No. 2009-1393

IN THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

PHOTOCURE ASA,

Plaintiff-Appellee,

v.

JOHN J. DOLL, ACTING UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY and ACTING DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE,

Defendant-Appellant.

Appeal from the United States District Court For the Eastern District of Virginia in Case No. 08cv718, Judge Liam O'Grady

REPLY BRIEF FOR DEFENDANT-APPELLANT

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REPLY BRIEF FOR DEFENDANT-APPELLANT

INTRODUCTION AND SUMMARY OF ARGUMENT

This case involves a challenge to the denial of a patent term extension application by the United States Patent and Trademark Office (USPTO) under 35 U.S.C. 156. The denial of the application ultimately rests on the USPTO's conclusion that the term "active ingredient" in 35 U.S.C. 156(f) means "active moiety." This Court interpreted "active ingredient" in Section 156(f) in precisely the same way in *Pfizer Inc. v. Dr. Reddy's Laboratories, Ltd.*, 359 F.3d 1361 (Fed. Cir. 2004), and *Pfizer* controls the outcome of this appeal. But even if the

meaning of "active ingredient" had not been resolved by *Pfizer*, the agency's interpretation of the term would be entitled to prevail, because it accords with the text, legislative history, and congressional purpose of the patent term extension provision, as well as the Food and Drug Administration's (FDA's) interpretation of the same term when it appears in the same context elsewhere in the Hatch-Waxman Act.

1. Photocure contends that the meaning of "active ingredient" is governed by *Glaxo Operations UK Limited v. Quigg*, 894 F.2d 392 (Fed. Cir. 1990), rather than by *Pfizer*. But *Glaxo* never addressed the meaning of "active ingredient," nor did it have any occasion to do so, because the parties in that case had agreed on the identity of the active ingredient and litigated the appeal based on that common understanding.

Photocure does not (and cannot) point to any passage in the *Glaxo* opinion where the Court defines "active ingredient," as the Court explicitly did in *Pfizer*. Rather, Photocure contends that *Glaxo implicitly* addressed the meaning of "active ingredient." But this Court has repeatedly held that "the disposition of an issue by an earlier decision does not bind later panels of this court unless the earlier opinion *explicitly* addressed and decided the issue." *Union Elec. Co.* v. *United States*, 363 F.3d 1292, 1297 (Fed. Cir. 2004) (emphasis added). Thus, even if

Photocure were correct (which it is not) that *Glaxo* addressed the meaning of "active ingredient" *sub silentio*, *Glaxo* would not have any precedential force with respect to that issue in later litigation.

Pfizer is the only decision of this Court to have addressed the term "active ingredient" in Section 156, and it holds that the term means "active moiety," which is what the USPTO decided here. Had *Glaxo* actually defined "active ingredient," *Pfizer* would not have been at liberty to reach a different conclusion. The fact that *Pfizer* never mentions *Glaxo* in the course of its analysis, including in Judge Mayer's dissent, despite the fact that the parties' briefs argued at length over the relevance of *Glaxo*, demonstrates that *Pfizer* understood *Glaxo* not to have reached the "active ingredient" issue. Photocure argues that *Pfizer*'s definition of "active ingredient" is "arguably dicta," but as we demonstrate below, there is no merit to that argument. Therefore, *Pfizer* is the controlling decision.

2. Only if the Court finds that neither *Pfizer* nor *Glaxo* governs will it need to address the merits of the parties' arguments regarding the meaning of "active ingredient" in 35 U.S.C. 156(f). In that case, the USPTO's interpretation should be approved by this Court, for the term "active ingredient" is ambiguous, and the agency's interpretation of that term as meaning "active moiety" is persuasive in light of the statutory language and context, legislative history, and public policy.

The core of the agency's argument is that the statute does not expressly define "active ingredient"; that, in the context of the phrase "active ingredient * * * including any salt or ester of the active ingredient," "active ingredient" is most appropriately construed to mean "active moiety"; that the FDA interprets virtually identical language in the market exclusivity provisions of the Hatch-Waxman Act the same way; and that interpreting "active ingredient" to mean "active moiety" comports with the legislative history demonstrating that Congress's intention was to provide additional incentives for only genuinely innovative drugs.

