose conflicts so we can manage them and ensure we make decisions in the best interest of USP.

What’s my role?

It isn’t possible to address every situation that could present a conflict, but there are certain situations where conflicts are more likely:

- Never solicit contributions for any charity or for any political candidate from any person or entity that does business or seeks to do business with USP.
- Do not take personal advantage of USP’s assets or business opportunities.
- Obtain approval before conducting USP business transactions with a family member.
- If you exercise supervision or other authority on behalf of USP over a counterparty who is also a family member or with whom you are financially involved, be sure to disclose the situation so that appropriate steps can be taken.

Learn from the experience of your colleagues.
Case Study: Jane Axelrad’s Secretive Dealings with USP

- Long-time FDA employee.
- From 1995-2012, served as the Director of the Office of Regulatory Policy in FDA’s Center for Drug Evaluation and Research (“CDER”).
- In 2012, became the Associate Director for Policy in CDER.
Case Study: Jane Axelrad’s Secretive Dealings with USP

b. General Chapter <797> Pharmaceutical Compounding—Sterile Preparations Subcommittee

Chair: Gigi Davidson

Members: Deborah Houston, Patricia Kienle, Keisha Lovoi, Linda McElhiney, William Mixon, Dave Newton, Keith St. John

FDA Liaisons: Jonathan Bray, Pamela Lee, John Metcalfe, Kristina Peters

CDC Liaisons: Nadine Shaw, Melissa Shaffer (via WebEx)

Invited guest: Jane Axelrad, FDA

The Chair convened the open meeting of the General Chapter <797> Subcommittee at 2:35 p.m. She welcomed Ms. Axelrad, Associate Director for Policy, Center for Drug Evaluation and Research (CDER) at FDA. Ms. Axelrad is the FDA lead on pharmacy compounding. Ms. Axelrad thanked the EC for inviting her to attend and explained that <797> is used by many states to regulate sterile compounding.

- On behalf of FDA, Ms. Axelrad begins consulting for the CEC from October 2013 forward in connection with the revisions for <797> as an “invited guest.”
The Chair noted that the EC would conduct a closed session to discuss General Chapter <797> Pharmaceutical Compounding–Sterile Preparations. Observers would leave the meeting at that time. Only USP staff, EC members, and government liaisons would attend this portion of the meeting.

• After Ms. Axelrad began attending CEC meetings, the Chapter <797> Subcommittee began to hold closed sessions.
Case Study: Jane Axelrad’s Secretive Dealings with USP

• Over time, Ms. Axelrad gained more influence in the Chapter <795> and <797> Subcommittees, and her amplified role curiously coincided with FDA’s increased focus on the CEC.

Source Document: Compounding Expert Committee Meeting Minutes (Sept. 9, 2015), at p.3.
Case Study: Jane Axelrad’s Secretive Dealings with USP

b. Creation of Subcommittees

Dr. Sun reported that EC members and FDA liaisons volunteered to serve on EC Subcommittees as follows:

1) <795> Pharmaceutical Compounding—Nonsterile Preparations

Chair: Bob Shrewsby
EC Members: Gus Bassani, Gigi Davidson, John Musil, David Newton, Alan Parr, Brenda Yuzdepski

FDA Liaisons: Jane Axelrad, Jonathan Bray, Ian Deveau, Susan Homire, John Metcalfe, Erika Pfeiler

2) <797> Pharmaceutical Compounding—Sterile Preparations

Chair: Gigi Davidson
EC Members: Deb Houston, Patti Kienle, Bill Mixon, Dave Newton, Abby Roth, Connie Sullivan, Jim Wagner

FDA Liaisons: Jane Axelrad, Jonathan Bray, Ian Deveau, Susan Homire, John Metcalfe, Erika Pfeiler

• For the 2015-2020 cycle, Ms. Axelrad became an official FDA Liaison to the Chapter <795> and <797> Subcommittees.
Case Study: Jane Axelrad’s Secretive Dealings with USP

Action Items

- Ms. Jane Axelrad will work with FDA colleagues to explore product labeling related to water used for reconstitution of nonsterile products and send an update to the EC.
- EC members will send comments on proposed <795> revisions to Dr. Shrewsbury.

- USP dispatched Ms. Axelrad to liaise directly with her “FDA colleagues” in order obtain information relevant to Chapter <795> from FDA and to report back to the CEC.
Case Study: Jane Axelrad’s Secretive Dealings with USP

When it enacted the CQA in 2013, Congress created the new voluntary category of outsourcing facilities. Instead of requiring compounding pharmacies to supply compounded drugs without obtaining prescriptions to become outsourcing facilities and adhere to higher standards, Congress decided to rely on market forces to encourage pharmacies to adopt this business model. More than 70 facilities have voluntarily registered with FDA as outsourcing facilities, providing millions of units of medications to healthcare facilities, doctors offices, and clinics. If Congress eliminates the prescription requirement, it would remove any incentive for compounding pharmacies to register as outsourcing facilities and comply with the standards that are necessary for the safety of higher volume, non-individualized compounding.

- While serving as an FDA Government Liaison to the CEC, Ms. Axelrad retired from the FDA in April 2016 after 25 years of service.
- Ms. Axelrad then launched a consulting firm called Axelrad Solutions, LLC and started calling for changes of law and tighter restrictions against the entire compounding industry.

In May 2017, USP hires a new “USP Expert Consultant” to finalize the <797> and <795> revisions:
Case Study: Jane Axelrad’s Secretive Dealings with USP

b. USP Expert Consultant

The Chair welcomed Jane Axelrad in her new role as USP Expert Consultant. In this role, Ms. Axelrad will serve as a volunteer, participate in discussion and document review, and provide expertise not otherwise represented in the EC membership. Ms. Axelrad played a key role in assisting the CMP EC in revising <797> during her work as an FDA liaison.
• Other than announcing her new role, **USP’s meeting minutes do not reflect any discussion of the propriety of Ms. Axelrad’s new position**, nor do they show any votes/approvals of the new “expert consultant” position.

• Nor is it clear whether Ms. Axelrad had voting power or whether she was actually a formal member of the CEC.

• USP evidently saw no impediment to Ms. Axelrad acting on behalf of USP despite acknowledging her “**key role**” in assisting the Chapter <797> revisions as a representative of FDA.
Case Study: Jane Axelrad’s Secretive Dealings with USP

The Chair announced that the following topic would be discussed in a closed session. Observers and government liaisons were asked to leave the meeting room. Observers and government liaisons were disconnected from the WebEx.

