
Facility Definition Under Section 503B of the Federal Food, Drug, and Cosmetic Act Guidance for Industry

**U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)**

**May 2018
Compounding and Related Documents**

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Facility Definition Under Section 503B of the Federal Food, Drug, and Cosmetic Act Guidance for Industry¹

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA office responsible for this guidance as listed on the title page.

I. INTRODUCTION

This guidance is intended for entities that are registered or are considering registering with FDA as an outsourcing facility under section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 353b).² Section 503B defines an outsourcing facility, in part, as “a facility at one geographic location or address.” FDA has received questions from outsourcing facilities and other stakeholders about the meaning of this term, such as whether multiple suites used for compounding human drugs at a single street address constitute one or multiple facilities, or whether a single location where human drugs are compounded can be subdivided into separate operations compounding under different standards. FDA is issuing this guidance to provide the agency’s current thinking on these issues, and related issues regarding how to ensure that the compounding of drugs in an outsourcing facility occurs only in accordance with section 503B.

In general, FDA’s guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency’s current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

Section 503A, added to the FD&C Act by the Food and Drug Administration Modernization Act of 1997, describes the conditions that must be satisfied for human drug products compounded by a licensed pharmacist in a State-licensed pharmacy or Federal facility, or by a licensed physician, to qualify for exemptions from three sections of the FD&C Act:

¹ This guidance has been prepared by the Center for Drug Evaluation and Research in cooperation with the Office of Regulatory Affairs at the Food and Drug Administration.

² A new section 503B was added to the FD&C Act by the Drug Quality and Security Act (DQSA). See Pub. L. No.113-54, § 102(a), 127 Stat. 587, 587-588 (2013).

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- section 501(a)(2)(B) (concerning current good manufacturing practice (CGMP) requirements);
- section 502(f)(1) (concerning the requirement to label drugs with adequate directions for use); and
- section 505 (concerning drug approval requirements).

One of the conditions that must be met for a compounded drug product to qualify for the exemptions under section 503A of the FD&C Act is that it must be “compounded for an identified individual patient based on the receipt of a valid prescription”³

Section 503B, added to the FD&C Act by the DQSA in 2013, created a new category of compounders called *outsourcing facilities*. Section 503B describes the conditions that must be satisfied for human drug products compounded by or under the direct supervision of a licensed pharmacist in an outsourcing facility to qualify for exemptions from three sections of the FD&C Act:

- section 502(f)(1) (concerning the requirement to label drugs with adequate directions for use);
- section 505 (concerning drug approval requirements); and
- section 582 (concerning Drug Supply Chain Security Act requirements).

Section 503B(d)(4) of the FD&C Act defines an outsourcing facility as a facility at one geographic location or address that— (i) is engaged in the compounding of sterile drugs; (ii) has elected to register as an outsourcing facility; and (iii) complies with all of the requirements of this section. An outsourcing facility is not required to be a licensed pharmacy, and it may or may not obtain prescriptions for identified individual patients.⁴ Because drugs compounded by outsourcing facilities are not exempt from section 501(a)(2)(B) of the FD&C Act, outsourcing facilities are subject to CGMP requirements.^{5,6}

One of the conditions that must be met for a compounded drug to qualify for the exemptions under section 503B is that it must be compounded in an outsourcing facility in which the compounding of drugs occurs only in accordance with this section (section 503B(a)(11)). FDA’s

³ See section 503A(a).

⁴ See section 503B(d)(4)(C).

⁵ See section 503B(a).

⁶ FDA has issued a draft guidance entitled, *Current Good Manufacturing Practice — Interim Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act* (“Interim CGMP Guidance”). The Interim CGMP Guidance, when finalized, will describe FDA’s current thinking regarding outsourcing facilities and the CGMP requirements in 21 Code of Federal Regulations (CFR) parts 210 and 211 until more specific CGMP regulations for outsourcing facilities are promulgated.

We update guidances periodically. To make sure you have the most recent version of a guidance, be sure to check the Agency’s guidance website at <http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234622.htm>.

