FDA U.S. FOOD & DRUG ADMINISTRATION

June 9, 2017

Erik Thygesen
Director, US Regulatory Affairs
Ferring Pharmaceuticals
100 Interpace Parkway
Parsippany, NJ 07054

Re: Ferring Pharmaceuticals, Inc.'s request for 5-year NCE exclusivity for Prepopik

Dear Mr. Thygesen:

This letter addresses Ferring Pharmaceuticals, Inc.'s (Ferring's) request for 5-year new chemical entity (NCE) exclusivity for Prepopik (sodium picosulfate, magnesium oxide, and citric acid) for Oral Solution (new drug application (NDA) 202535), pursuant to section 505(c)(4)(E)(ii) and (j)(5)(F)(ii) of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

As you are aware, in October 2014, the Food and Drug Administration (FDA or the Agency) adopted a new interpretation of the relevant statutory and regulatory provisions for 5-year NCE exclusivity as applied to certain fixed-combination drug products (fixed-combinations).[1] Under this interpretation, a drug substance (i.e., an active ingredient)[2] containing no previously approved active moiety would be eligible for 5-year NCE exclusivity even when such a drug substance is approved in a fixed-combination with another drug substance containing one or more previously approved active moieties (October 2014 interpretation).[3] In contrast, under the Agency's interpretation at the time it approved Prepopik (pre-October 2014 interpretation),[4] a fixed-combination was not eligible for 5-year NCE exclusivity if the drug product contained a previously approved active moiety, even if the product also contained a "new active moiety" (i.e., an active moiety that the Agency had not previously approved). Because the Agency decided to apply the October 2014 interpretation prospectively, Prepopik was ineligible for 5-year NCE exclusivity.

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[1] See FDA Guidance for Industry, *New Chemical Entity Exclusivity Determinations for Certain Fixed-Combination Drug Products* (October 2014). The guidance is available at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[2] 21 CFR 314.3 (defining "drug substance" as an active ingredient).

[3] See Section I.C. of this letter for a description of the Agency's current interpretation of the relevant statutory and regulatory provisions governing 5-year NCE exclusivity as applied to fixed-combinations beginning October 2014, which is referred to as the "October 2014 interpretation" in this letter.

[4] See Section I.C. of this letter for a description of the Agency's interpretation of the relevant statutory and regulatory provisions governing 5-year NCE exclusivity as applied to fixed-combinations prior to October 2014, which is referred to as the "pre-October 2014 interpretation" in this letter.

On June 1, 2015, Ferring filed an action challenging the Agency's pre-October 2014 interpretation as applied to Prepopik.[5] In a Memorandum Opinion and Order dated September 9, 2016, the U.S. District Court for the District of Columbia (District Court) concluded that FDA's pre-October 2014 interpretation of the word "drug" in the relevant statutory provisions governing 5-year NCE exclusivity was arbitrary and capricious in the context of certain fixed-combinations, and remanded the action to FDA for proceedings not inconsistent with the opinion.[6]

Upon careful consideration and review of the administrative record, FDA has determined that at the time it was approved, Prepopik did not contain any drug substance with no previously approved active moiety. All three drug substances in Prepopik — sodium picosulfate, magnesium oxide, and citric acid — contained previously approved active moieties. Therefore, FDA concludes that Prepopik is not eligible for 5-year NCE exclusivity under either the Agency's pre-October 2014 interpretation or the Agency's October 2014 interpretation. Rather, Prepopik was eligible for 3-year exclusivity, which expired on July 16, 2015.

I. BACKGROUND

A. Approval of Prepopik

FDA approved Prepopik on July 16, 2012, for cleansing of the colon as a preparation for colonoscopy in adults. Prepopik contains three active ingredients: magnesium oxide, citric acid, and sodium picosulfate. Both magnesium oxide and citric acid are previously approved active ingredients, and thus contain previously approved active moieties. The Agency had previously determined that picosulfate was the active moiety in sodium picosulfate, and that it had not been previously approved in any NDA prior to the approval of Prepopik (see section I.E. of this letter). Consistent with the Agency's pre-October 2014 interpretation, FDA determined that, because Prepopik (the drug product) contained at least one previously approved active moiety, it was not eligible for 5-year NCE exclusivity. The Agency determined that Prepopik was eligible for 3-year exclusivity pursuant to section 505(c)(4)(E)(iii) and 505(j)(5)(F)(iii) of the FD&C Act, with an expiration date of July 16, 2015.