- After Ms. Axelrad arrived as USP’s “Expert Consultant,” the CEC returned to holding closed sessions.
Problems with USP’s Development of the Revised Chapters: Conflicts of Interest Infected the Process
USP’s Definition of “Conflict of Interest”

2.03 Conflict of Interest

(a) **General.** Pursuant to Article VIII, Section 1, of the Bylaws and the Conflicts of Interest Policy in the Code of Ethics, all CoE/EC Expert members shall adhere to the Conflicts of Interest provisions set forth in this section. Expert Panel members are subject to the Conflict of Interest requirements contained in Section 5.05(a) of these Rules. As used in these Rules, “Conflict of Interest” includes, but is not limited to, any matter in which an Expert has a direct or indirect financial interest or any other personal interest of any kind which would preclude or appear to preclude such individual from exercising impartial judgment or otherwise acting in the best interest of USP.
USP Belatedly Discloses that Certain Unidentified CEC Members Had Conflicts of Interest

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**In accordance with USP’s rules and policies regarding conflicts of interest, all members of the CMP EC were invited to discuss the appeal. However, members with conflicts of interest related to the General Chapters under appeal recused themselves prior to final discussion and voting.**

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Source Document: Letter from Mario Sindaco to Derek Shaffer (Aug. 16, 2019).
2.03 Conflict of Interest

(a) General. Pursuant to Article VIII, Section 1, of the Bylaws and the Conflicts of Interest Policy in the Code of Ethics, all CoE/EC Expert members shall adhere to the Conflicts of Interest provisions set forth in this section. 

Expert Panel members are subject to the

* * *

(b) Recusal. No CoE/EC Expert shall vote nor take part in the final discussion or deliberation of any matter in which he or she has a Conflict of Interest. An Expert Panel member may participate in deliberations or recommendations regarding matters in which he or she has a Conflict of Interest provided disclosure of a Conflict of Interest is made pursuant to Section 5.05(a) of these Rules.
Disclosure of Conflicts Is Limited to USP

**2.05 Identification and Resolution of Conflict Issues.**

(a) **USP Responsibility.** USP staff, together with the chairperson of an Expert Committee or Expert Panel shall review Disclosure Statements on a periodic basis to identify potential conflicts.

(b) **Expert Responsibility.** Any CoE/EC Expert or Expert Panel member who believes or should have reason to believe that he or she may have an apparent or potential Conflict of Interest shall notify USP staff and the chairperson of the Expert Committee or Expert Panel, as applicable, prior to any work on or discussion of the matter in question. Conflict of Interest issues identified by a CoE/EC Expert shall be resolved as described in Section 2.05(a) above.

**5.05 Conflict of Interest and Confidentiality.**

(a) **Conflicts.** Conflicts of Interest, as defined in Section 2.03(a), will not be a bar to participation on an Expert Panel or in any deliberations or recommendations of the Expert Panel, including voting, provided the Expert Panel member timely and adequately discloses any Conflict of Interest as required by Sections 2.03, 2.04 and 2.05 of these Rules to other members of the Expert Panel including the chairperson.
The Coalition Requests Basic Information About these Conflicts

Fourth, the Coalition also requests additional information from USP concerning the unspecified conflicts of interests USP acknowledged in its August 16, 2019 initial denial of the Coalition’s appeal. See Appeal of Revisions of Beyond-Use Date Standards in General Chapters <795> and <797>, dated Aug. 16, 2019 at 2, fn. 2. In particular, USP acknowledged in that letter that various CEC members had conflicts of interest yet participated in the discussion of the merits of the Coalition’s appeal. To date, USP has not provided any information about the nature of these conflicts, the conflicted members, their involvement in the Coalition’s appeal, or the dates on which they ceased further participation in the new standards. To the extent the Appeals Panel is focusing, as you write, on addressing “the sufficiency of the process used by the responsible Expert Committee to develop and approve the standards under appeal,” it is incumbent upon USP, at a minimum, to provide information about these conflicts well in advance of any hearing. The Coalition therefore respectfully requests that USP promptly (i) identify all CMC members with conflicts of interests who may or may not have recused themselves prior to final discussion and voting on the new standards; (ii) the precise nature of those conflicts of interests; (iii) the date(s) upon which those conflicts of interests were disclosed to USP and/or the CMC; (iv) a full accounting of the conflicted members’ involvement in the Coalition’s appeal and/or their involvement in the creation of the new standards; (v) the dates on which their participation concluded; and (vi) all internal USP documents and communications concerning these conflicts of interests and the conflicted members.
Inquiry concerning Conflicts of Interest. The Coalition requests information concerning conflicts of interest for certain Expert Committee members, as referenced in a footnote of our August 16 response to the Coalition’s first-level appeal. Under Section 2 of the Rules and Procedures of the Council of Experts, USP is required to maintain confidentiality relating to the conflict-of-interest disclosures of its Expert Committee and Expert Panel members, who themselves have obligations to maintain confidentiality of information gained in the course of their participation in USP activities.

Kind regards,

Mario Sindaco
Vice President, Science—Operations and Executive Secretariat, Council of Experts
Section 2 of the Rules & Procedures Does Not Prevent Disclosure

2.05 Identification and Resolution of Conflict Issues.

(a) **USP Responsibility.** USP staff, together with the chairperson of an Expert Committee or Expert Panel shall review Disclosure Statements on a periodic basis identify potential Conflicts of Interest and to ensure that all interests disclosed on the Disclosure Statements are disclosed to the other members of the Expert Committee or Expert Panel. Where an apparent or potential Conflict of Interest is identified by a CoE/EC Expert and cannot be resolved through voluntary recusal and/or intervention by the EC chair, the matter shall be referred to the Chair of the Council of Experts (CoE Chairperson) and the USP Executive Secretariat for resolution. The CoE Chairperson shall have final authority for resolving matters involving Conflicts of Interest. The minutes of any meeting at which a Conflict of Interest issue has been identified shall reflect disclosure and resolution of such issue, including any recusal of a CoE/EC Expert due to Conflict of Interest.
Section 2 of the Rules & Procedures Does Not Prevent Disclosure

2.04 Disclosure Statements

(a) **Requirement.** Each COE/EC Expert and Expert Panel member shall submit to USP a Disclosure Statement disclosing all employment, professional research, organizational memberships, and other relevant interests. The Disclosure Statement, shall be updated by the member as necessary to keep current or as requested periodically by USP, and the member is also obligated to advise the Expert Committee or Expert Panel chair and USP staff of changing or emerging interests. Except as specified in Section 2.05 below (e.g., periodic disclosure to fellow Expert Committee or Expert Panel members), the information provided in Disclosure Statements shall be kept confidential.
Section 2 of the Rules & Procedures Does Not Prevent Disclosure

2.06 Confidentiality

(a) **Obligation to Maintain Confidentiality.** Each CoE/EC Expert member shall maintain the confidentiality of all information gained in the course of his or her activities as a CoE/EC Expert, and shall not use or disclose such information for any purpose, unless such information is already publicly available. In case of doubt as to whether information is deemed confidential, the information shall be treated as confidential until otherwise indicated by the USP Executive Secretariat or USP Secretary. Expert Panel members are obligated to maintain confidentiality of materials in accordance with Section 5.05(b) of these Rules. CoE/EC Experts and Expert Panel members should receive and send any confidential electronic communications (i.e. all communications in the case of Expert Committee members) from a private email address, not shared with or accessible to their employer or any other 3rd party.
The Coalition Requests USP Reconsider Its Refusal to Provide Conflicts Information