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guidance document, *For Entities Considering Whether to Register As Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act*,⁷ clarifies that:

If you register a facility as an outsourcing facility, you are indicating your intent for the facility's compounded drugs to be regulated under section 503B of the FD&C Act. Under section 503B(a)(11), a compounded drug can only qualify for the exemptions from sections 502(f)(1), 505, and 582 of the FD&C Act if **all** of the facility's compounded drugs are compounded in accordance with section 503B (page 4).

The guidance further states that:

By registering as an outsourcing facility, an entity is electing to have its compounded drugs regulated under section 503B of the FD&C Act, not section 503A. Drugs compounded at an outsourcing facility are not eligible for the exemptions provided in section 503A, even if the conditions in that section are met with respect to the particular drug (page 5).

Some outsourcing facilities compound drugs both according to patient-specific prescriptions as well as in response to orders that are not patient-specific, as section 503B permits them to do.⁸ FDA has been asked whether an outsourcing facility can create a separate area within its facility for compounding according to patient specific prescriptions under section 503A, and not follow CGMP requirements in that area. The Agency has also been asked whether drugs can be compounded according to patient-specific prescriptions in an adjacent area or room, or in a separate suite, but with the same staff and the same materials used in 503B compounding.

The CGMP regulations⁹ contain requirements for facility design, training and qualified staff, control of incoming components, aseptic processing, air quality, environmental monitoring, and related requirements designed to ensure the quality of the finished drug product. The application of CGMP requirements to only some drugs produced in an outsourcing facility, or application of the different conditions in section 503A and 503B to commingled compounding activities, could cause confusion about what requirements apply and could lead to the production of substandard drugs.

For that reason, and because all drug products compounded in an outsourcing facility must be compounded in accordance with section 503B and with CGMP requirements, this guidance clarifies FDA's current thinking on what constitutes a "facility at one geographic location or address" as that term is used in section 503B and addresses some related issues.

⁷ See the guidance, *For Entities Considering Whether to Register As Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act*.

⁸ Section 503B(d)(4).

⁹ See CGMP regulations at 21 CFR Parts 210 and 211.

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III. POLICY

Section 503B(d) defines an outsourcing facility, in part, as “a facility at one geographic location or address.” FDA interprets “facility,” as used in this section, to mean a business or other entity under one management, direct or indirect, engaged in the compounding of human drug products. The Agency considers all activities, equipment, and materials related to human drug compounding that are under the supervision of the facility’s management at the geographic location or address to be part of the facility, unless they are completely segregated from the facility by clearly identified boundaries. For purposes of this interpretation, such boundaries may include permanent physical barriers, such as walls, or doors that are locked to effectively exclude other human drug compounding.

Under this interpretation, a “facility” may be comprised of one or multiple suites within a single building, or one or multiple buildings “at one geographic location or address.” Further, a geographic location could include two or more addresses, provided that FDA is capable of inspecting the addresses within a single inspection.

The boundaries of the outsourcing facility should be clearly identified by management and communicated to staff. When the outsourcing facility registers its place of business with FDA to comply with section 503B(b)(1)(A)(i) of the Act, it should identify all of the facility’s rooms, suites, and buildings. This includes all locations at the geographic location or address used to support the outsourcing facility’s compounding operations.

As noted above, *all* drug products compounded in an outsourcing facility are regulated under section 503B¹⁰ and subject to CGMP requirements.¹¹ If the outsourcing facility intends to compound patient-specific prescriptions, it may do so within the facility subject to CGMP and consistent with the conditions of section 503B. If the owner or operator wishes to compound patient-specific prescriptions under the different conditions of section 503A, this must be done outside the outsourcing facility, in and by a separate establishment. This statutory condition cannot be avoided by subdividing the rooms of the outsourcing facility with a temporary barrier such as a curtain, or by limiting the compounding of patient-specific prescription compounding within the facility to certain periods of time. *All* compounding within the outsourcing facility is subject to regulation under section 503B, and CGMP requirements.

A. Segregating Compounding of Drug Products Under Section 503A From Compounding of Drug Products Under Section 503B

An entity that owns or manages an outsourcing facility may compound drugs under section 503A in a separate establishment located outside the boundaries of the outsourcing facility (a “section 503A establishment”). The section 503A establishment may be located near the outsourcing facility or in the same building, provided the compounding in the outsourcing facility is *completely segregated* from compounding by the section 503A establishment.

¹⁰ See section 503B(a)(11).

