August 31, 2020

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Submitted via www.regulations.gov

Re: Docket FDA-2020-N-1127 on Patent Listing Practices in the Orange Book

Dear Dockets Management Staff:

Intellectual Property Owners Association (IPO) thanks the Food & Drug Administration (FDA) for the opportunity to respond to the request for comments in "Listing of Patent Information in the Orange Book; Establishment of a Public Docket" (hereinafter referred to as the "FDA-2020-N-1127"), published in the *Federal Register* on June 1, 2020.

IPO is an international trade association representing companies and individuals in all industries and fields of technology who own, or are interested in, intellectual property rights. IPO's membership includes 175 companies and close to 12,000 individuals who are involved in the association either through their companies or as inventor, author, law firm, or attorney members. IPO advocates for effective and affordable IP ownership rights and provides a wide array of services to members, including supporting member interests relating to legislative and international issues; analyzing current intellectual property issues; information and educational services; and disseminating information to the general public on the importance of intellectual property rights.

The FDA asked for general comments concerning potential improvements to the Orange Book patent listing process, as well as responses to specific questions concerning:

(1) the listing of patents that claim a device constituent part of a combination product approved under section 505 of the FD&C Act;
(2) the listing of patents that claim a device whose use is referenced in approved drug labeling;
(3) the listing of patents associated with an established Risk Evaluation Mitigation Strategy ("REMS"); and
(4) the listing of patents associated with digital applications.

IPO commends the FDA's efforts to modernize the Orange Book and appreciates the agency's interest in stakeholders' opinions. IPO agrees that the Orange Book and associated patent information are valuable tools that serve important statutory requirements and public policy objectives for stakeholders including doctors, patients, and the pharmaceutical industry.

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In particular, IPO supports the public policy of promoting innovation. A clearer Orange Book, as proposed herein, will help promote innovation and maintain the balance between branded pharma and generic manufacturers, consistent with the Hatch-Waxman Act.

Modernizing the Orange Book to improve transparency and ease of use will also help the industry as a whole. As representatives of patent owners and innovator pharmaceutical companies, IPO considers its obligation to assist in modernizing the Orange Book as part of promoting public health and well-being. We look forward to working together toward that end.

Consistent with that obligation, IPO believes that any patent should be listed in the Orange Book as long as it reasonably relates to a Center for Drug Evaluation and Research (CDER)-approved drug substance, drug product, or method of treatment. This would generally include: (1) patents that claim a device constituent part of a combination product; (2) patents that claim a device whose use is referenced in approved drug labeling; (3) patents associated with an existing REMS; and (4) patents associated with digital applications in appropriate circumstances.

In addition to the below responses to the questions posed in the FDA's *Federal Register* notice, we ask that the FDA consider the proposed modifications to Form 3542 as described in an Appendix to these comments.

A. General Questions

1. Do 505(b)(2) and ANDA applicants currently encounter any challenges because certain types or categories of patents are not listed in FDA's Orange Book?

IPO provides no comment to this question.

2. Given the general increasing complexity of products approved in an NDA (e.g., drug-device combination products, complex delivery systems, associated digital applications), are there any aspects of FDA's interpretation of the statutory requirement for NDA holders to submit information on a patent that claims the drug or a method of using such drug that are not sufficiently clear? If there is a lack of clarity, how could this be resolved?

The statute requires NDA holders to identify the "patent number and expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the drug owner engaged in the manufacture, use, or sale of the drug." *See* 21 U.S.C. 355(b)(1).

In promulgating the statutory requirements, the agency requires that NDA applicants and holders timely submit completed Forms 3542a and 3542, as applicable, to list patents in the Orange Book. IPO believes that one of the agency's forms and practice in using the form discourage the complete identification of patent information required by the statute. Form 3542 may be improved in several ways to facilitate proper patent listing in the Orange Book. We provide detailed comments in this regard within the attached Appendix.