December 6, 2019

Mario P. Sindaco, M.S., MBA
Vice President, Science-Operations
Executive Secretary to the Council of Experts
United States Pharmacopeia
3201 Towbinbrook Parkway
Rockville, MD 20852-1900

Re: Appeal of New Standard for USP General Chapter 795

Dear Mr. Sindaco,

I write on behalf of Alliance for Pharmacy Compounding—Wedgebrook Village Pharmacy (collectively, “the Coalition”)

The Coalitions 2019 correspondence regarding the revised procedure for the new standard for USP General Chapter 795: Pharmaceutical Compounding—Nonsterile Product—Chapter 795: Pharmaceutical Compounding—Nonsterile Product, as well as additional dates for the Appeals Hearing. The Coalition is pleased to present this appeal, as well as to broaden the scope of the hearing. At the same time, the Coalition is disappointed that USP will not be making its employees or agents available to testify, which we continue to believe would properly aid the Coalition’s presentation and inform the Appeals Panel’s evaluation of the merits of the Coalition’s appeal. We respectfully urge USP to reconsider its position and we incorporate by reference the concerns we have raised above the absence of due process, while also respectfully reserving rights for the reasons we have previously stated.

That noted, one point requires further treatment. Specifically, the Coalition is perplexed by USP’s refusal to disclose key information that would shine light on conflicts that may have afflicted members of the Compounding Expert Committee (“CEC”) while those members developed, discussed, and considered the revisions to General Chapters 795 and 797. We fail to understand why USP is declining the Coalition’s request for basic information about these

82 Source Document: Letter from Derek Shaffer to Mario Sindaco (Dec. 6, 2019).
The Coalition Requests USP Reconsider Its Refusal to Provide Conflicts Information

December 6, 2019
Mario P. Sindaco, M.S., MBA
Vice President, Science-Operations
Executive Secretary to the Council of Experts
United States Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Re: Appeal of New Standard for USP General Chapter

Dear Mr. Sindaco,

I write on behalf of Alliance for Pharmacy Compounding Wedgewood Village Pharmacy (collectively, “The Coalition”), in response to the Coalition’s 83 correspondence regarding the revised protocol for the USP’s General Chapter 797: Pharmaceutical Compounding—Injectable. The Coalition’s basis for its appeal is the absence of due process. The Coalition’s position is that USP has not provided adequate information regarding conflicts of interest that may have influenced the decision-making process of the Expert Committee. The Coalition has requested additional information to support the appeal.

The Coalition seeks to ensure that all members of the Expert Committee are properly disclosed and that all relevant conflicts of interest are transparent. The Coalition believes that the Expert Committee was not adequately informed of all potential conflicts, leading to a decision that may have been influenced by undisclosed, improper influences. Additionally, the information is essential to ensuring that the Coalition receives a full and fair hearing before a duly informed Appeals Panel. Indeed, absent this information, the Coalition as well as the Appeals Panel will be left in the dark as to whether and to what extent the revisions under appeal may have been tainted by conflicts at the Expert Committee stage, and as to how, when, and to what extent USP sought to mitigate or obviate the conflicts it ultimately acknowledged (albeit while withholding particulars).

We cannot conceive of a legitimate reason why USP would keep secret basic information about the Coalition’s appeal.

That noted, one point requires further treatment. Specifically, the Coalition is perplexed by USP’s refusal to disclose key information that would shine light on conflicts that may have influenced the Expert Committee’s work. The Coalition has requested that USP disclose any communications with members of the Expert Committee regarding conflicts of interest. The Coalition believes that this information is necessary to ensure a fair and transparent appeal process.

We request that USP provide the necessary information to support the Coalition’s appeal and to ensure a fair and transparent appeal process.

Sincerely,

[Signature]

[Name]

[Title]

Source Document: Letter from Derek Shaffer to Mario Sindaco (Dec. 6, 2019).
The Coalition Requests USP Reconsider Its Refusal to Provide Conflicts Information

We cannot conceive of a legitimate reason why USP would keep secret basic information that stands to benefit all interested parties—including appellants, stakeholders, public observers, and the Appeals Panel itself—about identified conflicts of interest that may bear directly and profoundly upon the revisions proposed by the Expert Committee. For USP to persist in its stance is to say, in essence, that certain members of the Expert Committee did in fact face conflicts of interest while working and deliberating on the revisions, potentially right up until the point the revisions were put to a vote, but that USP is sworn to cover up those conflicts and its handling of same so as to thwart full and fair examination of these particulars on appeal. Needless to say, we are troubled by that stance and believe others should be too.

“[The Coalition] cannot conceive of a legitimate reason why USP would keep secret basic information that stands to benefit all interested parties . . . about identified conflicts of interest that may bear directly and profoundly upon the revisions proposed by the Expert Committee. For USP to persist in its stance is to say . . . that certain members of the Expert Committee did in fact face conflicts of interest while working and deliberating on the revisions . . . but that USP is sworn to cover up those conflicts and its handling of same so as to thwart full and fair examination of these particulars on appeal.”

Source Document: Letter from Derek Shaffer to Mario Sindaco (Dec. 6, 2019).
The Coalition Requests USP Reconsider Its Refusal to Provide Conflicts Information

If USP is nonetheless claiming the ability to shield from external scrutiny its official handling of an acknowledged conflict and its minutes reflecting same, then something is seriously amiss not only with USP’s reading of Section 2, but with its overall approach to conflicts and/or transparency.

“If USP is nonetheless claiming the ability to shield from external scrutiny its official handling of an acknowledged conflict and its minutes reflecting same, then something is seriously amiss not only with USP’s reading of Section 2, but with its overall approach to conflicts and/or transparency.”

Source Document: Letter from Derek Shaffer to Mario Sindaco (Dec. 6, 2019).
The Coalition Requests USP Reconsider Its Refusal to Provide Conflicts Information

In sum, nothing in USP’s Rules (or Bylaws) disables, limits, or otherwise inhibits USP’s disclosure of information about how it has addressed conflicts of interests among its Expert Committee. To the contrary, the Rules call for the disclosure of this information, and so does due process, basic fairness, and the ability of USP to claim public legitimacy as it makes pivotal judgments upon which industries, professions, and public health depend. We thank you for considering this one further submission and look forward to your prompt response. As always, we will be at your disposal if you wish to discuss.

“To the contrary, the Rules call for the disclosure of this information, and so does due process, basic fairness, and the ability of USP to claim public legitimacy as it makes pivotal judgments upon which industries, professions, and public health depend.”

Source Document: Letter from Derek Shaffer to Mario Sindaco (Dec. 6, 2019).
USP’s Response

NO!
Conflicts of Interest: Why It Matters to the Coalition?

- Conflicts information is critical to assessing the legitimacy of the revisions to Chapters <795> and <797> and the extent to which these revisions were propelled by undisclosed influence(s).

