EXHIBIT A

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 076596

Marc Goshko
Vice President
Product and Patent Strategy
Legal Affairs
Teva Pharmaceuticals – Americas
425 Privet Road, PO Box 1005
Horsham PA 19044-8005

Dear Mr. Goshko:

This is in further response to your letter of February 29, 2012 (February 29 Letter), addressed to David T. Read of the Food and Drug Administration (FDA), regarding abbreviated new drug application (ANDA) 076596 of Teva Pharmaceuticals USA., Inc., for Modafinil tablets, 100 mg and 200 mg. In your February 29, 2012 Letter you requested that FDA "confirm" that Teva is the sole first applicant entitled to 180-day exclusivity for generic modafinil tablets.

In a letter dated March 28, 2012, the agency sent you a preliminary response, noting that this matter involves novel and complicated legal and factual considerations, and a decision by the agency would be premature at that time. Teva's February 29 Letter addresses just one pertinent issue regarding 180-day exclusivity under section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act (the Act) Act[1] for ANDAs referencing PROVIGIL® Tablets. Our letter of March 28 noted other related issues that needed to be considered before any meaningful decision on Teva's eligibility for exclusivity could be made. Having carefully considered these issues, and because FDA is ready to act on a pending ANDA that has the potential to be delayed from approval only by Teva's eligibility for 180-day exclusivity, FDA is in a position to provide you the following information in response to your February 29 Letter.

New drug application (NDA) 020717 for PROVIGIL Tablets is held by Cephalon, Inc., which as of October 14, 2011, became a wholly owned subsidiary of Teva Pharmaceutical Industries Ltd.[2] Your February 29 Letter sets forth information that you state only recently came to Teva's attention by virtue of the acquisition of Cephalon and access to Cephalon's records. February 29 Letter, at 1. The information from these records pertains to the timing of Teva's certifications in ANDA 076596 to the two patents currently listed for PROVIGIL Tablets in FDA's publication *Approved Drug Products with Therapeutic Equivalence Evaluations*, (the Orange Book).

[1] Because your ANDA was filed before the date of enactment of the Medicare Prescription Drug, Improvement and Modernization Act (MMA) (Public Law 108-173) on December 8, 2003, references herein to the 180-day exclusivity provision are to the section of the Act as in effect prior to December 8, 2003. See MMA § 1102(b)(1).

[2] Teva Pharmaceuticals USA lists "Provigil® (modafinil) Tablets" as one of "Teva's Brand Products." See http://www.tevausa.com/default.aspx?pageid=3452&audience=hcp.

As described in more detail below, we are in basic agreement with the facts as set forth in the February 29 Letter and, in particular, we agree with your conclusion that –

> [N]o applicant other than Teva notified Cephalon of Paragraph IV certifications to *both* listed patents for PROVIGIL on the two dates that respectively would have corresponded to the first valid submission of such certifications to, and receipt of such certifications by, the Agency.

February 29 Letter, at 2 (emphasis in original). For the reasons discussed below, we also agree with your conclusion that Teva alone has 180-day generic drug exclusivity under section 505(j)(5)(B)(iv) of the Act. This claim to sole exclusivity arose when Teva became a first applicant with respect to a patent submitted to FDA and certified to by Teva on December 14, 2007.

Furthermore, we conclude that Teva's 180-day generic drug exclusivity was triggered on March 30, 2012, when Teva began commercial marketing of an authorized generic of PROVIGIL (modafinil) Tablets, and that this exclusivity period will expire on September 26, 2012.