In contrast to interpreting "active ingredient" in the context of Section 156 as the USPTO does, Photocure argues primarily that various words in Section 156(f), such as "active ingredient," had well-defined meanings prior to the enactment of the Hatch-Waxman Act and outside the text of that statute. But, the critical issue in this case is the meaning of "active ingredient," not in isolation, but rather as used in the statutory phrase, "active ingredient * * * including any salt or ester of the active ingredient * * *." That phrase was used for the first time in the Hatch-Waxman Act and thus had no well-defined meaning prior to that time. Accordingly, the sources relied upon by Photocure, all of which predate the Hatch-

Waxman Act, do not carry the weight Photocure assigns to them and do not undercut the agency's interpretation.

ARGUMENT

A. *Pfizer* Governs The Outcome In This Case.

1. In *Pfizer*, this Court squarely addressed the meaning of "active ingredient" in 35 U.S.C. 156 and held that it means "active moiety." 359 F.3d at 1365-66; see Opening Br. at 19-21. In no prior case had this Court addressed the meaning of "active ingredient" in Section 156. As a matter of *stare decisis*, therefore, *Pfizer* governs the outcome of this appeal and compels reversal of the district court's decision, which is predicated on that court's view that "active ingredient" does *not* mean "active moiety."

Photocure argues that *Pfizer*'s definition of "active ingredient" is "arguably dicta." Photocure Br. at 27. First, Photocure argues that *Pfizer* dealt with rights under 35 U.S.C. 156(b), not patent term extension under 35 U.S.C. 156(a)(5)(A). *Ibid.* But Section 156(f), by its very terms, states that the definition of "active ingredient" applies to all of Section 156, which makes Photocure's purported distinction meritless. See 35 U.S.C. 156(f)(1) ("For purposes of *this section* * * * [t]he term 'product' means * * * ") (emphasis added); *id.* § 156(f)(2) ("For

purposes of *this section* * * * [t]he term 'drug product' means * * * ") (emphasis added).

Second, Photocure makes a highly reticulated argument that *Pfizer* contained two holdings, one of which depended on the "active ingredient" determination and one of which did not, and that the latter holding, by itself, was sufficient for the Court to rule in Pfizer's favor. Photocure Br. at 28-30. The problem with the argument is that the "second holding" is not a holding at all. See Photocure Br. at 29 (quoting *Pfizer*, 359 F.3d at 1366). What Photocure characterizes as the second holding is actually the Court's discussion of an argument made by Dr. Reddy's (the other party in *Pfizer*). It is clear that the Court is merely reciting Dr. Reddy's argument, not adopting it, because in the next three sentences of the opinion the Court rejects that argument, making clear that the meaning of "active ingredient" in Section 156(f) was critical to the Court's conclusion that Dr. Reddy's product would infringe Pfizer's patent as extended by the USPTO. See *id.* at 1366 ("That provision does not contain any limitation regarding the form of the product subject to the extension. In fact, § 156(f) clearly provides otherwise, in defining the term 'product' as 'including any salt or ester of the active ingredient.' Thus, Dr. Reddy's attempt to limit the extension to the

specific approved salt on the basis of the 'rights derived' provision of § 156(b) to the approved product is unsound.").[1]

Finally, Photocure tries to distinguish *Pfizer* on the ground that it was "heavily influenced" by the fact that Dr. Reddy's had relied on the safety and efficacy data of Pfizer's drug product to support Dr. Reddy's request for approval of its own drug product. Photocure Br. at 30 n.11. But *Pfizer*'s holding was not dependent on, or confined to, that factor. Rather, the Court was simply making the important point that reading "active ingredient" to mean "active moiety" comports with Congress's goal of rewarding innovation. See 359 F.3d at 1365-66.[2]

2. Photocure contends that *Glaxo*, rather than *Pfizer*, is the controlling decision. Photocure Br. at 16-22. That argument suffers from several basic weaknesses.

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[1] Furthermore, the briefs in *Pfizer* demonstrate that the Court's resolution of the meaning of "active ingredient" was central to the decision because the parties fought hard over whether *Glaxo* addressed that issue. See Opening Br. at 23-24.

[2] In an apparent effort to avoid the point about rewarding innovation, Photocure suggests that Metvixia required research beyond that which the pioneer manufacturer conducted and also represented a therapeutic improvement over Levulan. Photocure Br. at 11-13, 30 n.11. That claim, which the USPTO did not consider to be "verified" (A748), may be important in the context of patentability, but has no bearing on the statutory interpretation question presented here.