- There is no way for the Panel to evaluate “the sufficiency of the process used by the responsible Expert Committee to develop and approve the standards under appeal” without knowing this information and the extent to which CEC members worked to push private and undisclosed interests. E-mail from M. Sindaco to S. Lerner (Oct. 30, 2019).
Conflicts of Interest: Why It Matters to USP?

1. GENERAL

1.01 Governance and Authority

As set forth in Article VII, Section 1 of the Bylaws, the Council of Experts and its Expert Committees are responsible for determining and approving content of the United States Pharmacopeia and National Formulary (USP-NF) and other compendia and information that may be published on behalf of the Council of Experts or an Expert Committee (including translations and line extensions of the USP-NF) and any associated reference standards. In order to fulfill these responsibilities, the Council of Experts is authorized under Article VII Section 5 of the Bylaws to make such Rules and Procedures, not in conflict with the Bylaws, that are sufficient to ensure the accuracy and adequacy of the content of the USP-NF and other authorized publications, and to provide for adequate notice and opportunity of impartial consideration of all proposed changes to such publications. Procedures of the Council of Experts (Rules) govern the actions of the USP-NF Secretariat and Joint Standard-Setting Subcommittees, Stakeholder Forums and Project Teams. USP staff may periodically also issue Guidelines publicly accessible on the USP website (e.g., Guidelines for USP-NF Submissions; Accelerated Revisions, and others) consistent with the Rules to promote transparency of USP’s internal processes and procedures.

• USP’s refusal to provide this information is contrary to USP’s oft-stated commitment to transparency in standard-setting.
As we set the course for 2020 and beyond, it is important that we remain true to the principles that have made us a trusted and respected standards-setting organization for nearly 200 years.
USP’s Purported Commitment to “Collaboration and Transparency”

for nearly 200 years. Our impact and achievements are deeply rooted in the rigorous evaluation of scientific data, collaboration and transparency in the standards-setting process, and the honest reporting of results.
This Code of Ethics reflects our continued commitment to integrity and includes resources we are all expected to use when faced with ethical questions or if we observe illegal or unethical conduct.
Conflict of Interest Case Study: Eric Kastango

- In October 2010, Eric Kastango was appointed by USP to chair the Chapter <797> Subcommittee.

- Mr. Kastango led the Chapter <797> Subcommittee’s efforts to revise the Chapter for nearly two and a half years, until April 2013.
Conflict of Interest Case Study: Eric Kastango

Transition: Mr. Eric Kastango announced that he has resigned from the CMP EC to protect the integrity of USP and its processes. His consulting work directly involves General Chapter <797>; he is involved with the application and enforcement of this General Chapter by state regulatory agencies. Although he will no longer be an EC member, USP will continue to engage him as an advisor on General Chapter <797> in accordance with Section 5.06 of the Rules and Procedures of the CoE, excerpted as follows:

An Expert Committee may also request assistance from an individual who is not a CoE/EC Expert to participate in discussion or review documents where such individual provides necessary expertise not available within the Council of Experts or Expert Committees. Such individual shall be required to sign a confidentiality agreement requiring that the confidentiality of all information provided to such individual be maintained.

The Chair, EC members, and USP staff recognized Mr. Kastango’s extensive contributions to the CMP EC and General Chapter <797>.

- After working on the <797> Subcommittee for nearly two and a half years, Mr. Kastango resigned as its Chairman in April 2013 for undisclosed conflict-of-interest reasons.
Conflict of Interest Case Study: Eric Kastango


The Chair announced that Mr. Kastango was conducting a <797> Compliance survey to establish the gaps in the Chapter and she asked him to inform the Committee of his efforts.
- Mr. Kastango reported that he is working on a project that will survey pharmacy facilities on the compliance of GC <797>. This project will be led from his consulting group, Clinical IQ. He said the survey asks pharmacists if they comply with all of <797> or not. The intent is to capture feedback and all problems associated with the compliance of <797>; the survey is an anonymous web-based gap analysis tool.
- Mr. Kastango said the survey will close in June or July and will be shared with the Committee and FDA. The goal is to publish the first-set of findings in the journal, Pharmacy, Purchasing & Products, by fall of this year. Dr. Allen said he would also be happy to consider publication of the results in his journal.

Although the precise nature of Mr. Kastango’s conflicts were never revealed, he had previously been a strong advocate for importing FDA guidelines into the Chapter <797> revisions and freely shared USP data with FDA.

b. <797> Subcommittee

Mr. Kastango explained that this subcommittee is revising <797> Pharmaceutical Compounding–Sterile Preparations to make the chapter more user friendly, incorporate frequently asked questions, and address the continuum of practitioners that practice sterile compounding. He emphasized the following key points discussed at the working meeting:
- The chapter should include the best science and procedures to ensure patient safety.
- Quality needs to be built into the process.
- The CDC has found that microbes can penetrate filters (e.g. Serratia). If microorganisms enter a clean room, they can contaminate a compounded preparation. Human and environmental factors must be controlled.
- The chapter should be harmonized with CDC and FDA guidances and Association for Professionals in Infection Control and Epidemiology (APIC) standards.
**Conflict of Interest Case Study: Eric Kastango**

**Transition:** Mr. Eric Kastango announced that he has resigned from the CMP EC to protect the integrity of USP and its processes. His consulting work directly involves General Chapter <797>; he is involved with the application and enforcement of this General Chapter by state regulatory agencies. Although he will no longer be an EC member, USP will continue to engage him as an advisor on General Chapter <797> in accordance with Section 5.06 of the Rules and Procedures of the CoE, excerpted as follows:

> An Expert Committee may also request assistance from an individual who is not a CoE/EC Expert to participate in discussion or review documents where such individual provides necessary expertise not available within the Council of Experts or Expert Committees. Such individual shall be required to sign a confidentiality agreement requiring that the confidentiality of all information provided to such individual be maintained.

The Chair, EC members, and USP staff recognized Mr. Kastango’s extensive contributions to the CMP EC and General Chapter <797>.

- Despite acknowledging Mr. Kastango’s “**extensive contributions**” to Chapter <797>, there is no **indication** USP ever reviewed Mr. Kastango’s work through April 2013 to determine whether it was tainted or otherwise influenced by his acknowledged conflicts.

Source Document: Compounding Expert Committee Meeting Minutes (April 25, 2013), at p.3.
Conflict of Interest Case Study: Eric Kastango

Transition: Mr. Eric Kastango announced that he has resigned from the CMP EC to protect the integrity of USP and its processes. His consulting work directly involves General Chapter <797>; he is involved with the application and enforcement of this General Chapter by state regulatory agencies. Although he will no longer be an EC member, USP will continue to engage him as an advisor on General Chapter <797> in accordance with Section 5.06 of the Rules and Procedures of the CoE, excerpted as follows:

An Expert Committee may also request assistance from an individual who is not a CoE/EC Expert to participate in discussion or review documents where such individual provides necessary expertise not available within the Council of Experts or Expert Committees. Such individual shall be required to sign a confidentiality agreement requiring that the confidentiality of all information provided to such individual be maintained.