I. Teva Alone Has 180-Day Generic Drug Exclusivity for Modafinil Tablets, 100 mg and 200 mg

A. Factual Background

The NDA for PROVIGIL tablets was approved on December 24, 1998 and was given five-year new chemical entity exclusivity.[3] No patent was submitted with Cephalon's submission of the PROVIGIL® application. Upon approval, no patents were listed for PROVIGIL. In 2001, United States Patent No. RE37,516 (the '516 patent) was listed for PROVIGIL in the Orange Book).[4] The first date on which ANDAs referencing PROVIGIL tablets were eligible for submission was the NCE-1 date, December 24, 2002. On that date, multiple ANDAs referencing PROVIGIL tablets and containing paragraph IV certifications to the '516 patent were submitted. According to information made public by the Federal Trade Commission (FTC), companies submitting ANDAs for modafinil tablets on that date include:

- Teva (Teva)
- Ranbaxy Pharmaceuticals Inc. (Ranbaxy)
- Mylan Pharmaceuticals Inc. (Mylan)
- Barr Pharmaceuticals (Barr)

[3] For a drug with five-year exclusivity, no ANDA may be submitted before the expiration of five years from the date of approval, except that an ANDA may be submitted after the expiration of four years (the NCE-1 date) if it contains a paragraph IV certification to one or more of the listed patents. See section 505(j)(5)(F)(ii) of the Act. For PROVIGIL tablets, the NCE-1 date was December 24, 2002.

[4] The '516 patent was a reissue of U.S. Patent No. 5,618,845, which was listed in the Orange Book for PROVIGIL® in 1999. Also listed in 1999 was U.S. Patent No. 4,927,855 which expired on May 22,2007 and is therefore not relevant to the exclusivity analysis.

In 2003, Cephalon sued Teva, Ranbaxy, Mylan, and Barr for patent infringement of the '516 patent. All four ANDAs were tentatively approved in the 2004-2005 timeframe. Teva's was the last to be tentatively approved, on December 16, 2005.[5] In late 2005 and early 2006, the parties entered into agreements under which Cephalon dismissed its patent infringement suit and each of the ANDA applicants agreed to refrain from marketing its generic products until April 6, 2012. The FTC investigated these agreements as potentially anticompetitive.[6]

On December 14, 2007, Cephalon submitted U.S. Patent No. 7,297,346 (the '346 patent), a later-obtained patent, to its PROVIGIL NDA. Teva submitted a paragraph IV certification to the '346 patent on December 14, 2007, and, in doing so, qualified as a first applicant to this later-listed patent. As indicated in the February 29 Letter, Teva acquired the NDA holder for PROVIGIL tablets, Cephalon, in 2011 (which acquisition apparently was finalized on October 14, 2011).[7] Under the Cephalon NDA, Teva currently markets modafinil both as PROVIGIL tablets and, separately, as an authorized generic.[8]

The FTC reviewed Teva's purchase of Cephalon, and, under a draft FTC decision and order, Teva has agreed to provide to Par Pharmaceuticals adequate supplies to market an authorized generic modafinil product for one year and, at Par's option, for two years.[9] The parties familiar with modafinil ANDAs appear to have operated under the assumption that there are multiple ANDAs that qualify for the 180-day exclusivity for modafinil. FTC expressly referenced this assumption in the December 2011 press release and Federal Register notice announcing the availability of the draft decision and order.[10]

B. Statutory Background

The statutory provision governing 180-day exclusivity states:

> If the application contains a certification described in subclause IV of paragraph (j)(2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection [containing] such a certification, the application shall be made effective not earlier than one hundred and eighty days after -