B. 5-Year NCE Exclusivity for Fixed-Combinations: Statute & Regulations

The FD&C Act provides for a 5-year exclusivity period to a "new chemical entity" by prohibiting the submission of 505(b)(2) applications and abbreviated new drug applications (ANDAs)[7] that contain the new chemical entity:

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[5] See Complaint for Declaratory, Injunctive, and Other Relief, Ferring Pharm., Inc. v. Burwell, No. CV 15-0802 (RC) (D.D.C. June 1, 2015).

[6] No. CV 15-0802 (RC), 2016 WL 4734333 (D.D.C. Sept. 9, 2016) (Sept. 2016 Opinion).

[7] A 505(b)(2) application allows an applicant to seek approval of an NDA for which some or all of the safety and efficacy investigations relied upon for approval were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use. An ANDA is an application for a generic drug submitted under section 505(j) of the FD&C Act and allows an applicant to rely on FDA's previous finding of safety and effectiveness for a reference listed drug (RLD). The ANDA applicant must show that, among other things, its proposed drug product is the same as the RLD with respect to active ingredient, dosage form, strength, route of administration, and with certain exceptions, labeling, and that its product is bioequivalent to the RLD. Section 505(j)(2) of the FD&C Act.

> If an application submitted under [section 505(b)] for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under [section 505(b)], is approved after September 24, 1984, *no application which refers to the drug for which the [section 505(b)] application was submitted and for which the investigations described in [section 505(b)(1)(A)] and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under [section 505(b)] before the expiration of five years from the date of the approval of the application under [section 505(b)], except that such an application may be submitted under [section 505(b)] after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A)...*[8]

In this provision, the first clause (underlined text) describes which "drugs" are new chemical entities (eligibility clause), and thus eligible for 5-year NCE exclusivity, while the second clause (italicized text) describes the applications that are blocked by such exclusivity (bar clause). Under the eligibility clause, a drug is eligible for 5-year NCE exclusivity if it contains "a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other" 505(b) application.

Once a drug has met the requirements of the eligibility clause, the bar clause prevents the submission of any 505(b)(2) application or ANDA that "refers to the drug for which the [505(b)] application was submitted." This bar (i.e., 5-year NCE exclusivity) does not block the submission, review, or approval of a 505(b)(1) application.[9] However, this bar on submission applies to 505(b)(2) and ANDA applications and lasts for "five years from the date of the approval of the [505(b)] application,"[10] except that a 505(b)(2) application or an ANDA may be submitted after the expiration of 4 years from the date of approval if the 505(b)(2) application or ANDA contains a certification of patent invalidity or noninfringement to a patent listed for the referenced drug. This certification is also referred to as a "paragraph IV certification."[11]

FDA's regulations contain definitions that further help determine the applications that are eligible for 5-year NCE exclusivity. "New chemical entity" is defined as "a drug that contains no active moiety that has been [previously] approved . . ."[12] "Active moiety" is defined as "the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt . . . , or other noncovalent derivative . . . of the molecule, responsible for the physiological or pharmacological action of the drug substance."[13]

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[8] Section 505(c)(3)(E)(ii) the FD&C Act (emphasis added). Section and 505(j)(5)(F)(ii) uses substantially the same language to apply these requirements to ANDAs.

[9] A 505(b)(1) application, also referred to as a stand-alone application, is an application that is supported entirely by investigations either conducted by the applicant or for which the applicant has a right of reference.

[10] Id.

[11] Section 505(b)(2)(A)(iv) and 505(j)(2)(A)(vii)(IV) of the FD&C Act; see 21 CFR 314.108(b)(2)-(3); see also 21 CFR 314.101(e)(2).

[12] 21 CFR 314.108(a).

[13] 21 CFR 314.3(b).