The Chair, EC members, and USP staff recognized Mr. Kastango’s extensive contributions to the CMP EC and General Chapter <797>.

Incredibly, USP continued to retain Mr. Kastango as an advisor on Chapter <797> despite his conflicts!!!
Conflict of Interest Case Study: Eric Kastango

Unable to Attend
Alan Parr, Brenda Yuzdepiski

Volunteer Observers
17. Eric Kastango, Compounding with Hazardous Drugs Expert Panel

Government Liaisons
Jane Axelrad, FDA; Jonathan Bray, FDA; Ian Deveau, FDA; John Metcalfe, FDA; Erika Pfeiler, FDA; Sara Rothman, FDA; Edisa Gozun, FDA; Nadine Shehab, CDC

• Indeed, Mr. Kastango continued to attend CEC meetings until at least September 2016 in his capacity as an expert for another USP Expert Committee.
Problems with USP’s Development of the Revised Chapters: *Key Input from FDA Withheld from the Public and the Coalition*
The Coalition submitted its 25 single-spaced page appeal of the revised Chapters <795> and <797> to USP on July 31, 2019.

The appeal set forth extensive factual and legal arguments as to how and why the revised standards are unsound scientifically, procedurally, and legally.

Attached to the appeal were several exhibits supporting the Coalition’s arguments.
The Compounding Expert Committee Holds a Meeting on August 8, 2019

Goals and Anticipated Outcomes
- Discuss and review Subcommittee activities and Workplan

Details:
- Attendees:
  - Attendee list provided on the day of the meeting
- Breakfast for Volunteers at the Hotel
- CLOSED TO ALL OBSERVERS AND GOVERNMENT LIAISONS

08:00 a.m.
1. Procedural Matters and Standards of Conduct
   a. Call Meeting to Order
   b. Establish Quorum
   c. Identification of Observers and Confidential Information
   d. Conflict of Interest
   e. Review of Appeals and Postponement Procedures

END CLOSED SESSION

09:45 a.m.
Break

10:00 a.m.
2. Open Meeting
   a. Welcome
   b. Introductions
   c. Approval of Agenda and Previous Meeting’s Minutes
   d. Review of Action Items
   e. Other Business

10:15 a.m.
3. Requests for Postponement/Appeals
   a. Overview of the requests
   b. Supporting Information

12:30 p.m.
LUNCH

1:00 p.m.
4. Requests for Postponement/Appeals
   a. Overview of the requests
   b. Supporting Information

1:30 p.m.
LUNCH

2:30 p.m.
Break

Empowering a healthy tomorrow
**Source Document:** Letter from FDA to Shawn Becker, Senior Director, Healthcare Quality Standards, USP (April 16, 2018).

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**The Compounding Expert Committee Discloses, for the First Time, a Key FDA Input**

At the August 8, 2019 meeting, Ms. Gigi Davidson, the Chair of USP’s CEC, disclosed for the **first time**, that in April 2018 it received a letter from the FDA that was described as a **critical input that USP relied upon in developing the revised <797> standards**.

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**Letter from FDA to Shawn Becker**

April 18, 2018

Ms. Shawn Becker  
Senior Director, Healthcare Quality Standards  
The United States Pharmacopeial Convention, Inc.  
12601 Twinbrook Parkway  
Rockville, MD 20852

Dear Ms. Becker:

FDA is setting to reiterate our concerns about the United States Pharmacopeial (USP)’s proposal to assign a draft <797> for the assignment of beyond-use-date (BUDs) to compounded sterile preparations (CSPs) based on the dating in the applicable USP monograph, if such a monograph exists. FDA is currently concerned about the proposal to assign BUDs based on a stability study. Stability studies are not sufficient to model the risk of microbiological contamination of a product each time it is produced, nor are they sufficient to predict the growth characteristics of any contaminating microorganisms. Assigning long BUDs that are not sufficiently supported by comprehensive, scientific microbiological data, and that are not reviewed by a regulatory agency with experience with such studies, could lead to significant microbial growth in a compounded sterile preparation (CSP) that has been contaminated. This could significantly exacerbate the harm caused by administration of a contaminated compounded drug.

**Assigning a BUD based on an applicable monograph**

For the following reasons, FDA recommends that the compounding USP monographs reference Table 8 in the draft <797> for assigning the BUD. The BUD for a CSP should exceed the shelf life specified in Table 8, and the BUD may be shorter if there are stability concerns that, as reflected in the monograph, necessitate a shorter date. This approach would recognize that a CSP with a monograph that demonstrates physical and chemical stability at a longer date is not any less prone to stability assurance concerns than a different substance that is not the subject of a monograph.

FDA recognizes that USP develops the dating in monographs based on robust stability studies that demonstrate the physical and chemical stability of the substance through the BUD. FDA also recognizes that the studies demonstrate that the container is appropriate such that it does not leak, rot or otherwise react with the drug product. However, stability studies do not sufficiently model the risk of microbiological contamination during production. For example, USP monographs do not specify manufacturing sterilization details, such as autoclave time and...
USP’s Reliance on the April 2018 FDA Letter Was Misguided

- For one, the FDA’s letter actually supports the arguments made in the Coalition’s Appeal that sterility testing does not ensure sterility of CSPs.

Sterility Testing

During a recent teleconference, USP suggested that performing a sterility test may mitigate FDA’s concern with CSPs being labeled with BUDs that exceed the default BUDs in table 8. However, merely passing a sterility test does not indicate that a CSP batch is, in fact, sterile; rather, adequate sterility assurance is a result of all activities that take place in a facility, including robust environmental and personnel monitoring. We note that the newest revision of the chapter has significantly decreased monitoring activities as compared to the initial draft chapter that appeared in the PF. Since not all these sterility assurance activities are accounted for in the monographs or in the newest revision of the chapter, BUDs unsupported by microbiological contamination risk data should be set conservatively, as reflected in table 8. The table 8 BUDs reflect a compromise that balance the quality risks associated with CSPs and the need for patient access to CSPs. Longer BUDs would require scientific support currently not required under the new revision to the chapter.

First, scientific consensus does not suggest any need to shorten BUDs for CSPs that are not sterility tested. Whether or not sterility testing has been performed does not determine the compounder’s ability to achieve or maintain sterility of a CSP. Indeed, relying upon “end-product sterility testing” over and above the “sterilization process” itself is “without scientific foundation and can lead to erroneous conclusions.” T.A. du Plessis, The Shelf Life of Sterile Medical Devices, 13 S. Afr. Orthopaedic J. 32, 33–34 (2014) (“It clearly follows that end-product sterility testing of a few medical devices following sterilization to ‘demonstrate’ or ‘prove’ that the entire batch is sterile, without a proper prior process validation, is without scientific foundation and can lead to erroneous conclusions with regard to the sterility of the batch as a whole. . . . Provided a properly validated sterilization process is used, and the integrity of the packaging is maintained, there is no reason to limit the shelf life of a sterile medical device—especially so in the case of radiation sterilization” (emphasis added)) (attached hereto as Exhibit A); see also Frances W. Bowmen, The Sterility Testing of Pharmaceuticals, 58 J. Pharmaceutical Sci. 1301 (1969) (attached hereto as Exhibit B).