¹¹ See section 503B(a).

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In determining whether a section 503A facility and an outsourcing facility are completely segregated, FDA intends to proceed case by case. Indicia of complete segregation include:

- The outsourcing facility and section 503A establishment do not share any rooms.
- The outsourcing facility and section 503A establishment do not share any fixed equipment or supplies for use in compounding.
- The outsourcing facility and section 503A establishment have separate entrance(s) and exit(s),¹² do not share an internal pass-through opening, and are separated by permanent physical barriers. For example, it should not be necessary to go through the outsourcing facility to reach any part of the section 503A establishment.

Furthermore, it is a compounder's responsibility to label, promote, and advertise its compounded drug products in a manner that does not mislead customers about whether the drug products were compounded in an outsourcing facility or a 503A establishment¹³ (e.g., the labeling should clearly identify the compounder who produced the drug product).

For example, the Agency generally intends to view the following as an instance in which compounding in an outsourcing facility is completely segregated from compounding under section 503A:

A compounder registers with FDA as an outsourcing facility at 1234 Maple Street Suite C. The outsourcing facility compounds its drugs at this address in accordance with the conditions of section 503B and CGMP requirements. The owner of the outsourcing facility also owns a facility that compounds drugs in accordance with the conditions of section 503A at 1234 Maple Street Suite D. Suites C and D are located within the same building, but each has separate entrances and exits, and they do not share any rooms in which compounding is conducted, an internal doorway, or other pass-through (i.e., a person cannot reach suite D directly from suite C). The two facilities do not share materials. The only compounded drugs distributed by the outsourcing facility from Suite C are drugs that were compounded within the outsourcing facility. The facilities' drug product labels clearly identify the compounder who produced the drug product.

However, if an entity purporting to compound drugs under section 503A is located near an outsourcing facility and the entity's operations are not completely segregated from the outsourcing facility, FDA generally intends to consider that entity to be part of the outsourcing facility and subject to the conditions of section 503B and CGMP requirements. For example, if an outsourcing facility compounds drugs in room A and a separate entity compounds drugs in an

¹² For example, each facility might have a separate entrance and exit within the same building or leading to the same hallway.

¹³ See section 502(a), (bb) (providing that a compounded drug is misbranded if its labeling, advertising, or promotion is false or misleading in any particular).

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adjacent room B, and the two rooms share an internal pass-through or window, FDA would likely consider the entity to be part of the outsourcing facility.

FDA's interpretation of "facility" is consistent with the intent of section 503B. To be eligible for the exemptions in section 503B(a), a drug product must be compounded in an outsourcing facility in which the compounding of drugs occurs only in accordance with section 503B (see section 503B(a)(11)). Outsourcing facilities may or may not obtain prescriptions for identified individual patients, and they are not subject to the interstate distribution conditions in section 503A. Therefore, the intent of this provision is to ensure that all drugs compounded in an outsourcing facility under section 503B are compounded in accordance with CGMP requirements, labeled appropriately, subject to the specific adverse event reporting requirements issued under section 503B, and otherwise compounded in accordance with the conditions of section 503B.

The statutory requirement that all compounding conducted within the outsourcing facility to be in accordance with section 503B prevents commingling of compounding activities under sections 503A and 503B. A drug product compounded under section 503A may be visually indistinguishable from a drug product compounded under section 503B regardless of the conditions under which it is compounded. It is important to be able to follow the production of drug products compounded in an outsourcing facility to ensure that the products are made under CGMP requirements from the time the bulk drug substances are received at the facility through production of the finished dosage form. If a firm compounds drug products in one facility under different standards, it could be difficult to ensure that all of the products were made under the correct standards, particularly if the activities are commingled (e.g., because compounding under both standards draws on the same supplies, equipment, storage, or processing areas), or if compounded drug products are marketed under the same firm name or from the same facility. Further, if drug products are compounded in neighboring suites in the same building that are not completely segregated, or in the same suite, it may be impossible to determine whether a prescription was obtained for the particular drug product before it was distributed, leading to potential circumvention of a condition of section 503A. The Agency's interpretation also provides clarity during inspections regarding which standards apply to the location that is being inspected.