C. FDA's Interpretation of the 5-Year NCE Exclusivity Provisions in the Context of Fixed-Combinations

At the time it approved Prepopik, FDA interpreted the word "drug" in the eligibility clause to refer to a "drug product." Under this interpretation, a "new chemical entity" referred to the entire drug product, which, in the case of a fixed-combination, included all the active ingredients in that fixed-combination. Accordingly, in making the eligibility determination, FDA evaluated whether the drug product contained a previously-approved active moiety. Under the applicable regulation, if the drug product contained at least one previously-approved active moiety, then that drug product was not eligible for 5-year NCE exclusivity.[14]

In 2013, Ferring petitioned the Agency to recognize 5-year NCE exclusivity for Prepopik.[15] Around the same time, two other citizen petitions were filed making similar requests for two other fixed-combinations. In a consolidated response to the three citizen petitions, FDA concluded that it intended to revise its interpretation of section 505(c)(3)(E)(ii) and (j)(5)(F)(ii) of the FD&C Act, as well as the applicable regulations.[16] FDA announced its decision to interpret the first "drug" in the statutory provision, and consequently, a "new chemical entity," to mean "drug substance" (i.e., active ingredient). This meant that rather than analyze the entire drug product, FDA would analyze each active ingredient separately to determine whether it meets the definition of new chemical entity. Therefore, a fixed-combination would be eligible for 5-year NCE exclusivity if it contained a new chemical entity (i.e., any active ingredient with no previously-approved active moiety). This would be true even if the fixed-combination also contained one or more active ingredients with previously-approved active moiety(ies).

In its citizen petition, in addition to requesting a revision to FDA's interpretation of the 5-year NCE exclusivity provisions, a request which FDA granted, Ferring asked FDA to apply the new interpretation retroactively to Prepopik, rather than applying the interpretation that was in effect at the time Prepopik was approved on July 16, 2012. Because Prepopik had been approved while FDA's pre-October 2014 interpretation was in place, the Agency denied this request. FDA concluded that the new interpretation would not be applied until after the Agency had finalized a guidance document announcing the new interpretation, and further, the Agency concluded that the new interpretation would only apply prospectively.[17] At the time the Agency issued the consolidated response, FDA issued a draft guidance that set out its reasoning for the existing interpretation, as well as the scientific and policy reasons underlying the change in its interpretation, and provided an opportunity for public comment.[18] After reviewing the public comments, which unanimously supported the change in policy, the Agency finalized the guidance

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[14] See 21 CFR 314.108(a) (defining new chemical entity).

[15] Letter from Theodore M. Sullivan and Edward J. Allera, Docket No. FDA-2013-P-0119 (Jan. 29, 2013).

[16] Letter from Janet Woodcock, Director, Center for Drug Evaluation and Research (CDER), to David M. Fox, Theodore M. Sullivan, Edward J. Allera, and Joy J. Liu, Docket Nos. FDA-2013-P-0058, FDA-2013-P-0119, and FDA-2013-P-0471 (Feb. 21, 2014) (consolidated response).

[17] Id. at 17.

[18] A petition for reconsideration was submitted on behalf of Ferring asking the Agency to reconsider its Feb. 21, 2014, decision denying Ferring's request for 5-year NCE exclusivity for Prepopik. That petition for reconsideration was also denied. See letter from Leslie Kux, Assistant Commissioner for Policy, to David M. Fox and Edward J. Allera, Docket Nos. FDA-2013-P-0058 and FDA-2013-P-0119 (Oct. 10, 2014).

for industry on *New Chemical Entity Exclusivity Determinations for Certain Fixed-Combination Drug Products* in October 2014.[19]

D. ***Ferring Pharmaceuticals, Inc. v. Burwell***

On June 1, 2015, Ferring filed suit in the U.S. District Court for the District of Columbia, challenging FDA's citizen petition response, and arguing that 1) FDA's prior interpretation was contrary to the plain meaning of the FD&C Act; 2) even if the relevant statutory provisions were ambiguous, FDA's prior interpretation was unreasonable; and 3) even if the prior interpretation was permissible, FDA's refusal to apply the October 2014 interpretation retroactively to Prepopik was arbitrary and capricious.[20]

The District Court issued a Memorandum Opinion on March 16, 2016, granting summary judgment in favor of FDA, and upholding FDA's pre-October 2014 interpretation of the 5-year NCE exclusivity provision as applied to fixed-combinations approved before FDA changed its interpretation.[21] The District Court did not resolve the question of retroactive application of FDA's new interpretation but instead ordered additional briefing on that issue. Ferring moved for reconsideration on certain factual matters, arguing that the District Court's March 16, 2016, opinion had left open the possibility that FDA's decision that Prepopik was ineligible for 5-year NCE exclusivity was arbitrary and capricious. Ferring argued that the scenario that the District Court had considered hypothetically was in fact true: "If there were, in fact, situations in which a drug was eligible for five-year exclusivity under the FDA's prevailing interpretation but failed to receive it because of the order in which it was approved, those circumstances might render the FDA's [prior] policy arbitrary and capricious."[22]