3. How would NDA holders and prospective 505(b)(2) and ANDA applicants weigh any advantages that may result from listing of additional types or categories of patent in the Orange Book against the potential need to submit additional patent certifications that could result in a delay of approval of a 505(b)(2) application or ANDA?

The FDA should not create additional categories or other identifiers for patents that can be listed in the Orange Book. Any patent is eligible to be listed in the Orange Book as long as it meets the statutory requirements. This would generally include: (1) patents that claim a device constituent part of a combination product; and (2) patents that claim a device whose use is referenced in approved drug labeling. This would generally also include (3) patents associated with an existing REMS; and (4) patents associated with digital applications, as long as they relate to a method of using an approved drug and, with respect to which a claim of patent infringement could reasonably be asserted, if a person not licensed by the drug owner engaged in the manufacture, use, or sale of the drug.

That said, IPO fully recognizes the uncertainty and potential that digital health technologies hold. Significant advancements in digital health have been made in the recent past and we agree with the FDA that future therapeutics will continue to integrate features and technologies that are complex and not contemplated by traditional features limited solely to active ingredients, formulations, and traditional method steps. In light of this variability and innovation, IPO urges continued evaluation of Orange Book practices in this area, provided that such policies continue to encourage disclosure of patent information. As noted above, such disclosure better serves all relevant stakeholders and encourages industry competition.

4. If you think FDA should clarify the type of patents that must be listed in the Orange Book, what factors should FDA consider in implementing this clarification? For example, should FDA consider specific factors in evaluating the timeliness of patent information submitted after such clarification?

As discussed in the response to Question A.3. above, IPO recommends that the agency not create additional types or categories of patents eligible to be listed in the Orange Book. Instead, the agency should encourage the identification of the those patents mentioned in the agency's *Federal Register* notice (e.g., patents that claim device constituents in combination products, devices used in approved drug labeling, established REMS, and digital applications) as generally required by statute, without reference to a category or other identifier. *See* 21 U.S.C. 355(b)(1).

If FDA clarifies that additional types of patents, if reasonably assertible, must be listed in the Orange Book, it should allow applicants a sufficient time period to file a supplemental listing request. Applicants might be filing multiple supplemental listing requests, so we recommend providing a period of at least 90 days from the issuance of clarification of Form 3542 for applicants to file supplemental listing requests.

5. Are there other issues related to the listing of patent information that we should consider?

Please refer to the Appendix for detailed suggestions to improve Form 3542.

B. Drug Product Patents

1. Are there elements of FDA's regulatory definition of drug product or dosage form in §314.3(b) that may be helpful to clarify to assist NDA holders in determining whether a patent claims the finished dosage form of an approved drug product?

21 CFR 314.3(b) defines a dosage form and drug product as follows:

> Dosage form is the physical manifestation containing the active and inactive ingredients that delivers a dose of the drug product. This includes such factors as: (1) The physical appearance of the drug product; (2) The physical form of the drug product prior to dispensing to the patient; (3) The way the product is administered; and (4) the design features that affect frequency of dosing.
>
> Drug product is a finished dosage form, e.g., tablet, capsule, or solution that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients.

It is unnecessary to modify these definitions to clarify whether patents claiming a device constituent part of a combination product should be listable as drug product patents in the Orange Book. Whether a patent claims a combination product that is (1) a formulation of two active drug substances or (2) active drug substance in combination with a device constituent part, both (1) and (2) can be properly considered to be dosage forms under the FDA's regulatory definition.

2. What factors should FDA consider in providing any clarifications related to whether device-related patents need to be submitted for listing as a patent that claims the drug? For example, what are the advantages and disadvantages of requiring patents that claim a device constituent part of a combination product approved under section 505 of the FD&C Act to also claim and/or disclose the active ingredient or formulation of the approved drug product (or the drug product class) to fall within the type of patent information that is required to be submitted to FDA for listing in the Orange Book? Also, how, if at all, should this analysis be affected by considerations about whether the device or specific component of device claimed in the patent is "integral" (see 68 FR 36676 at 36680) to the administration of the drug?