First, Photocure is unable to identify any passage in *Glaxo* where the Court actually set out a definition of "active ingredient." The absence of any such discussion is unremarkable, because it is indisputed that the parties in *Glaxo* had agreed on the identity of the active ingredient, so the Court did not have to address the meaning of the term. See Opening Br. at 21-24; *Glaxo*, 894 F.2d at 394 ("It is undisputed that cefuroxime axetil is the active ingredient of CEFTIN tablets."). See also Photocure Br. at 24 (acknowledging that "the parties may have agreed on the identity of the 'active ingredient'"). As a result of the agreement as to the active ingredient, the parties and the Court focused on the term "product," not "active ingredient," and on whether Glaxo's product (cefuroxime axetil, which is the ester of cefuroxime) had previously received FDA approval. No one, including the Court, focused on whether the "active ingredient" — meaning "active moiety" — had previously received such approval.[3] See Opening Br. at 21-23; *Glaxo*, 894 F.2d at 394 ("The Commissioner * * * argues that 'product' was not intended by Congress to have a literal meaning * * *"); and see Photocure Br. at 18 (same). In fact, *Glaxo* addressed only whether the USPTO was correct

[3] This indisputable point completely rebuts Photocure's contention that nothing in *Glaxo* suggests that the parties' arguments focused solely on whether the FDA had previously approved Glaxo's "precise product" — or any salt or ester of that product. Photocure Br. at 25 n.8, quoting Opening Br. at 22.

that Congress intended "product" to mean "any 'new chemical entity,'" that is, whether the term "product" meant "'new active moiety * * *.'" 894 F.2d at 394.[4]

In an effort to overcome the indisputable point that *Glaxo* does not define "active ingredient," Photocure argues that *Glaxo* is controlling because its facts are "virtually identical" to those at issue here (Photocure Br. 17) and because the position of the USPTO in both cases is "substantively identical" (*id.* at 18, 19). However, the USPTO's position on appeal in *Glaxo* in 1990 was vastly different from its position here. As noted in the USPTO's opening brief (at 22), the USPTO's position in *Glaxo* was that cefuroxime axetil (an ester of cefuroxime) was the active ingredient, whereas under USPTO's current construction of "active ingredient," the active ingredient in *Glaxo* would have been cefuroxime, the underlying molecule of that ester. The difference is critical because a focus on the phrase, "active ingredient * * * including any salt or ester of the active

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[4] Photocure also claims that the USPTO's current position that *Glaxo* did not address the meaning of "active ingredient" is undercut by a statement in a different patent term extension application in which the USPTO stated that "'Glaxo must be treated as overruled'" by *Pfizer*. Photocure Br. at 25 (quoting A855). First, that statement was not made in this case and therefore has no relevance to the current analysis. Second, even if the statement were considered, it does *not* state, or even suggest, that *Glaxo* established that "active ingredient" does *not* mean "active moiety.

ingredient," as a whole is necessary to determine whether the "product" at issue previously received FDA approval.

Photocure also suggests that, when *Glaxo* observed that "active ingredient" and other terms "had well-defined, ordinary, common meanings when Congress enacted the Act," the Court was implicitly addressing the meaning of "active ingredient" in Section 156(f). Photocure Br. at 19-20 (quoting 894 F.3d at 395), and *id.* at 23. The bare reference to pre-Hatch-Waxman definitions of "active ingredient" falls well short of being even an implicit holding about the meaning of that term in Section 156(f) itself. Moreover, this Court has "repeatedly held that the disposition of an issue by an earlier decision does not bind later panels of this court unless the earlier opinion *explicitly* addressed and decided the issue." *Union Elec. Co.*, 363 F.3d at 1297 (emphasis added). Photocure does not claim that *Glaxo* explicitly resolves the meaning of "active ingredient"; to the contrary, it concedes that the opinion does not do so. See Photocure Br. at 21 ("Although *not explicitly stated in the opinion*, the plain meaning was clearly that the ester cefuroxime axetil was the active ingredient in CEFTIN because 'each salt or ester of a therapeutic agent is a unique active drug ingredient.'") (emphasis added).[5] It