Source Document: Letter from FDA to Shawn Becker, USP (April 16, 2018); Appeal Letter from the Coalition to Compounding Expert Committee (July 31, 2019).
USP’s Reliance on the April 2018 FDA Letter Was Misguided

Further, it is FDA’s understanding that a concern that prompted USP to initiate the process of revising chapter <797> was that the standards in the current chapter can be interpreted in a variety of ways and have, therefore, presented difficulties both for compounders that seek to comply with them and states that seek to enforce them. For the standards that USP is developing to have a meaningful public health impact, it is critical that they be specific enough for compounders and regulatory authorities to understand what is expected. A provision for stability studies, without any guidance on what that entails, would likely be difficult to interpret and enforce uniformly.

Further, as USP is aware, FDA does not conduct inspections of the vast majority of compounding pharmacies in the United States. States have primary day-to-day oversight over such pharmacies and may not have the expertise to review stability studies, which are not typically required by states’ laws. As noted above, long BUDs based on flawed stability studies could have significant public health implications.

- FDA’s enlistment of <797> is misplaced.
- The problem is not that <797> is not up to the task.
- The problem is that a limited number of facilities were not complying with <797>, and the States do not, according to FDA, “have the expertise” needed to ensure compliance.
- The stated concerns do not hold for a facility like Wedgewood, which has not shown any contamination in any of the thousands of batches it has tested since 2014.
USP’s Reliance on the April 2018 FDA Letter Was Misguided

Conclusion

As USP is aware, once a drug intended to be sterile is contaminated and the longer it is held before administration, the greater the potential for microbial proliferation. FDA has investigated numerous outbreaks associated with patients who received contaminated compounded drug products labeled with a long BUD.

FDA’s concerns associated with the proposals to assign BUDs based on the dating in the monograph or a stability study are rooted in our experience responding to outbreaks associated with compounded drugs. Pharmacies, federal facilities, and physicians that compound sterile drug products look to USP standards to understand the practices and conditions that must be met to produce a sterile and otherwise high quality product. Many states similarly look to USP standards for inspections and enforcement. The revisions pertaining to BUDs would send a concerning signal to these entities that assigning a BUD based on monograph dating that is divorced from sterility assurance, or based on any stability study that they conduct no matter its content or rigor, is acceptable. This would constitute a significant loosening of the standards that USP initially proposed to raise the bar for sterile compounding broadly and decrease the potential for serious patient harm associated with contaminated compounded drug products.

- FDA’s focus on “numerous outbreaks” involving patients who received contaminated CSPs “labeled with a long BUD” is unsupported.
- FDA does not identify (i) what outbreaks it is referring to; (ii) what facilities were at issue; (iii) whether these facilities were complying with <797>; or (iv) what products were at issue.
- USP needs specific information to evaluate FDA’s reliance on these “numerous outbreaks.”
USP’s Reliance on the April 2018 FDA Letter Was Misguided

However, even if USP did provide detailed standards for conducting stability studies, concerns would remain. For example, FDA is concerned about the quality of the stability studies that compouders are not subject to current good manufacturing practice requirements may conduct. To conduct a meaningful study that demonstrates that a drug product is sterile and stable through its BUD, an entity must conduct a number of tests that, in FDA’s experience, state-licensed pharmacies, federal facilities, and physicians do not typically perform and are beyond their capabilities. When FDA has reviewed or become aware of stability studies conducted by compounding pharmacies, they have been deficient. For example, during a recent inspection, FDA noted that although a compounding pharmacy assigned a BUD to a drug product based on a stability study, FDA laboratory analysis of the drug product, which was within its BUD, revealed that it was 1% of its labeled potency.

July 31, 2019
Compounding Expert Committee
United States Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852-1790

Re: Appeal of Revisions of Beyond-Use Date Standards in General Chapters <795> and <797>

Dear Compounding Expert Committee:

I write respectfully to appeal on behalf of a coalition of compounding pharmacies and professional associations (“Coalition”) pursuant to Article VII, Section 7 of the Bylaws of the United States Pharmacopeia Convention (“USPC”). Specifically, the undersigned Coalition is to work with stakeholders to ensure patient access and safety. At the same time, the Coalition stands ready, willing, and able to assist the Expert Committee in arriving at appropriate BUD dates along with other protocols that both protect the interests of the public and ensure patient access to needed medications.

Source Document: Letter from FDA to Shawn Becker, USP (April 16, 2018); Appeal Letter from the Coalition to Compounding Expert Committee (July 31, 2019).
Problem with USP’s Reliance on the April 2018 FDA Letter

- All interested and relevant parties must be involved in the standard-setting process.
- USP cannot rely upon FDA’s private, unilateral submissions (sent outside official notice and comment channels) without informing the public of those submissions or making them available to the public for comment.
- The withholding of the FDA letter renders the notice and comment period deficient and unreliable as it prevents USP from obtaining a balanced set of inputs.
Problems with USP’s Development of the Revised Chapters: *USP Overlooked Scientific Evidence and Practical Realities*
By revising Chapter <797> so as to incorporate substantially shortened BUDs with no allowance to extend BUDs, **USP ignored overwhelming scientific evidence and consensus to the contrary.**
• USP decided inexplicably that compounders are unlikely to achieve or maintain sterility when preparing CSPs in accordance with Chapter <797> unless they also perform unnecessary and expensive sterility testing.

Source Document: USP General Chapter <797> (June 2019), Sec. 12.2.
USP’s Revisions Depart from and Ignore Scientific Consensus

It clearly follows that end-product sterility testing of a few medical devices following sterilisation to ‘demonstrate’ or ‘prove’ that the entire batch is sterile, without a proper prior process validation, is without scientific foundation and can lead to erroneous conclusions with regard to the sterility of the batch as a whole.

Provided a properly validated sterilisation process is used, and the integrity of the packaging is maintained, there is no reason to limit the shelf life of a sterile medical device – especially so in the case of radiation sterilisation.

• Whether or not sterility testing has been performed does not determine the compounder’s ability to achieve or maintain sterility of a CSP.
USP’s Revisions Depart from and Ignore Scientific Consensus

• Even FDA guidance casts doubt on the need for sterility testing to ensure sterility: “sterility tests are not recommended as a component of a stability program for confirming the continued sterility throughout a product’s shelf life or dating period.”
Instead, what matters most is **whether a compounder strictly adheres to best practices for establishing and maintaining a sterile environment**, as other provisions of the USP standards recognize.
USP’s Revisions Depart from and Ignore Scientific Consensus

- **USP casually dismisses** the Coalition’s arguments as to:
  - the **lack of scientific consensus for shortening the BUD** for CSPs that have not undergone sterility testing;
  - the **illogical differences** between the maximum BUDs for room temperature, refrigerated, and frozen BUDs;
  - the **internal inconsistency** between the revised BUD standards in Chapters <795> and <797> and sterility assurance protocols in other USP General Chapters;
  - why sterility testing is preferable to policing the actual sterilization processes and methods used to prepare the CSPs.