As long as a claim of patent infringement could reasonably be asserted for the device-related patent, it should be listable. *See* 21 U.S.C. 355(b)(1). The FDA has previously stated:

> Most comments agreed that patents claiming packaging should not be submitted for listing. However, some comments stated that patents claiming devices or containers that are ''integral'' to the drug product or require prior FDA approval should be submitted and listed. These comments distinguished between packaging and devices

> such as metered dose inhalers and transdermal patches, which are drug delivery systems used and approved in combination with a drug.
>
> (Response) We agree that patents claiming a package or container must not be submitted. Such packaging and containers are distinct from the drug product and thus fall outside of the requirements for patent submission. However, we have clarified the rule to ensure that if the patent claims the drug product as defined in § 314.3, the patent must be submitted for listing. Section 314.3 defines a ''drug product'' as ''* * * a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients.'' The appendix in the Orange Book lists current dosage forms for approved drug products. The list includes metered aerosols, capsules, metered sprays, gels, and pre-filled drug delivery systems. The key factor is whether the patent being submitted claims the finished dosage form of the approved drug product. Patents must not be submitted for bottles or containers and other packaging, as these are not ''dosage forms.''

68 Fed. Reg. 36,676; 36,680 (June 18, 2003).

Following this reasoning, device-related patents, such as pre-filled cartridges and disposable pens, should be listable as long as a claim of patent infringement could reasonably be asserted.

C. Method-of-Use Patents

1. What information should FDA consider regarding when a patent that claims a method of using a device constituent part, or only a component of a device constituent part, might or might not meet the statutory standard for submission by the NDA holder for listing in the Orange Book as a method-of-use patent? Should FDA consider whether: (1) The patent claims and/or discloses the active ingredient or formulation of the approved drug product (or the drug product class)?; (2) the device constituent part is described in certain sections of the listed drug labeling?; or (3) use of the device is described in labeling for the listed drug, but the device is not a constituent part of the drug product? Should FDA consider whether the drug product labeling states that the drug is only for use with the specific device? Should FDA also consider device labeling, for example whether the device labeling indicates the device is for use with the specific drug?

If a patent claims a device constituent part and an approved active ingredient, approved drug product or drug product class, it should be eligible for listing in the Orange Book. Also, if a patent claims a device constituent part described in certain sections of the listed drug labeling, then it should be eligible for listing in the Orange Book as long as a claim of patent infringement could reasonably be asserted. *See* 21 U.S.C. 355(b)(1).

When drug product labeling states that the drug is only for use with a specific device, the patent claiming that specific device should be listed as long as a claim of patent infringement could reasonably be asserted. Similarly, when device labeling indicates the device should be used with a

specific drug, a patent claiming that device should be listed in the Orange Book as long as a claim of patent infringement could reasonably be asserted. *See* 21 U.S.C. 355(b)(1).

2. What information should FDA consider regarding whether there are circumstances in which a patent claiming the way an approved drug product is administered would meet the statutory standard for submission by the NDA holder for listing in the Orange Book as a drug product patent rather than a method-of-use patent?

When a patent claims an approved drug substance in combination with a device, whether that device is a constituent part of the drug product or it is referenced in the approved drug labeling, it should be treated as a "drug product patent" for Orange Book identification.

3. What information should FDA consider regarding whether there are circumstances in which a method-of-use patent claiming the way an approved drug product is administered that is not described in FDA-approved product labeling would meet the statutory standard for listing in the Orange Book?

The statute governs in all circumstances. As long as a claim of patent infringement could reasonably be asserted for the device-related patent, it should be listable. *See* 21 U.S.C. 355(b)(1).

The NDA applicant is in the best position to assess whether a method-of-use patent claiming the way an approved drug product is administered that is not described in FDA-approved product labeling would meet the statutory requirements. The FDA's role in patent listing matters is purely ministerial. Accordingly, we submit that the statute, and its corresponding regulations, should govern in this and all circumstances.

