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Alliance for Pharmacy Compounding

December 13, 2021

Name
Organization
Address
City, ST ZIP

Dear [firstname]:

I write to make you aware of proposed changes to USP <795> and <797> that could affect patient access to compounded preparations in your state and how your agency regulates pharmacy compounding.

The Alliance for Pharmacy Compounding (formerly IACP) is the voice for pharmacy compounding, representing compounding pharmacists and technicians in 503A state-licensed pharmacies, 503B outsourcing facilities, and in both 503A and 503B hospital and health system pharmacies. Compounding pharmacists work directly with prescribers to create customized medication solutions for patients and animals whose health care needs cannot be met by manufactured medications.

As you may know, due to a 2019 appeal of beyond-use date restrictions in the previously proposed USP Chapters <795> and <797>, USP's Compounding Expert Committee has spent much of this year developing revised recommendations. This past Autumn, USP released its proposed changes to the beyond-use dating protocols in the chapters. While we see substantive improvements in the new proposals, some of USP's recommendations are still quite problematic, and to our thinking USP continues to fail to demonstrate both the science and the necessity behind its proposed BUDs.

Because many states adopt USP's compounding in whole or in part into their state regulatory framework, it's important that USP hear feedback from state boards of pharmacy about the proposed recommendations before the comment period ends January 31, 2022. Without your input, it's possible your state will find itself saddled with certain regulations that limit patient access to compounded preparations while creating considerable waste and cost containment issues for the pharmacies that compound those preparations.

I have included here comments APC offered to USP's Compounding Expert Committee when we were invited to address the committee in October. Those comments may be helpful to you and your board members as you investigate this issue.

At a minimum, please take a look at the proposed changes to USP Chapters <795> and <797>, which can be found on USP's website, and provide written input to USP before the January 31 comment deadline.

If I can be helpful to you or your board members, please contact me directly at scott@a4pc.org.

Sincerely,

Scott Brunner, CAE
Chief Executive Officer

COMMENTS: ALLIANCE FOR PHARMACY COMPOUNDING to USP CEC | October 5, 2021

BLAIRE: My name is Michael Blaire, and I am a compounding pharmacist and the current president of the Alliance for Pharmacy Compounding. On behalf of the Alliance for Pharmacy Compounding – and the compounding professionals and patients we represent – thank you for the opportunities USP and the Compounding Expert Committee have given us to provide input and to be a part of this process on setting standards for extending – or not extending – beyond-use dates for non-sterile and sterile compounded preparations. We have felt engaged and heard in this process, and we're grateful to you for that.

In the comments that follow, we will be candid in stating both what we think this committee gets right, as well as our concerns about where we believe the current proposal goes astray. Please do not take our disagreement as disrespect. *We fully value your work and we support the need for USP compounding standards that are necessary and rooted in science*. We also recognize the difficulty in getting to agreement on not only what the science dictates, but what a wide and diverse group of stakeholders wants and expects from those standards.

Before I turn the presentation over to my colleagues, I want to introduce a bit of reality for your consideration. For the past 20 months, we have seen healthcare providers like physicians and pharmacists working with regulatory agencies like FDA and State Boards of Pharmacy in order to save lives and combat COVID-19. We have seen the suspension of a number of regulations in order to enable life-saving medications to find their way to the patients that need them. Under emergency guidance from FDA, and in collaboration with State Boards of Pharmacy, over 90 hospitals across the US availed themselves of compounded sterile preparations from 503A compounding pharmacies, with no adverse events reported. These compounding pharmacies were operating under the USP guidelines currently in place. I ask the Compounding Expert Committee to seriously question what changes to the current guidelines are really necessary, and remind them that added stringency does not necessarily promote better quality.

Congress has unequivocally carved out a place for traditional prescription-based 503A compounding in federal law. In doing so, Congress recognized the extraordinary need for compounded preparations when, in the judgment of a prescriber, those customized medications are needed to treat patients. Congress recognized that, despite the fact that those preparations are not themselves FDA-approved, they could be compounded in compliance with standards that ensure patient safety. Notably, it did not require that 503A compounders adhere to Current Good Manufacturing Practices. Nor did it assert that drugs not compounded under CGMP were any less appropriate for patients than manufactured drugs.

I share this not to lecture the committee, but to remind us all that at the heart of what we're talking about here are real patients with real medical needs – needs that manufactured drugs often do not meet. What the USP standards require or don't require can have considerable implications for those patients' access to their medications.

Tenille Davis of Scottdale, Arizona, chairs APC's BUD Task Force, and will speak next. She'll be followed by APC Vice President Anthony Grzib from Swedesboro, NJ.

DAVIS: Thank you to the members of the USP CEC and to the people who worked so hard in the subcommittees to come up with changes to the Chapters that were published in early September. It is encouraging that USP granted our appeals and appears to have taken some of the compounding communities' recommendations to heart in the revisions to 795 and 797. The biggest issue that our members had was that there wasn't a pathway to extend BUDs beyond the defaults in the 2019 version of USP <797>. APC's BUD committee had recommended the creation of a Category 3 for CSPs.