[5] In a similar vein, Photocure argues that *Glaxo* addressed the meaning of "active ingredient" because the district court in *Glaxo* addressed that term, and this Court (continued...)

is a "longstanding rule that if a decision does not 'squarely address[ ][an] issue,' a court remains 'free to address the issue on the merits' in a subsequent case." *Boeing North American, Inc.* v. *Roche*, 298 F.3d 1274, 1282 (Fed. Cir. 2002) (quoting *Brecht* v. *Abrahamson*, 507 U.S. 619, 631 (1993)). As a result, nothing in *Glaxo* constrained this Court when it expressly addressed the meaning of "active ingredient" in *Pfizer*, nor does *Glaxo* govern this Court's disposition of that issue in this appeal.

B. Even if *Pfizer* Does not Control, the USPTO's Interpretation is Persuasive and Should be Upheld.

If the Court were to find that neither *Pfizer* nor *Glaxo* controls, it would have to address the meaning of "active ingredient" in Section 156 as a matter of first impression. As used in the context of Section 156(f), "active ingredient" is ambiguous, and the statute itself does not define the term. The core of the agency's position is that (1) in the context of the phrase "active ingredient * * *

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[5](...continued)
subsequently "endorsed" the district court decision. See Photocure Br. at 23 n.7 (citing *Glaxo Operations UK Limited v. Quigg*, 706 F. Supp. 1224, 1227 (E.D. Va. 1989), *aff'd* 894 F.2d 392 (Fed. Cir. 1990)). The argument on its face concedes that *this* Court did not actually address the meaning of "active ingredient." In any event, the Federal Register entries cited in *Glaxo* for the proposition that "active ingredient" had a well-defined meaning prior to enactment of the Hatch-Waxman Act, address a more limited phrase (*e.g.*, "identical active drug ingredient") than is at issue here. See 44 Fed. Reg. 2932, 2938 (1979) (col. 1); 45 Fed. Reg. 72,582, 72,591 (1980) (col. 3).

including any salt or ester of the active ingredient," it is reasonable to interpret "active ingredient" to mean "active moiety" (Opening Br. at 24-26); (2) the FDA interprets virtually identical language in the market exclusivity provisions of the Hatch-Waxman Act the same way (*id.* at 26-29); and (3) interpreting "active ingredient" to mean "active moiety" comports with the legislative history demonstrating that Congress's intention was to provide additional incentives only for genuinely innovative drugs (*id.* at 31-34). For these reasons, the agency's interpretation is a persuasive one that is entitled to *Skidmore* deference. See *id.* at 24 n.8 and, *infra*, a pp. 24-26.

1. Section 156(f) defines "drug product" to mean "the active ingredient * * *, including any salt or ester of the active ingredient," but does not define the term "active ingredient" itself. Parsing the language of Section 156(f), the USPTO concluded that the definition of "drug product" encompasses three categories of molecules: (1) a non-salified and non-esterified form of a molecule, (2) any salt of that molecule; and (3) any ester of that molecule. See Opening Br. at 24-25, citing A743. The agency interpreted "active ingredient" to refer to the first category of molecule, which is the "active moiety" of the drug — the pharmacologically active molecule to which components can be added to make it a salt or ester. *Ibid.*

Photocure argues that the agency bases its interpretation on the theory that "there is a salt and an ester of each active ingredient." Photocure Br. at 37-38. But, as the foregoing demonstrates, the agency's interpretation does not rest on that premise. Instead, it is based on a strict adherence to the words of the statute, which permit but do not require an active ingredient to have a salt and an ester form. The agency has never taken the position that there must be a salt or ester of every active ingredient. Indeed, as Photocure itself observed, there are some active ingredients that cannot be formulated as a salt or an ester "because they lack the necessary chemical group." Photocure Br. at 38. Nor does the USPTO rely on the theory that "one cannot have a salt or ester of a compound that is itself a salt or ester." Photocure Br. at 38.[6] The agency has all along understood that Metvixia (MAL HCl) is an ester of a salt. See A745 & A746 (noting that Metvixia is an ester of ALA hydrochloride); see also A4 n.2 (same).

2. Although it is indisputable that the statute does not provide a definition of "active ingredient," Photocure claims that the meaning of the term is clear and unambiguous, citing two FDA regulations, two Federal Register notices cited in *Glaxo*, and a dictionary definition of the word "ingredient" also cited in *Glaxo*.