D. REMS-Related Patents

1. What information should FDA consider regarding whether patents that claim how the sponsor has implemented a particular REMS requirement meet the statutory requirement for the type of patent information that is required to be submitted to FDA for listing in the Orange Book? What factors should be considered in making this determination?

The statute and corresponding regulations govern in all circumstances and already identify the factors that govern whether a REMS-related patent must be listed. Again, because the FDA provides a ministerial role in patent listing, we do not believe the agency should develop an alternative framework beyond what is listed in the statute.

2. Are there other issues related to patents that claim how the sponsor has implemented a particular REMS requirement that FDA should consider with regard to listing patent information in the Orange Book, including any potential impact listing such patents in the Orange Book could have on development of REMS for generic versions of products? For example, does listing patent

information in the Orange Book for such patents pose difficulties for ANDA applicants in developing a single, shared system REMS for that product?

The statute and corresponding regulations govern in all circumstances. As long as a claim of patent infringement could reasonably be asserted for a patent implementing a particular REMS requirement, it should be listable. *See* 21 U.S.C. 355(b)(1).

E. Patents for Digital Applications

1. If an approved drug product has an associated digital application (e.g., a mobile application that accepts and records information from an ingestible sensor in a drug product), what factors should be considered in determining whether a patent that claims an aspect of that digital application meets the standards for listing in the Orange Book?

As noted above, if a patent claims a method of using an approved drug product in combination with an associated digital application, and this digital application is referenced in the approved drug labeling, then the patent should be listed in the Orange Book "as long as a claim of patent infringement could reasonably be asserted." *See* 21 U.S.C. 355(b)(1).

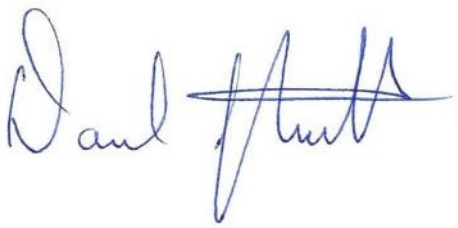
However, given the promise and nascency of digital health technologies, IPO urges continued evaluation of Orange Book practices in this area, provided that such policies continue to encourage disclosure of patent information. IPO strongly believes that such disclosure better serves all relevant stakeholders and encourages industry competition.

2. Are there other issues related to patents for digital applications associated with approved drugs that should be considered with regard to listing patent information in the Orange Book?

IPO provides no comment to this question.

Thank you for considering these comments. We welcome further dialogue or opportunity to provide additional information to assist your efforts.

Best regards,



Daniel J. Staudt
President

APPENDIX

IPO provides its suggestions for modifying Form 3542 in markup below. We believe these modifications would improve transparency and efficiency in the patent listing process. In our comments and markups, we often suggest replacement of a term like "does the patent claim" with a phrase that addresses "at least one claim," as U.S. patents most often have more than one claim. All references herein to "patent" refer to a U.S. patent.

IPO recommends the following changes to Form 3542:

In the instructions immediately prior to Section 2:

> *For the patent referenced above, provide the following information on whether the patent claims the drug substance, drug product, or method of use that is the subject of the approved NDA or supplement. FDA will not list patent information if the patent declaration does not contain the information required by 21 CFR § 314.53(c)(2) or the patent declaration indicates the patent is not eligible for listing.*
> - *If the patent is eligible for listing as claiming the drug substance and section 2 is completed, it is ~~not~~ still necessary to complete section 3, ~~even if~~whether or not the patent is also eligible for listing as a drug product.*
> - *If the patent is eligible for listing as claiming the drug product and section 3 is completed, it is ~~not~~ still necessary to complete section 2, ~~even if~~whether or not the patent is also eligible for listing as drug substance.*
>
> *FDA will consider incomplete a patent declaration that does not include a response to all required questions contained within each section below applicable to the patent referenced above.*

Rationale: Because the Orange Book indicates whether each patent claims the drug substance or drug product, applicants should be required to fill out both sections 2 and 3 or the Orange Book will be inaccurate in the majority of circumstances.

