

application, the patent would be ineligible for listing because the patent would violate a specific provision in patent law.

In contrast, three comments supported listing product-by-process patents. These comments agreed that product-by-process patents are a form of a product patent. Two comments stated that we did not need to revise the rule to distinguish between product-by-process patents (which must be listed) and process patents (which must not be listed). The comment suggested revising § 314.53(b) to replace its mention of product-by-process patents with “patents that claim the drug substance or drug product at least in part in terms of its method of manufacture (product-by-process patents).”

(Response) We agree that, to be submitted for listing, the product-by-process patent must claim the drug product that is the subject of the NDA. We explained in the proposed rule why a product-by-process patent is a type of product patent (see 67 FR 65448 at 65452). We also agree that the declaration should be clear enough to ensure that the patents that are submitted for listing are product-by-process patents and not process patents. In the response to comment 12 in section II.A of this document we detail the changes we have made to the declaration (including declaration forms) to help ensure that the patents submitted for listing are patents that claim the drug product that is the subject of the NDA and do not claim the process that is used to manufacture the drug product.

The declaration forms include a question which requires the NDA applicant or holder or patent owner to certify whether the patent being submitted is a product-by-process patent in which the product claimed is novel. Although we do not adopt the wording suggested by several comments, we agree that a requirement to identify the product as novel will help ensure that the patent is a product-by-process patent. We acknowledge that when the PTO issues a patent, the PTO necessarily determines that some aspect of the patent claims is “novel.” We want to make sure that the NDA applicant or holder or patent owner is identifying the product claim as the novel aspect. This clarification should eliminate the submission of patents that may be mistakenly identified as product-by-process patents but, in reality, are process patents which cannot be submitted for listing.

We expect that product-by-process patents will not be submitted often. Drug products approved under section

505 of the act typically are capable of being described by their chemical formula. Most such drug products approved are not of the type that can be described only in terms of the process used to produce the product. We decline to add any additional questions to the declaration relating to the patented product's length of time in the commercial market or other related questions, as we believe that the declaration questions we have added will accomplish the clarification necessary to prevent the submission of process patents.

c. *Patents Claiming Packaging—Do We Consider Containers and Delivery Systems to be “Packaging?”* Proposed § 314.53(b) would not have allowed an applicant to list a patent that claimed packaging.

(Comment 3) 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.” The revised declaration requirements, described in the response to comment 12 in section II.A of this document, detail the information required for submission.

d. *Patents Claiming Metabolites—Are Any Patents Claiming Metabolites Eligible for Submission and Listing?* The

proposed rule would prohibit submission and listing of a patent claiming a metabolite of the approved drug. A metabolite is the chemical compound that results after the active ingredient of the drug has broken down inside the body. We explained that a patent claiming a metabolite does not claim the approved drug, as required by the act, because the metabolite exists only after the approved drug has been broken down inside the body (see 67 FR at 65451).

(Comment 4) Most comments agreed with our exclusion of patents claiming a metabolite. One comment, however, asked whether we would list “a patent that claims a method of using an approved drug to administer a metabolite.” The comment distinguished a method-of-use patent from a patent that claimed the metabolite.

(Response) The final rule prohibits submission of patents claiming metabolites when the metabolite is not the active ingredient described in the NDA. The submission of a metabolite patent does not meet the legal requirements for patent submissions as discussed in the proposed rule (see 67 FR 65448 at 65451). By contrast, if a patent submitted for listing claimed an approved method of using an approved drug to administer a metabolite, the submission of the patent would be permissible as long as all the conditions for submitting “method-of-use” patents are met. We describe the requirements for submission of method-of-use patents in the response to comment 7 in section II.A of this document. Briefly, if a method of use is described in the labeling for the drug product, and there is a patent claiming that method of use, the patent must be submitted for listing in the Orange Book, the method-of-use claim must be identified in the declaration forms, and the labeling language related to the method-of-use claim must be provided in the declaration forms.

e. *Patents Claiming Intermediates—Must We Allow Them to Be Submitted?* The proposed rule would not allow the submission of patents that claimed an intermediate. We explained that intermediates are materials that are produced during preparation of the active ingredient and are not present in the finished drug product. We consider intermediates to be “in-process materials” rather than drug substances or components in the finished drug product (see 67 FR 65448 at 65451 to 65452).

(Comment 5 and Response) The comments that addressed this issue agreed with the proposal. Consequently,