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[6] Contrary to Photocure's contention, we do not think we implied that *Pfizer* had adopted this theory either. See Photocure Br. at 38 n.17 (citing Opening Br. at 15, 19-20).

See Photocure Br. at 32-33 & nn.12-15. All of these sources, however, are irrelevant, because all of them define the term "active ingredient" in isolation. None of them addresses "active ingredient" in the specific context in which it is used in Section 156(f), *i.e.*, "active ingredient * * * including any salt or ester of the active ingredient." The critical inquiry in this case is what the term means in that specific statutory context. Thus, there was no well-defined, unambiguous meaning for "active ingredient" in the context in which it appears in Section 156(f). See Opening Br. at 25-26, citing *United States v. Santos*, 128 S. Ct. 2020, 2024 (2008) ("context gives meaning"); and *Fort Stewart Schools v. Federal Labor Relations Authority*, 495 U.S. 641, 645-46 (1990) ("[the term in question] is not in isolation, but forms part of a paragraph whose structure, as a whole, lends support to the [agency's] * * * reading.").

For the same reason, it does not help Photocure's cause to argue that "active moiety" had a well-defined meaning prior to enactment of the Hatch-Waxman Act and that Congress's decision not to use that term is significant. Photocure Br. at 40-41. The legislative history of Section 156 (see Opening Br. at 31-32) is silent as to why Congress chose certain words over others. And just because Congress included the term "active ingredient" instead of "active moiety" in Section 156(f)

does not prove that Congress did not intend to define "active ingredient" to mean "active moiety."

Photocure's reliance on the FDA's regulations at 21 C.F.R. 210.3(b)(7) (1979) and 21 C.F.R. 60.3(b)(2) (1986) (Photocure Br. at 32, 43-44), ignores the FDA's later and more germane interpretation of the market exclusivity provisions of the Hatch-Waxman Act where the FDA interpreted "active ingredient" to mean "active moiety" in a phrase virtually identical to the phrase in Section 156(f). See Opening Br. at 27-28 (discussing 59 Fed. Reg. 50338, 50357-38 (1994)).[7] Photocure gives particular emphasis to 21 C.F.R. 60.3(b)(2), a regulation adopted by the FDA in 1986 that construed "active ingredient" in Section 156(f) and did not define it in terms of "active moiety." Photocure Br. 43-44; see also *id.* at 45 (citing informal "FAQ" on the FDA web site regarding the meaning of "active ingredient" in Section 60.3(b)(2)). But that regulation does not refer to, or otherwise take account of, the "including any salt or ester" clause. See Opening Br. at 27-28 and *id.* at 29 n.9. And, as just noted, when FDA subsequently did address the meaning of "active ingredient" in connection with the salt/ester clause

[7] 21 U.S.C. 355(j)(5)(F)(ii), for example, provides non-patent related market exclusivity "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 subsection (b) of this section * * *." See also Opening Br. at 9.

in the agency's 1994 rulemaking regarding the Hatch-Waxman marketing exclusivity provisions, the FDA expressly concluded that "active ingredient" *does* mean "active moiety" when used in that context. See Opening Br. at 27-28, quoting 59 Fed. Reg. at 50357-58. The interpretation arrived at in that rulemaking, rather than the approach adopted almost a decade earlier in Section 60.3(b)(2) (or in the informal "FAQ" discussing Section 60.3(b)(2)), represents FDA's prevailing interpretation of "active ingredient" as it is actually used in a context like the one found in Section 156(f). As a result, Photocure's further contention that "active ingredient" would have to be interpreted to mean "active moiety" in "all portions of the statute" (Photocure Br. at 37) is without merit because it clearly misses the distinction between "active ingredient" in the context of Section 156(f) (where the term appears in the larger phrase) and "active ingredient" in other contexts (where the term appears in isolation).