A clear separation between 503A and 503B facilities helps ensure that those obtaining the drugs will know the standards under which they were compounded. Furthermore, the public health is best served, and an important objective of section 503B is achieved, if all drug products compounded in an outsourcing facility, whether patient-specific or non-patient specific, are compounded in accordance with CGMP requirements and the requirements in section 503B of the FD&C Act.

B. Compounding Drug Products Under Section 503B and Conventionally Manufacturing Drug Products at the Same Facility

If a section 510-registered manufacturer registers a facility as an outsourcing facility and makes both approved drug products and compounded drug products in the outsourcing facility, the

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compounded drug products would need to meet the conditions of section 503B to qualify for the exemptions from sections 502(f)(1), 505, and 582.¹⁴

All drug products produced at the facility would be subject to the CGMP requirements in Title 21, Parts 210 and 211 of the CFR. As stated above,¹⁵ FDA has issued a draft guidance that, when finalized, will describe FDA's current thinking regarding outsourcing facilities and these CGMP requirements. When a facility both manufactures conventional drug products and compounds drug products under section 503B, the policies described in FDA's CGMP guidance would apply to the facility's compounded drug products, except with respect to CGMP requirements that must be implemented throughout a manufacturing facility and cannot be applied differently to different drug products in the same facility, such as environmental monitoring and pressure differential monitoring requirements.

Under FDA's interpretation, approved drug products and drug products compounded under section 503B may be produced in the same facility (e.g., without separation by a permanent physical barrier) because this activity does not present the concerns described above.¹⁶ For example, an outsourcing facility could not commingle its compounded and conventional drug products to avoid manufacturing the conventional drug products in accordance with applicable CGMP requirements or to avoid compounding drug products in accordance with the conditions of section 503B. An outsourcing facility's compounded drug products may be more easily differentiated from its conventional drug products; the conventional drug products may be the subject of approved drug applications and are listed with FDA under section 510 of the FD&C Act, while drug products compounded under section 503A are unapproved¹⁷ and are generally not listed. Furthermore, outsourcing facilities must label compounded drug products with the statement, "This is a compounded drug,"¹⁸ so purchasers of compounded drug products from an outsourcing facility that also manufactures conventional drug products will know that the drug products that they purchased were compounded. FDA verifies during inspections that outsourcing facilities are producing their compounded and conventional drug products in accordance with the applicable standards, including that the drug products are labeled appropriately.

¹⁴ We do not read *compounding* in section 503B(a)(11) of the FD&C Act to refer to the manufacture of a conventional drug product. Therefore, a drug product may be compounded in an outsourcing facility in accordance with section 503B even if a conventional drug product is manufactured in that outsourcing facility not in accordance with section 503B.

¹⁵ See footnote 6.

¹⁶ However, CGMP may require segregation of certain drug products or activities in certain circumstances. For example, 21 CFR 211(42)(d) requires that operations relating to the manufacture, processing, and packing of penicillin shall be performed in facilities separate from those used for other drug products for human use.

¹⁷ Drug products compounded under section 503B are similarly unapproved.

¹⁸ See section 503B(a)(10).

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C. Registering an Outsourcing Facility's Place of Business

When a facility registers with FDA as an outsourcing facility, it is required, among other things, to register its place of business. Section 503B(b)(1)(A)(i). The facility's registration should identify as its place of business the address, or the addresses at one geographic location, where the outsourcing facility's compounded drugs are manufactured, processed, packed, or held,¹⁹ and should identify any and all suites and buildings that are part of the facility. Examples are provided below.

- If the outsourcing facility occupies only one portion of a building, its registration should include enough information to identify that portion. For example, if the outsourcing facility occupies suites B and C of a building located at 1234 Maple Street, it should register 1234 Maple Street, Suites B and C, as its place of business. The outsourcing facility can identify both suites B and C in a single registration.
- If the outsourcing facility occupies more than one building, its registration should identify each building. For example, if the outsourcing facility has a storage facility for bulk drug substances and other supplies at 100 Main Street, prepares finished drugs at 101 Main Street, and then stores, repackages, and ships the finished drugs from 102 Main Street, the outsourcing facility should register 100-102 Main St. as its place of business.

¹⁹ The facility may not submit the address of a business office that handles administrative or executive work if this is at a separate geographic location.