[5] The basis of the tentative approval was the unexpired period described in sections 505(j)(5)(B)(iii) and 505(j)(5)(F)(ii) of the Act, i.e., 7½ years from the date of approval of Provigil, which would be June 24, 2006.
[6] See *FTC Press Release: FTC Requires Sale of Generic Cancer Pain Drug and Muscle Relaxant as Conditions of Teva's $6.8 Billion Acquisition of Cephalon*, at 1 (Oct. 7, 2011), *available at* http://www ftc.gov/opa/2011/10/tevacephalon.shtm.
[7] See, e.g., London Stock Exchange Aggregated Regulatory News Service, *Immupharma PLC Preliminary Results*, at 1 (Mar. 27, 2012).
[8] See note 2, above. See also Teva Press Release March 30, 2012 announcing Teva's launch of an authorized generic for modafinil tablets, available at http://www.tevapharm.com/Media/News/Pages/2012/1678505.aspx..
[9] See In re. Teva Pharmaceuticals Industries Ltd. and Cephalon, Inc., Decision and Order (Draft), at 33, available at http://www ftc.gov/os/caselist/1110166/111007tevacephalondo.pdf.
[10] See FTC Press Release: FTC Requires Sale of Generic Cancer Pain Drug and Muscle Relaxant as Conditions of Teva's $6.8 Billion Acquisition of Cephalon, available at http://www.ftc.gov/opa/2011/10/tevacephalon.shtm; *Teva Pharmaceutical Industries Ltd. and Cephalon, Inc.; Analysis of Agreement Containing Consent Orders To Aid Public Comment*, 76 Fed. Reg. 64945, 64947 (Teva, Ranbaxy, Mylan and Barr "all filed on the first day that the FDA would accept such an application, making them all eligible for the 180-day marketing exclusivity period provided under the Hatch-Waxman Act. Subsequently, each of the companies agreed with Cephalon to refrain from marketing generic Provigil until April 2012").

> (I) the date the Secretary receives notice from the applicant under the previous application of first commercial marketing of the drug under the previous application, or
>
> (I) the date of a decision of a court in action described in clause (ii) holding the patent which is the subject of the certification to be invalid or not infringed,
>
> whichever is earlier.

Section 505(j)(5)(B)(iv).[11]

The 180-day exclusivity provisions of the Act give the first ANDA applicant to submit a paragraph IV certification challenging a patent an incentive in the form of the opportunity to be the only generic drug manufacturer to compete with the innovator for a 180-day period. *See* Section 505(j)(5)(B)(iv). The statute addresses the effect of an ANDA's exclusivity on *other* ANDAs; it delays the approval of an ANDA containing a paragraph IV certification for a drug "for which a previous [ANDA] has been submitted [containing a paragraph IV] certification" until 180 days after the exclusivity is triggered. *Id*.

C. Development of FDA's Shared 180-Day Exclusivity Approach

One theory under which applicants other than Teva may have believed they were eligible for exclusivity was under a "shared exclusivity" theory. In an August 2, 1999 response to petitions from two generic drug firms addressing the exclusivity issue associated with the approval of ANDAs for cisplatin, FDA stated that, at least with respect to the situation presented in the citizen petitions, the regulations governing 180-day exclusivity should be interpreted to award such exclusivity on a patent-by-patent basis.[12] That is, eligibility for 180-day exclusivity would be based on which company submitted the first paragraph IV certification for each listed patent. Therefore, in cases where multiple patents are listed, multiple ANDA applicants may simultaneously be eligible for 180-day exclusivity.

The agency has recognized, however, that with eligibility for exclusivity determined on a patent-by-patent basis, the agency could be prevented from approving ANDAs referencing a particular drug product by multiple conflicting exclusivities ("mutually blocking exclusivity").[13] An exclusivity stand-off (*i.e.*, A's exclusivity blocks approval of B and B's exclusivity blocks approval of A) whereby each ANDA applicant's approval is delayed indefinitely would be so at

[11] The referenced provision governing paragraph IV certifications at section 505(j)(2)(a)(vii)(IV) states that an ANDA must contain: "a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c)… (IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted."

[12] See Letter fr. J. Woodcock to R. Green, S. Sklar, and K.Beardsley, FDA Docket No. 99P-1271/PSA1 and PSA2, at 4 (Aug. 2, 1999).