In a subsequent opinion dated September 9, 2016, the District Court granted Ferring's motion for reconsideration, concluding "that there is good reason to correct a clear error in its prior opinion, that Ferring would be harmed by the District Court's failure to do so, and that Ferring's motion for summary judgment should have been granted."[23] On reconsideration, rather than ruling on the question of retroactivity, or its previous ruling that FDA's longstanding interpretation was reasonable, the District Court concluded that Ferring had provided examples in its motion for reconsideration showing that the temporal sequence of approval was outcome determinative under FDA's prior interpretation, thus rendering that interpretation arbitrary and capricious.[24]

The District Court explained:

> The relevant point is that certain drug substances received a five-year period of marketing exclusivity—in which later fixed-combination drug products that included those drug substances were able to share, as a consequence of the umbrella policy—while others were denied the same marketing exclusivity period because a fixed-combination drug product was

[19] See http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

[20] See footnote 4.

[21] No. 1:15-cv-00802 (D.D.C. Mar. 16, 2016) (March 2016 Opinion) at 15-18.

[22] March 2016 Opinion at 28; see also Sept. 2016 Opinion at 17.

[23] Sept. 2016 Opinion at 22-23.

[24] Sept. 2016 Opinion at 21-22.

approved first.[25]

The District Court continued: "If a drug substance is sufficiently novel to warrant protection under a five-year exclusivity period—and sufficiently novel that other products containing that drug substance should also be protected through the umbrella policy—it is not apparent why timing, or the order in which the drugs were approved, should alter that assessment."[26] In summary, the District Court concluded that because FDA had not justified the outcome-determinative role the order of approval seemed to play, in certain circumstances, when its pre-October 2014 interpretation was applied, that prior interpretation was arbitrary and capricious.[27] The District Court then remanded the matter to FDA "for further proceedings not inconsistent with [the] opinion."[28]

The government filed a Notice of Appeal with the U.S. Court of Appeals for the District of Columbia Circuit on November 7, 2016. On March 14, 2017, the government filed an Unopposed Motion for Voluntary Dismissal of this appeal, and the order dismissing the appeal was issued on March 17, 2017.[29]

E. FDA's Analysis of Sodium Picosulfate as an NCE

In determining whether a drug product is eligible for 5-year NCE exclusivity, FDA's analysis begins with the chemical structure of each drug substance (or active ingredient) in the drug product. The Agency starts with the molecule that comprises that drug substance in the drug product, and excludes the ester and salt-bonded portions of the molecule (consistent with the statutory language stating that "no active ingredient (including any ester or salt of the active ingredient . . .)" is eligible for 5-year NCE exclusivity). Once the portions of the molecule comprising esters, salts, and other non-covalent derivatives of a drug substance are excluded, the molecule or ion that remains will be considered the active moiety.[30]

A drug substance (or active ingredient) is considered an NCE if it does not contain a molecule or ion that has been previously approved as an active moiety.[31] FDA applied this interpretation of the 5-year NCE

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[25] Id. In the preamble to the proposed rule for 21 CFR 314.108, FDA explained that after a drug product becomes eligible for 5-year NCE exclusivity, certain later-approved drug products that contain the same active moiety would also benefit from the original product's 5-year NCE exclusivity until the exclusivity period for the original product expired. See Abbreviated New Drug Application Regulations, Proposed Rule, 54 FR 28872, 28898-28899 (July 10, 1989). Under the "umbrella policy," 5-year NCE exclusivity does not benefit only the first approved drug product that was eligible for 5-year NCE exclusivity, but also benefits the line of products containing the same active moiety. Such subsequent drug products will be protected in the same way as the first approved drug product for the balance of the 5-year period, which runs from the date of approval of the first approved drug product. As the District Court acknowledged in its initial opinion, "[b]ecause the FDA did not 'believe the Congress intended the exclusivity provisions to discourage innovators from making improvements in their drug products nor from authorizing the marketing of competitive products,' the FDA concluded that the 'broader interpretation of the scope of exclusivity [the umbrella policy] should be applied.'" Sept. 2016 Opinion at 9.

[26] Sept. 2016 Opinion at 22.

[27] Id.

[28] Id. at 23.