Photocure appears to suggest that if FDA's views regarding the meaning of "active ingredient" in Section 156(f) had changed as a result of the 1994 rulemaking, the agency would have amended 21 C.F.R. 60.3(b)(2) to reflect the change in its position. Photocure Br. at 44-45. A formal revision by the FDA of the regulation might or might not have been desirable, but it was clearly unnecessary for the interpretive task at hand. Because 35 U.S.C. 156(e)(1)

delegates to the USPTO, alone, the authority to decide patent term extension applications, the USPTO has never argued that the FDA's regulations are controlling.[8] The USPTO's position all along has simply been that the FDA regulations are relevant to the extent they provide persuasive support for the precise statutory issue presented in this case. In that regard, only the FDA's 1994 Federal Register notice has any relevance because only that statement has addressed language virtually identical to Section 156(f)). And that position remains in effect today; no drug manufacturer has directly challenged the FDA's regulatory approach in litigation in the intervening fifteen years. See Opening Br. at 28.

3. Photocure argues that only its interpretation makes sense of the "including" clause. Photocure Br. at 39. But USPTO's interpretation does, too. As a textual matter, if "active ingredient" is understood to mean active moiety, it is entirely coherent to speak of salts and esters of the active moiety. Reading "active ingredient" in this fashion means that "drug product" encompasses (1) the non-salified and non-esterified form of a molecule, and also "include[s]" (2) any salt of

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[8] In making patent term extension determination, the USPTO only seeks confirmation from the FDA.

that molecule and (3) any ester of that molecule. See A743 (USPTO Final Decision).

In any event, Photocure's definition produces an illogical result. Photocure says that, under its definition, the "including" clause would serve to "'add' (i) salts to the definition of 'product' when the 'active ingredient' is an ester, (ii) esters to the definition of 'product' when the 'active ingredient' is a salt, and (iii) salts and esters to the definition of 'product' when the 'active ingredient' is an acid." Photocure Br. at 39-40. But Photocure's definition would also mean that "esters of esters" and "salts of salts" would be possible, and yet Photocure fails to discuss or account for this difficulty in its definition.

4. Photocure does not dispute that an important congressional purpose for enacting the patent term extension provisions was to provide additional incentives for innovative research. See Opening Br. at 31-32. Instead, Photocure argues that the legislative history is irrelevant because the statute is clear. Photocure Br. at 46-47. But as we have already shown, "active ingredient" is not a self-explanatory term, nor does it have a settled meaning in the context in which it appears in Section 156(f). Because the text of Section 156(f) does not resolve the meaning of "active ingredient," resort to the legislative history to shed light on what Congress meant is entirely proper. See *Merck & Co., Inc. v. U.S.*, 499 F.3d 1348, 1355 (Fed.

Cir. 2007) ("[I]f the bare language of the statute fails to provide adequate guidance * * *, the court must resort to the purpose and legislative history of the statute to determine the intent of Congress in enacting the statute.") (citation and internal quotation marks omitted). And, in this regard, the USPTO looks to legislative history to confirm its interpretation, not to supplant the words of the statute. See, *e.g.*, *Chamberlain Group, Inc. v. Skylink Technologies, Inc.*, 381 F.3d 1178, 1196 (Fed. Cir. 2004) ("Though we do not resort to legislative history to cloud a statutory text that is clear, * * * we nevertheless recognize that words are inexact tools at best, and hence it is essential that we place the words of a statute in their proper context by resort to the legislative history.") (internal quotation marks and citations omitted).

As we pointed out in our opening brief, if "active ingredient" were not construed to mean "active moiety," the eligibility for a patent term extension could turn on the sequence of drug approvals rather than innovation as Congress intended. Opening Br. at 33.[9] Photocure argues that such an "asymmetrical"

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[9] This case is illustrative. Had Metvixia been the earlier approved product and Levulan the latter approved product, Metvixia would have barred extension of a patent claiming Levulan. This is so because (a) the "product" for Levulan under Section 156(f) includes ALA HCl (active ingredient), any salt of ALA HCl (a salt of the active ingredient) and any ester of ALA HCl (an ester of the active ingredient) and (b) Metvixia is an ester of ALA HCl. See, *e.g.*, A4 n.2.

result is what "Congress *may* have intended * * *." Photocure Br. at 47 (emphasis added). But, in *Abbott Labs. v. Young*, 920 F.2d 984, 989 (D.C. Cir. 1990), the D.C. Circuit found no legislative purpose in having the FDA's market exclusivity provisions depend on the sequence of drug approvals: such a result "fails to serve any conceivable statutory purpose." *Ibid.* Photocure's suggestion that obtaining useful salts and esters from an acid is more difficult than the reverse (see Photocure Br. at 47-48) is nothing more than speculation, and Photocure offers no evidence that Congress itself relied on such speculation or desired the resulting "asymmetrical" results.