[13] See generally, *Proposed Rule: 180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications*, 64 Fed. Reg. 42873, 42875-76 (Aug. 6, 1999), *withdrawn on unrelated grounds*, *Proposed rule; Withdrawal, 180-Day Generic Drug Exclusivity for Abbreviated New Drug Applications*, 67 Fed. Reg. 66593, 66593 (Nov. 1, 2002).

odds with both the narrow purpose of the 180-day exclusivity provision, to reward the first ANDA applicant to challenge a listed patent,[14] and the broader purpose of the Drug Price Competition and Patent Term Restoration Act of 1984 (hereafter "Hatch-Waxman Act"), to encourage generic competition, as to defeat the purpose of the generic drug provisions.[15]

To avoid results that cannot be reconciled with the purposes of the 180-day exclusivity provisions, in particular, and the Hatch-Waxman Act, in general, the agency has taken an approach to "mutually blocking" 180-day exclusivities that both hews as closely as possible to statutory language and is consistent with congressional intent. When different applicants have submitted first paragraph IV certifications to different listed patents and thus become eligible for exclusivity as to different patents, but each applicant is blocked by a previous paragraph IV certification as to a patent to which it did not have the first paragraph IV certification, FDA will approve the ANDA for either of the applicants that qualifies for exclusivity as soon as it is otherwise eligible for approval. That is, if two or more applicants are each eligible for exclusivity based upon paragraph IV certifications to different patents and each is blocked by previous paragraph IV certifications on another patent to which it was not first to certify, FDA will conclude that neither application blocks approval of the other. Exclusivity for all of the ANDAs eligible for 180-day exclusivity as to any patent at that time will be shared, and it will be triggered by the earlier of either first commercial marketing of any first applicant or a court decision on any one of the patents that qualified any applicant for exclusivity. During that "shared" exclusivity period, FDA may approve any ANDA eligible for exclusivity, but no other ANDAs. If, however, there are multiple patents and there is an application that is not blocked by another applicant's eligibility for exclusivity (because that applicant is a first filer on all of the relevant patents), that applicant would be entitled to sole exclusivity for the drug product at issue.[16]

D. FDA's Shared Exclusivity Approach Is Not Applicable In the Case of Modafinil Tablets

As noted above, there are currently two patents listed for PROVIGIL Tablets: the '516 patent, and the '346 patent. Each has a six-month period of pediatric exclusivity attached pursuant to section 505A of the act. These pediatric exclusivity periods expire on April 6, 2015, and May 29, 2024, respectively.

For the five years that preceded the submission of the '346 patent, it appeared that there were multiple first applicants for modafinil tablets who would be eligible for 180-day exclusivity , i.e.,

[14] See, e.g., *Mova Pharmaceutical Corp. v. Shalala*, 140 F.3d 1060, 1075 (D.C. Cir. 1998).

[15] We note that for ANDAs that are covered by the 2003 MMA amendments to the statute, this problem was rectified by Congress when it amended the statute to award exclusivity only to the first applicant to submit a paragraph IV certification to any patent listed for the drug product. See Section 505(j)(5)(B)((iv)(II)(bb)(defining "first applicant"). The issue of shared exclusivity discussed in this letter, therefore, applies only to ANDAs not subject to the 2003 MMA amendments.

[16] The agency has confronted this situation at least once before, in the case of generic metformin extended-release tablets. In that case there was only one first-filer to all relevant patents. See ANDA 76-863 approval letter dated October 14, 2004. Barr Laboratories was the only applicant to be a first filer on the two patents that were not listed at the same time for that product.

Teva and the other applicants who submitted ANDAs containing paragraph IV certifications to the '516 patent on December 24, 2002. See, *Guidance for Industry, 180-Day Exclusivity When Multiple ANDAs Are Submitted on the Same Day*, July 2003.