Source Document: Letter from Mario Sindaco to Derek Shaffer (Aug. 16, 2019).
USP’s Revisions Depart from and Ignore Scientific Consensus

- Practiced compounding pharmaceuticals in the community and hospital settings.

- As a professor, taught courses in compounding pharmacy as well as formulations, physical chemistry, pharmaceutical analysis, and dispensing.

- Published extensively on compounding topics, including authoring *The Art, Science, and Technology of Pharmaceutical Compounding* (5 editions) and *Allen’s Compounded Formulations: A Complete U.S. Pharmacist Collection*.


- Extensive experience on USP’s compounding pharmaceutical committees. See, *e.g.*, Pharmacy Compounding Practice Advisory Panel (1990-2000); USP Expert Committee on Nonsterile Compounding (2000-2013).
USP’s Revisions Depart from and Ignore Scientific Consensus

Dr. Loyd Allen

- “My view of the revised Chapters <795> and <797> is that they are generally not scientifically supported by any evidence, but rather by ‘opinions’ and what some individuals think ‘should be done.’ It seems that in many cases the new requirements for compounding activities are similar or the same as the requirements for manufacturing facilities. Thus, there is only a threshold level of compliance and not a graduated hierarchy to allow lower-risk facilities some leeway to serve their patients safely and effectively. The risk factors are different, but are not addressed in the standards. There is, evidently, no scientific data showing that the previous Chapters <795> and <797> were problematic and required revisions—only opinions.” Letter from L. Allen to USP Appeals Panel (Jan. 21, 2020), at 4.

- “[T]he issue of greatest concern regarding the revised compounding chapters is their failure to account for the differences in small- versus large-scale compounding. In the past, these chapters have been fairly reasonable and achievable with the goal of enhancing the quality of compounded preparations... However, the standards recently published by USP are far more onerous, cost-prohibitive, and appear to be patterned after industry standards where tens of thousands of dosage units are made.” Id.

- “In particular, a serious problem is that there are no graduated levels for nonsterile or sterile compounding based upon the number of preparations compounded daily. In other words, there is no relationship between the USP standards and the level of compounding activity a pharmacy does. For example, if a compounding pharmacy does one (1) compounded prescription per day— whether sterile or nonsterile or hazardous, etc.—it is required to be completely compliant with the Chapters the same as if they do five hundred compounded prescriptions a day, whether sterile or nonsterile or hazardous, etc. This does not seem rational, as the risk levels are considerably different for the pharmacies and personnel involved.” Id. at 5.

USP’s Revisions Overlook Practical Realities

• USP’s revisions to Chapters <795> and <797> will have a number of harmful consequences that will severely impact patients and compounders alike, including:

  1. Making essential compounds more difficult to obtain or altogether unavailable, thereby disrupting the continuity of care for various patient groups, including pregnant women, patients undergoing fertility treatments, cancer patients, elderly patients, and pets, and the list goes on…;

  2. Raising unit costs to a degree that imposes extreme financial hardship on patients, particularly those who are socio-economically disadvantaged;

  3. Forcing compounders to make smaller batches that introduce greater risk of error and reduce overall safety; and

  4. Disrupting the entire compounding industry and throwing it into upheaval.

• In denying the Coalition’s appeal, USP did not even purport to address these arguments raised by the Coalition (and others).
Roadmap of the Coalition’s Appeal

1. Threshold Legal Concerns
2. Problems with USP’s Development of the Revised Chapters
3. Problems with the Adequacy of this Appeal Hearing
4. Remand to New, Fairly Informed CEC
USP Has Not Issued Formal “Rules and Procedures” for this Appeal

Section 7. Appeals.
The Council of Experts shall adopt rules and procedures for appealing any standard adopted by the Council. The appeals process shall be consistent with the following provisions:

- A request for an appeal shall be made in writing within sixty (60) days after the date of publication of the standard as official text.

- The panel shall be chaired by the President.

- The panel shall be convened within ninety (90) days after the request for further review is received, and the appellant shall be given the right to appear at a hearing of the panel. The decision of the panel shall be final.

- The date by which conformance with the standard is required shall be postponed while the appeal is pending. If the standard is upheld, the date by which conformance is required shall be reestablished so that the period allowed for implementation is not less than that provided for upon original publication of the standard.
Specifically, the Panel intends to consider the sufficiency of the process used by the responsible Expert Committee to develop and approve the standards under appeal. They will consider issues such as whether

- Despite purporting to address the “sufficiency of the process,” USP has refused to provide the Coalition and this Panel with critical information relevant thereto, including:
  - Information concerning known and undisclosed conflicts of interest;
  - Key witness testimony; and
  - Communications with FDA.

- USP has made it impossible for this Panel to fulfill its mandate.

Source Document: Email from Mario Sindaco to Scott Lerner (Oct. 30, 2019).
The Panel Was Not Permitted to Review Information Related to Conflicts of Interest

In accordance with USP’s rules and policies regarding conflicts of interest, all members of the CMP EC were invited to discuss the appeal. However, members with conflicts of interest related to the General Chapters under appeal recused themselves prior to final discussion and voting.


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1 We recognize that your submission included points related to USP’s standards setting authority and process. The appeal provisions set forth in USP’s policies contemplate standards to be adopted by the Council of Experts. This response is limited in scope to addressing your scientific and substantive challenges to the standards themselves.
The Panel Was Not Permitted to Hear Testimony from USP or FDA

First, your letter does not shine light on the relevant procedures for the appeals hearing. As you know, the Coalition previously requested that it be provided a full and fair hearing so as to enable a meaningful presentation and consideration of the merits of its appeal. See Ltr. from D. Shaffer to M. Sindaco, dated Sept. 13, 2019. The appeals process you have described in your recent correspondence, however, affords the Coalition no such rights or protections. To the contrary, the process outlined in your letter appears designed to limit the Coalition’s ability to make such a meaningful presentation. For example, USP is limiting the Coalition’s participation at the hearing to a mere 1-hour presentation. Such a strict, tight limitation does not afford the opportunity for the Coalition to present and examine witnesses, as we had hoped to do. Unless we can present live testimonial evidence to the Appeals Panel, the Coalition will be severely inhibited in its ability to make a complete record of the procedural and substantive defects in USP’s new standards. As such, the Coalition respectfully requests that USP reconsider the current procedures for the upcoming hearing and that it promptly clarify that the Coalition is, in fact, permitted to call live witnesses, including expert witnesses and certain adverse witnesses from or associated with USP. The Coalition is, of course, willing to work with USP (as well as other appellants) to develop a more clear and concrete set of procedures that will allow for an efficient yet fair presentation of all relevant evidence.
The Panel Was Not Permitted to Hear Testimony from USP or FDA

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**Source Document:** Letter from Mario Sindaco to Derek Shaffer (Nov. 20, 2019).

