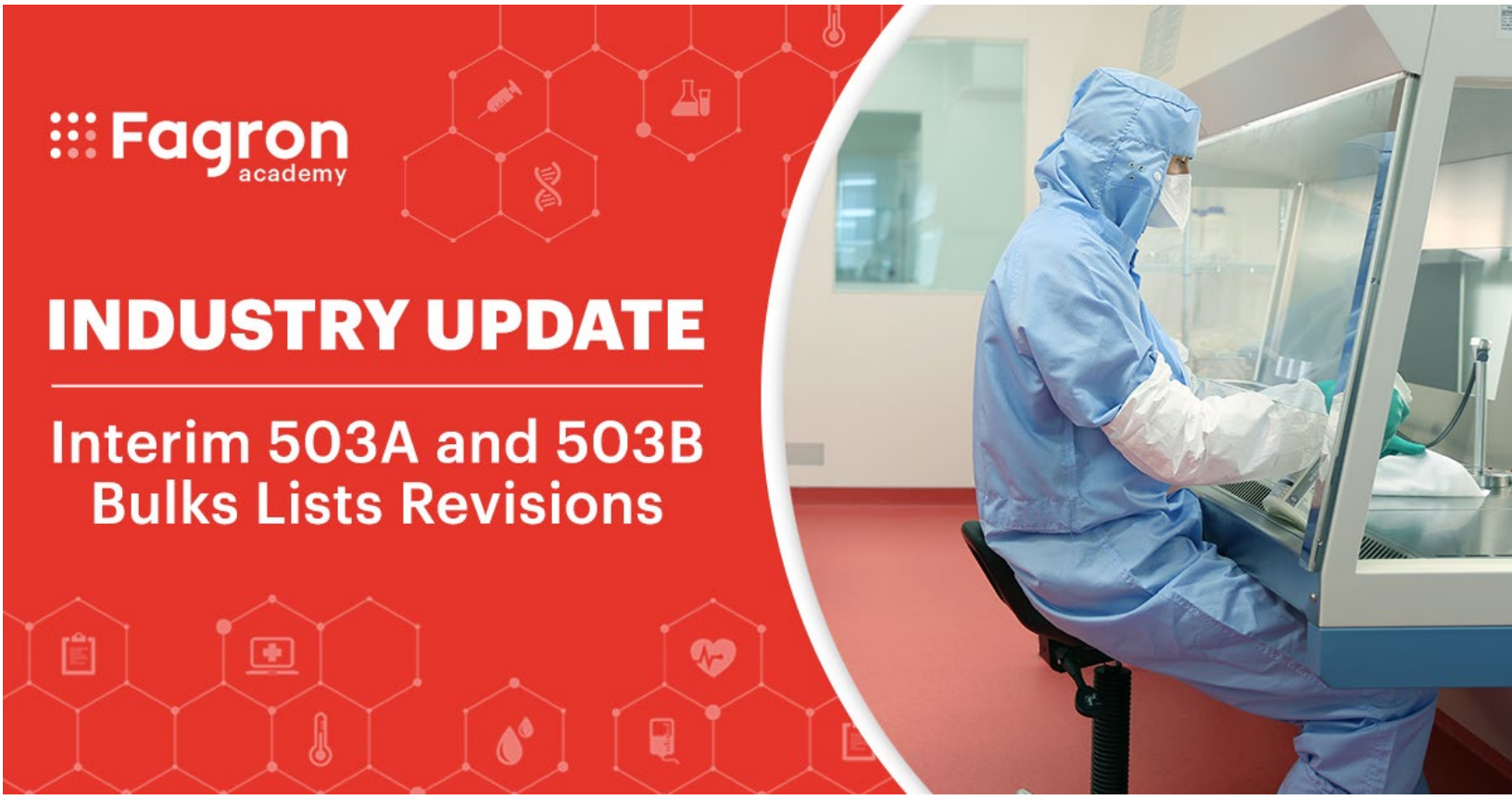

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To remain compliant, compounding pharmacies must keep abreast of constantly changing and updating regulation from a variety of different regulatory agencies. Recently, the FDA released updated 503A and 503B interim bulks lists. The complete documents released can be viewed here:

- Safety Risks Associated with Certain Bulk Drug Substances Nominated for Use in Compounding | FDA
- Interim 503B Bulks List: download (fda.gov)
- Interim 503A Bulks List: 503A Categories Update for September 2023 (fda.gov)

What Are the 503A and 503B Bulks Lists?[1,2,3]