5. In our opening brief, we explained that the district court was wrong to think that the dictionary definition of "ingredient" supported its "plain language" conclusion, because the court ignored elements of the definition that contradicted its reading and because the elements on which the court did rely would exclude components that are obvious ingredients of a particular product. See Opening Br. at 34-35. Photocure responds by arguing that the aspect of the definition relied on by the district court ("a component part, constituent or element") is more germane than the aspect that the court disregarded ("[s]omething that enters into the formation of a compound or mixture"). That response misses our point. When a word such as "ingredient" has more than one dictionary definition, no single

definition can be held out as the "plain meaning" of the word. And when an agency's interpretation accords with one of the dictionary definitions, as USPTO's does, it can hardly be dismissed as contrary to the "plain meaning" simply because it does not embrace one of the other definitions. Put simply, when a word is defined in more than one way in the dictionary, the dictionary cannot reveal which of the definitions Congress had in mind, or which definition best accords with the overall structure and purpose of the statute.

In our opening brief, we also argued that the active moiety, ALA, "is present [in the final compound] in the form of the particular salt or ester of the moiety." Opening Br. at 35. Photocure argues that *Hoechst-Roussel v. Lehman*, 109 F.3d 756 (Fed. Cir. 1997), "hold[s] * * * that 'th[e] active ingredient must be present in the drug product when administered.'" Photocure Br. at 36, quoting *id.* at 759 n.3. But as we pointed out in our opening brief, this language is dicta, *not* a holding, and, in any event, consistent with our point regarding the presence of ALA. Opening Br. at 35 n.13.

Photocure contends that "there is no compound in Metvixia having the chemical structure of ALA, and thus it is not correct to say that ALA is present in Metvixia." Photocure Br. at 34 n.16. That argument fails, however, because it makes a distinction between esters and salts that the statute does not make. For

example, it is clear that ALA *is* found in the structure of the salt, ALA HCl. See Photocure Br. at 9 (diagram); and A4 (district court "diagram showing the chemical structure for ALA hydrochloride, which reflects *the addition* of HCl") (emphasis added). Thus, this argument cannot succeed because Congress has already made the choice to treat salts and esters the same way, no doubt based on the common understanding that rendering a drug molecule in the form of a salt or ester may modify certain characteristics of the molecule, but generally does not change the basic pharmacologic and therapeutic properties of the molecule. See Opening Br. at 7-9.[10]

Photocure relatedly argues that "it is wrong to say that [Metvixia] * * * ha[s] the same 'activity'" as Levulan, contending that "[Metvixia] has a number of advantages over [Levulan], some of which *arguably* make it have a different 'activity' than ALA HCL." Photocure Br. at 36 (emphasis added). Such anecdotal evidence regarding Metvixia, however, has no force for the statutory interpretation question at issue here. See, *supra*, at n.2. But even if there were some relevance to this anecdotal evidence, Photocure only suggests that it is "arguable" that

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[10] Photocure contends that we "appear[] to concede" that ALA is not in Metvixia. Photocure Br. at 34 n.16 (citing Opening Br. at 14). The portion of our brief that Photocure cites is our recitation of the district court decision, *not* our own argument.

Metvixia has a different activity, and as far as the record is concerned, that fact was not "verified" (A748).

Photocure also argues (Br. at 35-36) that our understanding of "ingredient" would make "intermediates" an ingredient of the drug product, which would be contrary to the district court's conclusion in *Glaxo*, 706 F. Supp. at 1227-28. However, an intermediate does *not* enter into the formation of a compound, which is the dictionary definition of "ingredient." Rather, an intermediate is a momentary compound that is produced during the synthesis of the final compound. See Merriam Webster's Online Dictionary (defining "intermediate" as "a chemical compound synthesized from simpler compounds and usually intended to be used in later syntheses of more complex products" or "a usually short-lived chemical species formed in a reaction as an intermediate step between the starting material and the final product"). Neither Metvixia nor Levulan are "intermediates." Therefore, the USPTO's position on whether an "intermediate" would be an "ingredient" is not relevant to the dispute herein. Opening Br. at 35.