[29] Order, Ferring Pharms. Inc. v. Price, No. 16-5326 (D.C. Cir. March 17, 2017).

[30] See 21 CFR 314.3(b) for definition of active moiety.

[31] In fact, a drug substance is considered an NCE even if it contains a molecule that can be metabolically converted to a previously approved active moiety. What matters is whether the active moiety as a whole has not been previously approved.

exclusivity provisions in its decision to recognize 5-year NCE exclusivity for Vyvanse (lisdexamfetamine dimesylate) Capsules. FDA's "structure-centric" approach was upheld in *Actavis Elizabeth LLC v. FDA*.[32]

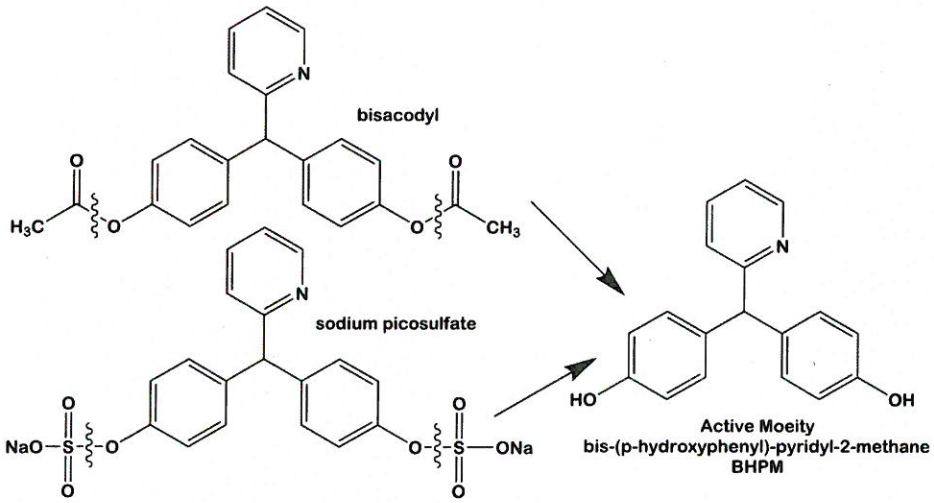

Figure 1: Compare chemical structure of bisacodyl and sodium picosulfate

At the time the Prepopik application was submitted, the Agency determined that sodium picosulfate was a new molecular entity[33] (NME).[34] It was believed that picosulfate was the active moiety of the drug substance sodium picosulfate, and that this active moiety had not been previously approved by FDA. It is not clear from the administrative record how the Agency determined that sodium picosulfate was considered to be an NME, as no documentation of a structural analysis of this active ingredient has been found. Upon further evaluation of the structure of sodium picosulfate during FDA's consideration on remand, the Agency determined that sodium picosulfate is the di-sodium salt of a di-sulfate derivative of bis-(p-hydroxyphenyl)-pyridyl-2-methane (BHPM) (Figure 1). After excluding the salt and ester portions of sodium picosulfate, as FDA's regulations require, what remains is BHPM. Therefore, BHPM is the active moiety in sodium picosulfate. BHPM is also the same active moiety as that of the drug substance bisacodyl, which was approved years before Prepopik.[35]

In reaching this decision, the Agency considered whether a di-sulfate derivative is an "ester" derivative from both a scientific and regulatory standpoint. Under standard scientific definitions, picosulfate is an ester of sulfuric acid.[36] Esters are substances that result from the splitting-out of water from combining an

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[32] *Actavis Elizabeth LLC v. FDA*, 625 F.3d 760 (D.C. Cir. 2010).

[33] See e.g., July 16, 2012, memorandum from Terrance Ocheltree, available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2012/202535Orig1s000ChemR.pdf.

[34] NME is a distinct term from NCE. The differences are both substantive and historical, but do not bear analyzing here since, for the purposes of this letter, there are no substantive differences between an NME (which FDA uses to classify certain applications when they are submitted) and an NCE (which determines whether an approved drug is eligible for 5-year NCE exclusivity.

[35] See e.g., NDA 021551 for Halflytely (bisacodyl; polyethylene glycol 3350; potassium chloride; sodium bicarbonate; sodium chloride), approved on May 10, 2004.