Your latest published draft included this recommendation, along with increased environmental and personnel monitoring as we suggested. Compounding pharmacies that want to extend BUDs will have to adhere to more stringent standards and conduct stability studies in order to provide these needed compounded medications to patients. Our main issue with the new revisions has to do with the batch size limitation and the BUDs themselves. If the argument for a maximum batch size of 250 units is because of the number of units required to be tested does not exceed 10, why could we not increase the number of units required to be tested, for example 4% of the total batch, whatever size it is? The batch size limitation should be based on the maximum number of units a facility can produce in one day, and this limit can be validated with media fills.

As far as BUDs, essentially, the CEC just "doubled" the default BUD of category 2 items. It indicates that it would be a rare occurrence for a patient to need more than a 180 day supply of a medication, but we argue that many patients may need a **90 day supply** at a time. Many of the aseptically processed compounds dispensed by pharmacies are not appropriate for frozen storage or terminal sterilization and wouldn't be able to be given a 90 day or even a 180 day BUD. It sounds hopeful to say that BUDs for Category 3 items are able to be extended to 180 days, but there are simply not many items that will be eligible for this dating. With stability studies costing upwards of $15K each, <u>USP will be disincentivizing pharmacies from performing these studies as the cost will be impossible to justify for the BUDs allowed.</u> I'd like to mention that some USP Monographs, which supersede the chapters, have sterile BUDs up to 180 days without any additional testing, environmental monitoring or media fills for items that do not require frozen storage or terminal sterilization.

As compounding pharmacists, we have **patients** at the forefront, and we strive to follow guidelines set for us to compound the safest medications possible. We must not forget that patient access is an important consideration. Patients rely on our compounded drug products – and decreasing access and increasing costs will surely harm our ability to provide patient care.

We appreciate the CEC's commitment to stakeholder engagement and will comment on the proposed changes by the January 31st deadline. I'd like to turn the time over to Anthony Grzib.

GRZIB: Thanks Tenille. I'd like to take a moment to provide the Committee with some insight about the current state of the compounding industry and some unintended consequences of these limitations on batch size and BUD assignment, particular for sterile compounds.

The restrictions on BUDs and batch sizes proposed in 797 aren't going to drive the majority of existing sterile compounders to downsize their business, or decrease the number of sterile preparations they make, or convert to 503Bs. The sterile compounders that exist today have already evaluated these possibilities over the past few years and determined that they're not options.

What these proposed restrictions WILL do is force compounders to implement whatever practice changes are necessary for them to continue to serve their patients, without cutting corners or skipping processes, WHILE meeting the proposed USP standards. Which sounds great! Until you get into some of the actual practices that will be implemented. A few examples:

- Shorter BUDs and batch size limits aren't going to reduce the total number of sterile compounds produced – it'll just mean compounders will make smaller batches of the same sterile preparations more frequently. This means to meet patient demand compounders will double, triple, or quadruple the number of times they perform critical tasks such as selecting and weighing ingredients, performing hand hygiene, and donning garb and sterile gloves. I'm sure everyone here knows that the risk of contamination and errors actually increases when you take a single batch and divide it into smaller, more frequent batches.
- Compounders are also likely to begin storing room temperature sterile preparations in the refrigerator or freezer to extend BUDs. Again, I don't think you need me to explain the potential quality issues this could create – stability issues with precipitation, crystallization, or phase separation of emulsions or ophthalmic ointments; container-closer integrity issues with materials shrinking or cracking.

And you should know that these aren't just theoretical examples of what might happen – because these BUD and batch size restrictions present REAL threats to patient access, there are compounders right now today having conversations NOT about IF they should make these practice changes, but WHEN they should begin implementing them. And these practice changes won't just increase the risk to patient safety, they'll also cost more, and those costs will be passed on to patients.

I doubt anyone on this committee intended to INCREASE both the safety risks and costs to patients using compounds, but that's the result the restrictions on BUDs and batch sizes will produce.

The good news is there is a way to avoid these unintended patient safety risks. The compounding industry is full of pharmacies that for decades have been able to produce compounds that are safe AND accessible. And those compounders have achieved this because of one important thing - they refuse to accept that these two things are mutually exclusive. For them, finding a "balance" between product safety and patient access is not an option – both must be achieved. It's clear the committee has begun

shifted its thinking in this direction, but our concern is that as long as the committee retains any “either or” thinking – the idea that compounds are somehow either safe OR readily accessible – it will continue to put forth standards that are ultimately just agreed-upon compromises that pose unintended risks to patients, such as those I’ve described here.

We offer this perspective respectfully. At the end of the day, we see this committee, each of you, as our partners in ensuring patient safety. We appreciate the time today and as always look forward to the opportunity to continue supporting your efforts to achieve both patient safety and patient access to compounded medication.

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