As pharmacies or outsourcing facilities operating under 503Aor 503B of the Federal Food, Drug, and Cosmetic (FD&C) Act, we are restricted to working with only certain materials as bulk active pharmaceutical ingredients. 503A compounding pharmacies may work with materials which, in addition to being accompanied by a valid certificate of analysis (CoA) and manufactured in an FDA registered facility, must meet one of the below three requirements:

1. Complies with an applicable USP or NF monograph if one exists*
2. Is a component of an FDA-approved drug product if an applicable USP or NF monograph does not exist; or
3. Appears on the 503A bulks list or *503A Category 1 – Bulk Drug Substances Under Evaluation* list (i.e., the “interim 503A bulks list”) provided by the FDA if requirements one or two are not met

**note that the FDA's position is that specifically refers to USP/NF drug monographs, not dietary supplement monographs*

503B outsourcing facilities are even further restricted in their allowed bulk materials and may not compound a drug product unless the relevant bulk drug product, in addition to being accompanied by a valid CoA and manufactured in an FDA registered facility, meets one of the below requirements:

1. Appears on the list identifying bulk drug substances for which there is a clinical need (503B bulks list *or 503B Category1: Bulk Drug Substances Under Evaluation* (i.e., the "interim 503B bulks list"); *or*
2. Appears on the FDA's Drug Shortage List at the time of compounding, distribution, and dispensing

The interim lists for both 503A and 503B facilities are divided into three categories. The full description of each category should be read on the FDA's website, but in short, materials listed in Category 1 may be used as bulk drug substances provided that all other relevant legal and regulatory conditions are met. The FDA states that the agency "does not intend to take action against a compounder for compounding drugs using bulk drug substances listed in Category 1". Substances in Category 2 (deemed to have safety risks) and Category 3 (deemed to have insufficient evidence for FDA evaluation) may not be compounded. The FDA states that the agency "would consider taking action against a compounder for compounding drug products with this bulk drug substance".

Relevant Updates to the Interim Bulk Drug Substances List for 503A Pharmacies[2,4,5,6]

For a full list of updates, please download the complete *Bulk Drug Substances Nominated for Use in Compounding Under Section 503A of the Federal Food, Drug, and Cosmetic Act* document linked above. Some updates of particular interest include further guidance on peptides. Many compounders have expressed interest in working with peptides such as AOD 9604, BPC-157,Ipamorelin Acetate, and Kisspeptin-10 among others. These materials have historically not been acceptable for compounding because they do not meet any of the requirements for 503A compounding. Now rather than being prohibited by omission, these ingredients are specifically referenced in the interim 503Abulks list as Category 2 substances. Category 2 substances are deemed by the FDA to have significant safety risks and compounding of those substances by503A pharmacies could result in FDA or state action.

Vasoactive Intestinal Peptide remains on Category 1. Another peptide, GHK-Cu, is being studied for potential cosmetic benefits such as for photoaging and hair loss and was added to the Category 1 list (but not for injectable routes of administration). L-theanine, an amino acid found in green tea that is being evaluated for potential benefit for some stress related symptoms as well as for cognitive function, was also added to the Category 1list.

Relevant Updates to the Interim Bulk Drug Substances List for 503BOutsourcing Facilities[3,7-13]

For a full list of updates, please download the complete *Bulk Drug Substances Nominated for Use in Compounding Under Section 503B of the Federal Food, Drug, and Cosmetic Act* document linked above. Some changes were made with regards to compounding with bulk peptides to this interim bulks list update as well. Gonadorelin Acetate, a peptide previously FDA approved as LutrePulse for the induction of ovulation in women with primary hypothalamic amenorrhea and sometimes used off label for conditions such as hypogonadism, has been added to the Category 1 list. On the other hand, Ipamorelin Acetate has been added to Category 2, consistent with its classification on the 503Abulks list. Oddly, GHRP-2, a growth hormone secretagogue peptide which remains Category 3 on the interim 503A bulks list, was moved to Category 1 on the interim503B bulks list specifically for non-injectable and non-nasal routes of administration. Other additions to Category 1 include ruxolitinib phosphate, a JAK1and JAK2 inhibitor currently commercially available orally and topically for conditions such as myelofibrosis or atopic dermatitis respectively and dimercaprol,a chelating drug currently commercially-available as an injectable.

For a full list of bulk drugs added, removed, and moved within the 503Aand 503B interim bulks lists, please view the documents in their entirety at the links above. For further questions on these bulk lists as they pertain to503A pharmacies and 503B outsourcing facilities, please reach out to the FACTS team!

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For further information or questions, please feel free to reach out to us by heading to www.fagronacademy.us!