[36] See e.g., Hawley's Condensed Chemical Dictionary 13th ed., Richard J. Lewis, New York: Van Nostrand (1997); IUPAC, Compendium of Chemical Terminology, 2nd ed. (the "Gold Book"), compiled by A. D. McNaught and A. Wilkinson, Blackwell Scientific Publications, Oxford (1997), XML on-line corrected version: http://goldbook.iupac.org (2006-) created by M. Nic, J.

alcohol and an acid, where the acid may be organic (e.g. acetic acid) or inorganic (e.g. sulfuric acid). FDA treats the combined product of an alcohol and sulfuric acid, like sodium picosulfate, as an ester.[37] Finally, throughout the NDA for Prepopik, Ferring identified sodium picosulfate as an "ester".[38]

II. DISCUSSION

In light of the District Court's opinion, FDA has reconsidered whether Prepopik is eligible for 5-year NCE exclusivity. Upon further review of the administrative record, the Agency has determined that Prepopik was not eligible for 5-year NCE exclusivity under either interpretation of the statute, because it does not contain a drug substance with no previously approved active moiety. Despite the Agency's prior statements that sodium picosulfate was an NME and an NCE, it is now evident that those statements were incorrect because this drug substance contained a previously approved active moiety when it was approved in Prepopik. As explained above, in evaluating the structure of sodium picosulfate, the Agency has determined that the active moiety of sodium picosulfate is not picosulfate, but BHPM, which was previously approved in bisacodyl.

Ferring claims that FDA has recognized that esters contain a central carbon atom or a central atom that is "usually" carbon.[39] Ferring further states that, to its knowledge, "FDA has never described the term 'ester' as including functional groups with a central sulfur atom."[40] However, contrary to Ferring's assertions, FDA, in accordance with established scientific principles, has not limited the term ester to only those molecules derived from an organic acid, i.e., molecules that contain a central carbon atom, but one that also includes molecules derived from inorganic acids. Specifically, the Agency has considered organosulfates to be sulfur-centric esters.[41] Further, Ferring's own NDA submission for Prepopik recognizes and identifies sodium picosulfate as an ester.

Previously, the Agency incorrectly believed that Prepopik contained a drug substance that had not been previously approved in the US, and was thus an NME. FDA regrets this error and apologizes for informing Ferring of this determination almost 5 years after Prepopik's approval and after litigation related to the exclusivity determination. However, under the applicable regulations,[42] the Agency must evaluate the chemical structure of each drug substance in a drug product. If a drug substance contains a previously approved active moiety, it is not an NCE. If none of the drug substances in a fixed-combination is an NCE,

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Jirat, B. Kosata; updates compiled by A. Jenkins. ISBN 0-9678550-9-8, available at http://goldbook.iupac.org/html/E/E02219.html.

[37] See e.g., NDA 017856, Topicort (Desoximetasone) Ointment ("Studies with other similarly structured steroids have shown that predominant metabolite reaction occurs through conjugation to form the glucuronide and sulfate ester") available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2004/17856slr024,18309slr013_topicort_lbl.pdf; see also, NDA 016042, Dyazide (hydrochlorothiazide/triamterene) Capsules, available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/016042s078lbl.pdf.

[38] See e.g., Module 3.2.S.1.1.6. Nomenclature – sodium picosulfate, Other non-proprietary name(s).

[39] Letter from David M. Fox and Susan M. Cook, counsel for Ferring Pharmaceuticals, Inc., to Kendra Stewart, Orange Book Staff in Center for Drug Evaluation and Research (May 10, 2017), at 8.

[40] Id.

[41] See footnote 37.

[42] See 21 CFR 314.3 & 314.108.

then that drug product will not be eligible for 5-year NCE exclusivity. Upon further review on remand, FDA has concluded that each drug substance in Prepopik contained a previously approved active moiety and none is an NCE. Thus, Prepopik is not eligible for 5-year NCE exclusivity under either the Agency's pre-October 2014 interpretation or the new interpretation put forth in October 2014.

III. CONCLUSION

For the reasons described above, FDA concludes that Prepopik is not eligible for 5-year NCE exclusivity, because it did not contain a drug substance with no previously approved active moiety when it was approved in 2012. Prepopik was eligible for 3-year exclusivity, which expired on July 16, 2015. In light of this conclusion, the exclusivity designation for Prepopik will remain unchanged in the *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book).

Sincerely,

Kathleen Uhl M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Cc: David Fox, Hogan Lovells US LLP
Susan Cook, Hogan Lovells US LLP