The situation changed, however, on December 14, 2007, when Cephalon listed the '346 patent. That same day, Teva submitted a paragraph IV certification to the '346 patent and sent notification to Cephalon. Aside from Teva, none of the other applicants who had submitted a paragraph IV certification to the '516 patent on December 24, 2002, also submitted a paragraph IV certification to the '346 patent on December 14, 2007. Teva, therefore, is uniquely positioned relative to other ANDA applicants for modafinil tablets. Although there are multiple first applicants with respect to both listed patents, only Teva is a first applicant as to both patents. FDA has only applied "shared exclusivity" when two applicants each have submitted paragraph IV certifications to two different patents, and one applicant was first to file a paragraph IV certification on one patent and the other was first to file on a different patent. The Agency has not extended shared exclusivity to a situation like the one at hand, where one applicant (in this case, Teva) was the only applicant to be among the first to file paragraph IV certifications to both listed patents. There are no "mutually blocking" 180-day exclusivities; Teva is not blocked by anyone else's eligibility for 180-day exclusivity and is, therefore, the sole first applicant eligible for exclusivity for modafinil tablets.

We therefore conclude that Teva alone has 180-day exclusivity for modafinil tablets.

II. Teva's 180-Day Exclusivity Was Triggered with Teva's Commercial Marketing of an Authorized Generic on March 30, 2012

Once we have determined that Teva, alone, is eligible for 180-day exclusivity for modafinil, we must consider whether that exclusivity has been triggered. As noted above, there are two events that can begin the running of ("trigger") a first applicant's 180-day exclusivity period: either the date of a decision of a court holding the patent that is the subject of the paragraph IV certification to be invalid or not infringed, or the date the Secretary receives notice from the first applicant of first commercial marketing of the drug under the ANDA. It is the commercial marketing trigger that is the subject of this discussion.[17]

[17] Two recent court actions are noted, however. In an October 31, 2011 Memorandum Opinion, the court determined that the '516 patent was invalid pursuant to the on-sale bar, for derivation, for obviousness, and for lack of a written description. The court also found the patent unenforceable due to inequitable conduct by Cephalon in its prosecution of the patent. *Apotex v. Cephalon, Inc.*, Civil Action No. 06-2768, 2011 U.S. Dist. LEXIS 125859, at *85 (E.D. Pa. Oct. 31, 2011). In a March 28, 2012 Memorandum Opinion, the court further determined that manufacture of ANDA applicant Apotex, Inc.'s modafinil product will not infringe on the '516 patent. *Apotex v. Cephalon, Inc.*, Civil Action No. 06-2768, 2012 U.S. Dist. LEXIS 43479, at *54 (E.D. Pa. Mar. 28, 2012). FDA just recently became aware of these decisions and is still reviewing them to determine whether one or the other satisfies the court decision trigger.

Following its acquisition of Cephalon on October 14, 2011, Teva immediately began marketing PROVIGIL under Cephalon's NDA.[18] On March 30, 2012, Teva announced the launch of an authorized generic version of modafinil tablets.[19]

FDA has determined that Teva's commercial marketing of an authorized generic version of modafinil triggered the running of its 180-day exclusivity. The agency addressed a very similar situation with respect to the drug nifedipine approximately eleven years ago. That case also involved the marketing of an authorized generic by a first applicant and the effect of such marketing on 180-day exclusivity. Teva (a subsequent applicant in that case), in a citizen petition submitted on August 9, 2000, stated its view that the marketing of an authorized generic by a first applicant eligible for 180-day exclusivity triggered the first applicant's exclusivity.[20] In granting Teva's petition, the agency stated that "FDA believes that Mylan's [the first applicant's] marketing of the Pfizer drug was commercial marketing that began the exclusivity period and that such an interpretation is fully consistent with the goals of Hatch-Waxman." FDA response, at 7; February 6, 2001 (Docket No. 200P-1446). This interpretation was upheld in *Mylan Pharmaceuticals, Inc. v. Thompson*, 207 F. Supp. 2d 476 (N.D.W.Va. 2001).