> **Section 2.1 Does the patent contain at least one claim that is directed to the drug substance ~~that is the active ingredient~~ in the drug product described in the approved NDA or supplement? ~~If yes, skip to Question 2.5.~~**

Rationale: First, since a patent typically has multiple claims, the addition of "at least one claim" provides a more accurate question. Second, because we also recommend modifications to 2.2 and elimination of 2.3 and 2.4, we recommend deleting "If yes, skip to Question 2.5."

> **Section 2.2 ~~Does the~~Is the only basis for potential listability of the patent at least one claim ~~only~~ directed to a drug substance that is a different polymorph of the active ingredient described in the NDA or supplement?**

Rationale: Because a patent typically has multiple claims, the use of "only" in present 2.2, is confusing. This revision makes clear that the answer to 2.2 is "No" if the patent has one or more

other appropriate bases for listing such as having one or more claims directed to the approved drug substance.

~~**Section 2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).**~~

Rationale: We recommend that if the only potential basis for listability of a patent is that it has one or more claims directed to a drug substance that is a different polymorph of the active ingredient described in the NDA or a supplement, then that patent should not be listed. In other words, if the answer to Section 2.2 is "yes", then the patent should not be listed.

~~**Section 2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.**~~

Rationale: Same rationale as stated in Section 2.3.

Section 2.5 ~~**Does the patent claim only a metabolite of the approved active ingredient?** ***(Complete the information in section 4 below if the patent claims an approved method using the approved drug product to administer the metabolite.)***~~**Are all of the claims in the patent that are being relied upon for listing the patent in the Orange Book as covering the approved drug substance directed to a metabolite of the drug substance as described in the approved NDA or supplement?**

Rationale: This revision makes clear that the answer to 2.5 is "Yes" only if all claims that form a basis for listability of the patent are directed to a metabolite of the approved drug substance described in the approved NDA or supplement. But if 2.5 is yes, then 2.1 must be no. If the answer to 2.5 is no, then there might be other claims in the same patent providing a basis for listability of the patent. The parenthetical "(Complete the information in Section 4 below, if the patent contains at least one claim directed to an approved method of using the approved drug product to administer the metabolite)" is confusing. If relevant, that parenthetical information will be subsumed in Section 4.1.

Section 2.6 ~~**Does the patent claim only an intermediate?**~~**Are all of the claims in the patent that are being relied upon for listing directed to a non-drug substance, synthetic intermediate of the drug substance described in the approved NDA or supplement? If so, the correct answer is "Yes."**

Rationale: We recommend a more precise definition to distinguish true synthetic intermediates from drug substances. For example, in GFI#126-BACPAC 1: Intermediates in Drug Substance synthesis, intermediate is defined at p. 22 as: "A material produced during steps of the synthesis of a drug substance that undergoes further molecular change before it becomes a drug substance." See "Guidance for Industry BACPAC I: Intermediates in Drug Substance Synthesis Bulk Actives Postapproval Changes: Chemistry, Manufacturing, and Controls Documentation," U.S.

Department of Health and Human Services Food and Drug Administration Center for Veterinary Medicine (CVM), June 1, 2006, p. 22.

See also: Intermediate defined as: "A material produced during the steps in the synthesis of an API that must undergo further molecular change or processing before it becomes an API. Source:

https://www.pharmaguideline.com/2011/09/terminology-definitions-in.html#gsc.tab=0"

Hence, for FDA, an intermediate is NOT a drug substance but is a synthetic compound that undergoes further molecular change before it becomes a drug substance.

~~Section 2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel?~~

Rationale: If all claims, even though they are in product-by-process form, are listed based on 2.1, then the drug substance(s) claimed must be novel in accord with Abbott v. Sandoz, 566 F.3d 1282 (Fed. Cir. 2009) (en banc) and Atlantic Thermoplastics Co. v. Faytex Corp., 970 F.2d 834 (Fed. Cir. 1992), holding that process limitations are not taken into account in assessing the patentability of the product in a product-by-process claim. Otherwise, the claims of the patent could not, or at least should not, have issued. Hence, 2.7 is rendered redundant and can be eliminated.