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**Scope of the Hearing.** The hearing is intended to be your opportunity to present. The Panel will reserve time at the end to ask clarifying questions. USP does not intend to make any members of staff or volunteer bodies (e.g., Expert Committee members) available to serve as witnesses for the hearing. The Coalition is free to present any evidence that it feels is relevant to further review of the Expert Committee’s decision on the appeal, which may include scientific evidence, data, and expert witness testimony. Further, the Coalition is free to present on information made available after its submission of the original appeal. In short, it is our hope that the Coalition will utilize the 2 hours of hearing presentation time to share any scientific and other information that it feels warrants further review by the Appeals Panel.
The Panel Does Not Have Key Documents Relevant to the Appeal

Document Disclosure

USP provides disclosure of information and records regarding USP standards-setting activities consistent with:

- The rights of individuals to privacy
- USP’s need to protect the confidentiality of trade secrets and other proprietary commercial or financial information
- USP’s need to promote frank internal deliberations and to pursue standards-setting activities without disruption

Pursuant to this policy, general information pertaining to standards-setting and other activities, including information regarding the work and deliberations of USP’s Council of Experts and Expert Committees, is posted and maintained on the USP website.

In addition, communications between USP and third parties relating to standards-setting activities will be made available upon specific written request, including copies of written correspondence to and from third parties and memoranda of telephone conversations and meetings with third parties. Such third-party communications do not include communications of personal nature between USP staff and members of the Board of Trustees.

All requests for documents shall be made to the USP Executive Secretariat, which shall be responsible for decisions about disclosure of information. A request may be refused solely on the basis that it is unduly burdensome or if USP determines that diversion of personnel from higher-priority duties would be unreasonable.

The Panel Does Not Have Key Documents Relevant to the Appeal

5. All Communications from January 1, 2015 through the date of this request between the USP and the FDA concerning the USP’s 2019 revisions to USP Reference Standards, General Chapters <797> and <795>.

Source Document: Letter from Derek Shaffer to USP (Aug. 1, 2019).
The Panel Does Not Have Key Documents Relevant to the Appeal

Source Document: Letter from Derek Shaffer to USP (Aug. 1, 2019).

3. All scientific materials or authorities consulted by the USP in connection with the revisions to General Chapters <795> and <797>, particularly with respect to changes in BUD assignment rules.
The Panel Does Not Include Compounding Pharmacy Experts

November 7, 2019
Mario P. Sindaco, M.S., MBA
Vice President, Science-Operations
Executive Secretary to the Council of Experts
United States Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852-7001

Re: Appeal of New Standard for USP General Chap

Dear Mr. Sindaco:

I write on behalf of International Academy of Compounding, and Wedgewood Village Pharmacy, with reference to your October 30, 2019 correspondence reporting additions to the Coalition’s appeal of the United States Pharmacopeia General Chapter <755>—Pharmaceutical Compounding—Nonsterile—section 755.5—Pharmaceutical Compounding—Nonsterile detail below, your letter raises new, additional concerns. As such, the Coalition is requesting to address the concerns raised herein before scheduling any additional hearing.

First, your letter does not provide any meaningful information about the composition of the Appeals Panel. Article VII, Section 7(c) of the USP Bylaws states that all appeals will be heard “by a panel of three members of the Council of Experts appointed by the Chair, three members of the Board of Trustees appointed by the Chair of the Board, and up to three additional experts appointed by the President in consultation with the Chair of the Council of Expert.” Please identify all members of the Appeals Panel, including by specifically identifying (i) the three members of the Council of Experts who were appointed to the Appeals Panel by the Chair; (ii) the three members of the Board of Trustees who were appointed to the Appeals Panel by the Chair of the Board; and (iii) any additional experts who were appointed to the Appeals Panel by the USP President. For each Panel member selected by USP, please explain how and why each member was selected. To state the obvious, composition of the Appeals Panel directly affects resolution by the Appeals Panel. The Coalition wants to know whom it’s appealing to and how the relevant individuals were appointed before arguing its case.

Third, your letter also fails to provide any meaningful information about the composition of the Appeals Panel. Article VII, Section 7(c) of the USP Bylaws states that all appeals will be heard “by a panel of three members of the Council of Experts appointed by the Chair, three members of the Board of Trustees appointed by the Chair of the Board, and up to three additional experts appointed by the President in consultation with the Chair of the Council of Expert.” Please identify all members of the Appeals Panel, including by specifically identifying (i) the three members of the Council of Experts who were appointed to the Appeals Panel by the Chair; (ii) the three members of the Board of Trustees who were appointed to the Appeals Panel by the Chair of the Board; and (iii) any additional experts who were appointed to the Appeals Panel by the USP President. For each Panel member selected by USP, please explain how and why each member was selected. To state the obvious, composition of the Appeals Panel directly affects resolution by the Appeals Panel. The Coalition wants to know whom it’s appealing to and how the relevant individuals were appointed before arguing its case.

Source Document: Letter from Derek Shaffer to Mario Sindaco (Nov. 7, 2019).
Composition of the Appeals Panel. Consistent with the USP Bylaws, the Appeals Panel is constituted specifically for the appeals concerning the proposed revisions to the compounding chapters. None of the members of the Appeals Panel served on the Expert Committee that developed and approved the standards under appeal. The Appeals Panel was selected to include relevant scientific and USP process expertise. It will be well-positioned to evaluate information and arguments presented by the Coalition and to assess the presentation in light of the development and approval of the provisions being challenged.
Section 7. Appeals.
The Council of Experts shall adopt rules and procedures for appealing any standard adopted by the Council. The appeals process shall be consistent with the following provisions:

a. A request for an appeal shall be made in writing within sixty (60) days after the date of publication of the standard as official text.

b. The Council or Expert Committee establishing the standard shall work with a sense of urgency and have up to ninety (90) days to reconsider the standard and issue a decision.

c. The appellant shall have thirty (30) days following receipt of the decision to request in writing further review by a panel consisting of three members of the Council of Experts appointed by the Chair, three members of the Board of Trustees appointed by the Chair of the Board, and up to three additional experts appointed by the President in consultation with the Chair of the Council of Experts. The panel shall be chaired by the President.
In Addition to No Subject Matter Experts, the Panel Is Not Fully Assembled

- Seven members on the Appeals Panel;
- Two not present today;
- One Panel Member, Tim Franson, is not participating in today’s hearing; and
- Another Panel Member, Mary Foster, is participating remotely.
1. Threshold Legal Concerns

2. Problems with USP’s Development of the Revised Chapters

3. Problems with the Adequacy of this Appeal Hearing

4. Remand to New, Fairly Informed CEC
Where Do We Go from Here?

• Cannot defer to “expertise” of prior CEC on the current record;
• Remand to newly constituted CEC that is fairly informed; and
• Start anew with full transparency and public participation.