6. Finally, Photocure argues against *Skidmore* deference because, it claims, the USPTO has been inconsistent in its application of Section 156(f). Photocure Br. at 50-51. There is no merit to this argument.

First, Photocure characterizes the agency's final decision as contrary to the position set out in Section 2751 of its Manual of Patent Examining Procedure. Photocure Br. at 50. We fully explained in our opening brief why the Manual provision should not affect *Skidmore* deference, see Opening Br. at 35-37, and there is therefore no need to add any further comment on that issue here.

Second, Photocure contends that the agency reached "inconsistent" decisions as to the identity of the active ingredient in Metvixia in its initial decision versus its final decision. Photocure Br. at 50-51. Review of agency decisions under the Administrative Procedure Act, however, is based on "final agency action," 5 U.S.C. 704, so the fact that agency may have taken a different position at an intermediate level is irrelevant to the validity of the final action. Final agency action exists to correct intermediate errors and to permit the agency to provide a final considered view of the matter. See, *e.g.*, *FTC v. Standard Oil Co.*, 449 U.S. 232, 242 (1980) (the "final agency action" requirement serves to provide the agency with "an opportunity to correct its own mistakes and to apply its expertise").[11]

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[11] Photocure also points to the fact that the FDA, in response to the USPTO's contact, answered that the active ingredient in Metvixia was MAL HCl and that the active ingredient in Levulan was ALA HCl. Photocure Br. at 45. However, what is important is that the FDA ultimately concluded that Metvixia was not the

(continued...)

Third, Photocure claims that the agency has shown inconsistency in its grant of patent term extensions in the period between *Glaxo* and *Pfizer*. See Photocure Br. at 51 & n.27. The agency's grant of extensions for the patents protecting Daunoxome and Etopophos, however, do not establish an inconsistency with the USPTO's decision here. Photocure does not cite any text from any one of the decisions demonstrating the basis for the USPTO's decisions in those cases. Nor could it because the USPTO never articulated such a position. Cf. *Cooper Industries, Inc. v. Aviall Services, Inc.*, 543 U.S. 157, 170 (2004) ("'Questions which merely lurk in the record, neither brought to the attention of the court nor ruled upon, are not to be considered as having been so decided as to constitute precedents.'") (quoting *Webster v. Fall*, 266 U.S. 507, 511 (1925)). In any event, the reason for the agency's claim to *Skidmore* deference *now* is the persuasiveness of the reasoning underlying its current decision, in which the agency carefully explained the basis for its determination that "active ingredient" in Section 156(f) means "active moiety." See pp. 12-13, *supra*. In this regard, contrary to Photocure's argument, the agency's interpretation does not "'run afoul'"

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[11](...continued)
first approval of the product at issue, which could only have been based on the common active moiety of the two products, ALA. See A517.

(Photocure Br. at 50, quoting the district court) of the plain language of the statute but, rather, is entirely consistent with it.

CONCLUSION

For the foregoing reasons and the reasons set forth in our opening brief, the judgment of the district court should be reversed.

Respectfully submitted,

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AUGUST 2009

CERTIFICATE OF SERVICE

I hereby certify that on August 11, 2009, I filed and served the foregoing REPLY BRIEF FOR DEFENDANT-APPELLANT by causing an original and twelve copies to be delivered to the Clerk of the Court by hand delivery and by causing two copies to be delivered to the following counsel as indicated:

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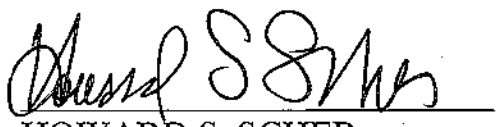

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CERTIFICATE OF COMPLIANCE WITH RULE 32(a)
OF THE FEDERAL RULES OF APPELLATE PROCEDURE

1. Pursuant to Fed. R. App. P. 32(a)(7), I certify that the attached BRIEF FOR DEFENDANT-APPELLANT complies with the type-volume limitation of Fed. R. App. P. 32(a)(7)(B). The brief contains **5,994** words, as counted by Word Perfect 12, excluding the parts of the brief exempted by Fed. R. App. P. 32(a)(7)(B)(iii) and Federal Circuit Rule 32(b).

2. I also certify that this brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6). The brief has been prepared in a proportionally-spaced typeface using Word Perfect 12 in 14-point Times New Roman.

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