Summary of Section 2
FDA will not list the patent in the Orange Book as claiming the drug substance if:

- **the answers to 2.1 is "No" and 2.2 ~~are~~is "~~No~~ Yes," or,**
- **~~the answer to 2.2 is "Yes" and the answer to 2.3 is "No," or,~~**
- **~~the answer to 2.3 is "Yes" and there is no response to 2.4, or,~~**
- **the answer to 2.5 or 2.6 is "Yes,"**
- **~~the answer to 2.7 is "No."~~**

and there is no alternative rationale for listing provided in answers to questions posed in Sections 3 and 4.

Rationale: See above where we propose to change the instructions immediately preceding Section 2 and delete Sections 2.3, 2.4, and 2.7.

Section 3.1 Does the patent ~~claim the approved drug product as defined in 21 CFR 314.3?~~contain at least one claim that is directed to the drug product described in the approved NDA or supplement? If so, the answer is "Yes".

Rationale: The change to "at least one claim" provides a more accurate question.

Section 3.2 ~~Does the patent claim only an intermediate?~~Are all of the claims in the patent that are being relied upon for listing directed to a non-drug substance, synthetic intermediate of the drug substance in the drug product described in the approved NDA or supplement? If so, the answer is "Yes."

Rationale: While patents claiming merely synthetic intermediates or formulations of synthetic intermediates are not listable, synthetic intermediates have specific definitions, as indicated above. For example, assume that all claim(s) providing the basis for listability of the patent are directed to a drug product, not a synthetic intermediate, that upon formulation, such as tabletting, or storage, converts to the approved drug product described in the approved NDA or supplement. If so, the patent is to be listed under Section 3.1.

~~**Section 3.3 If the patent reference in 3.1 is a product-by process patent, is the product claimed in the patent novel?**~~

Rationale: Same reasoning given above for Section 2.7.

Summary of Section 3
FDA will not list the patent in the Orange Book as claiming the drug product if:

- **the answer to question 3.1 is "No," or,**
- **the answer to question 3.2 is "Yes~~,"~~ ."**
- ~~**the answer to 3.3 is "No."**~~

Rationale: We propose to delete section 3.3.

Section 4 METHOD OF USE
NDA holders must submit the information in section 4 for each approved method of using the approved drug product claimed by the patent. An NDA holder may list together multiple patent claims for each approved method of use; however, each approved method of use claimed by the patent must be separately identified within this section. Continuation pages may be used to separately list method of use information within this section. For each approved method of use claimed by the patent, provide the following information:

Section 4.1 Does the patent claim one or more approved methods of using the approved drug product?
(Select one)
___ Yes (patent claims only one approved method of use)
___ Yes (patent claims more than one approved method of use)
___ No

Similarly, if the patent claims only one approved method of use, complete Fields 4.2, 4.2a, and 4.2b.

If you answer yes to question 4.1, you are also required to state whether the patent also claims the drug substance/active ingredient or drug product. Accordingly, make sure you have completed section 2 or section 3, if appropriate.

If the patent claims more than one approved method of use, separately identify and complete Fields 4.2, 4.2a, and 4.2b for each approved method of use claimed by the patent. Click the

“Add section 4.2” button to add a new set of section 4.2 entries for each approved method of use claimed by the patent.

The “Add section 4.2” button is at the end of Section 4.