We do not believe any factual differences meaningfully distinguish the nifedipine decision from the case at hand. If anything, the argument that 180-day exclusivity has been triggered is stronger in this case than it was with nifedipine. In the case of nifedipine, the NDA holder and the authorized generic were not related corporate entities. In contrast, here the NDA holder, Cephalon, is wholly owned and controlled by Teva, the ANDA applicant who holds the sole exclusivity seat. With control of the marketing of PROVIGIL, and of an authorized generic, Teva has every reason not to pursue final approval of ANDA 076596 and not to market a "true" generic under that application.[21] Unless FDA finds here, as Teva successfully urged us to do in nifedipine, that marketing of an authorized generic triggers exclusivity, Teva has no incentive to trigger its exclusivity.[22] If Teva does not trigger its exclusivity, that exclusivity will not run and all

[18] We have considered finding that Teva's marketing of PROVIGIL upon its acquisition of Cephalon triggered its 180-day exclusivity, and believe that there is a strong argument for finding so. We have refrained from adopting that interpretation in this case, however, because that exclusivity, if it were triggered by Teva's acquisition of Cephalon, would expire on April 11, 2012 and, given the multiple uncertainties in this case, Teva had no notice that FDA considered it to be running. Because of the potential for collusion between NDA holders and captive first generics, and the subversion of the statutory scheme that could result, the agency may in the future provide guidance on the effect of such a relationship between NDA holder and first applicant upon any claim for 180-day exclusivity.

[19] See, http://ir.tevapharm.com/phoenix.zhtml?c=73925&p=irol-newsArticle&ID=1678505&highlight=

[20] See Citizen Petition from Teva re: Nifedipine Extended Release Tablets, at 1-2; August 9, 2000 (Docket No. 2000P-1446).

[21] Only within the last few days has Teva initiated any activity in pursuit of approval ANDA 076596. Teva made its first submission to its ANDA in over two years on April 2, 2012, following a letter from FDA dated March 28, 2012, that noted, among other issues, that Teva had made no submissions to its ANDA since 2009 and questioned whether Teva was pursuing ANDA approval. We note that if FDA determines that a first applicant is "not actively seeking approval of its application", that applicant will not maintain its eligibility for 180-day exclusivity.

[22] It is informative to note how Congress, understanding the opportunities for mischief that such agreements can bring, addressed these kinds of arrangements when it passed the MMA in 2003. The MMA adopts the position that FDA took with respect to nifedipine and states that "commercial marketing of the listed drug" by any first applicant would trigger the 180-day exclusivity period. See the current Act, at section 505(j)(5)(B)(iv)(I).

subsequent ANDAs for modafinil will be blocked from approval until one or more of the relevant patents expires.[23]

We conclude, therefore, that Teva triggered its 180-day exclusivity on March 30, 2012, when it began commercial marketing of an authorized generic of PROVIGIL (modafinil) Tablets. During this period, Teva will be able to obtain the benefits of sale of both the innovator and a generic forms of modafinil tablets. The 180-day exclusivity period will expire on September 26, 2012.

III. Conclusion

For the reasons set forth above, we conclude that Teva alone is entitled to 180-day generic drug exclusivity under section 505(j)(5)(B)(iv) of the Act. We also conclude that Teva's 180-day generic drug exclusivity was triggered on March 30, 2012, when Teva launched an authorized generic of PROVIGIL (modafinil) Tablets, and that this exclusivity period will expire on September 26, 2012.

Sincerely,

{See appended electronic signature page}

Keith O. Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

[23] As Teva itself noted in its Citizen Petition on nifedipine, "[i]t is universally accepted that the 180-day exclusivity clause was never intended to create opportunities for drug companies to indefinitely obstruct the market entry of generic drugs by entering into commercial arrangements which . . . prevent the 180-day period from ever being triggered." See Citizen Petition from Teva re: Nifedipine Extended Release Tablets, at 4; August 9, 2000 (Docket No. 2000P-1446).

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT L WEST on behalf of KEITH O WEBBER

04/04/2012

Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.