Section 4.2 Patent Claim Number(s) (as listed in the patent) (Please separate numbers with commas.)	~~**Does (Do) the patent claim(s) referenced in 4.2 claim an approved method of use of the approved drug product?**~~

Section 4.2a ~~**If the answer to 4.2 is “Yes,” f**~~**For each approved method of use, separately identify the specific section(s) (please list each section on a separate line and within each line, separate each subsection with a comma), and subsection(s) of the approved labeling for the drug product that describe the approved method of use claimed by the patent. If there is no applicable subsection, insert “subsection N/A”. If there is more than one approved method of use, please use the “Add Section 4.2” button for additional entries as needed.**	~~**Use (In your answer below, please list each section on a separate line. Within each line, separate each subsection with a comma.)**~~

Section 4.2b For each approved method of use, provide the description of the specific approved method of use claimed by the patent that FDA should include as the “use code” in the Orange Book. Each use code must describe only an approved method of use claimed by the patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the patent owner engaged in the manufacture, use, or sale of the drug product.*	~~**Use (Submit the description of the specific approved method of use claimed by the patent that FDA should include as the “Use Code” in the Orange Book, using no more than 250 total characters including spaces.)**~~

*In other words, the scope of the use code must not extend beyond the scope of the patent claim(s) and, within the boundary established by the patent claim(s), the use code must only describe a patented method of use that has been approved by FDA as reflected in approved product labeling. The use code must contain adequate information to assist 505(b)(2) application and abbreviated new drug applications (ANDA) applicants in determining whether a listed method-of use patent

claims a use for which the 505(b)(2) application or ANDA applicant is not seeking approval (see 21 CFR 314.53(c)(2)(ii)(P)(3)). If you intend to use an existing use code that satisfies the current requirements of the statute and regulations, submit the existing use code for listing in the Orange Book. Use a maximum of 250 characters for each use code, and follow the general principles described below.

- Patent method of use is broader than an indication or other approved condition of use in the labeling: The use code must only describe a patented method of use that is described in FDA-approved product labeling. If the method of use claimed by the patent uses different terminology than the approved labeling and/or is broader than an indication or other approved condition of use, then the use code would need to be phrased more narrowly than the patent claim to only describe the specific patented method of use that is described in FDA-approved product labeling.
- Patented method of use is co-extensive with an indication or other approved condition of use in the labeling: The use code must describe only the specific approved method of use claimed by the patent.
- Patented method of use is narrower than an indication or other approved condition or use in the labeling. If the method of use claimed by the patent does not cover an indication or other approved condition of use in its entirety, then the NDA holder must describe only the specific approved method claimed by the patent for which a claim of patent infringement could reasonably be asserted if a person not licensed by the patent owner engaged in the manufacture, use, or sale of the drug product - not the broader indication or other approved condition of use that may include, but is broader than, the use claimed by the patent.

In line with these principles just expressed, the practitioner, if and only if appropriate, should use existing codes to the extent possible to make the choice easier on the listing person and easier for the FDA to review.

Rationale: Our concern with 4.2b is that it leaves the individual completing the listing form, who usually is a patent attorney, with no guidance in Form 3542 itself regarding the use code. But, looking at the instructions for filling out Form 3542 section 4.2b, they seem to be in harmony with the guiding principles of the case law. The revision includes information verbatim from the instructions.

Summary of Section 4

FDA will not list the patent in the Orange Book as claiming the method of use if the answer to 4.1 is no. Even if the answer to section 4.1 is yes, FDA will not list the patent in the Orange Book if sections 4.2, 4.2a and 4.2b are not completed. ~~:~~
~~**the answer to question 4.1 or 4.2 is "No," or**~~
~~**the answer to 4.2 is "Yes" and the information requested in 4.2a and 4.2b is not provided in full.**~~

SECTION 6 – DECLARATION CERTIFICATION

Fields 6.1 through 6.3: Read the required declaration, then date and sign the form in Field 6.2. If the person signing the form in field 6.2 does not reside or have a place of business in the United States, the form must also be dated and countersigned in Field 6.3 by an ~~attorney, agent, or other authorized official who resides or maintains a place of business within the United States~~ **agent or representative who resides or maintains a place of business in the United States**. Check the

applicable box that describes the authorized signature provided in Field 6.2, and provide the name, street address, city, state/province/region, country, zip or postal code, telephone number and, if available, the fax number and e-mail address of the person signing the form in Field 6.2. Complete each required section, including country, and provide the area code or country code, as applicable, for the telephone or fax number.

Rationale: To conform to SECTION 1e.