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COLLEEN R. BUTCHER
PATENT AGENT
JOSEPH F. MURPHY, PH.D.

A.D. CAESAR (1901-1995)
CHARLES RIVISE (1900-1951)
COUNSEL
ALLAN H. FRIED, PH.D.

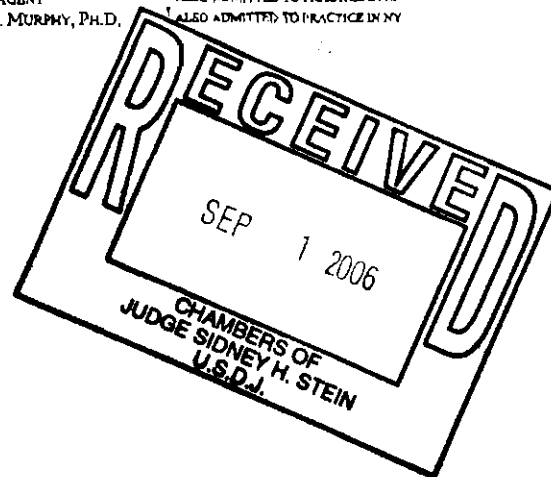
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September 1, 2006

Honorable Sidney H. Stein
U.S. District Judge
Southern District of New York
500 Pearl Street, Room 1010
New York, NY 10007

RE: **SANOFI SYNTHELABO ET AL v.
APOTEX, INC. ET AL**

SUB: **CIVIL ACTION NO. 02-CV-2255
OUR REFERENCE NO.: A1047/40021**



Dear Judge Stein:

Apotex submits this Letter Motion requesting the Court to stay the preliminary injunction pending an appeal to the Court of Appeals for the Federal Circuit because Apotex has raised substantial questions regarding the validity of the '265 patent. Apotex submits this letter via facsimile as the Court so graciously allowed.

Although Apotex believes that each and every one of its defenses raise substantial questions of invalidity, Apotex specifically directs the Court's attention to its anticipation defense under 35 U.S.C. § 102(b).

As this Court explained, "[a] prior art reference renders a patented invention anticipated – and thus invalid – if it discloses every feature of the claimed invention, either explicitly or inherently." Order at p. 14 (internal quotations omitted). Furthermore, a prior art reference discloses the features of the claimed invention where it "describe[s] every element of the claimed invention, either expressly or inherently, such that a person of ordinary skill in the art could practice the invention without undue experimentation." *Id.* That is, the reference must be enabling. *See Id.*

The prior art reference at issue is Sanofi's own patent, U.S. Patent No. 4,529,596 ("the '596 patent"). The Court agreed that the '596 patent is prior art to the patent in suit, and moreover noted that "the parties have stipulated that clopidogrel bisulfate is a compound that is within the genus of claim one of the '596 patent." *Id.* at 14-15 (internal quotations omitted). The Court however held that the '596 patent does not (1) describe clopidogrel bisulfate (2) so as to enable one skilled in the art to create it absent undue experimentation. Order at pp. 20-28.

9/1/06
Motion denied
So ordered
Sidney H. Stein
U.S.D.J.

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Thus, the Court found that although Apotex successfully raised a substantial question of invalidity insofar as anticipation is concerned, Sanofi demonstrated that such question "lacks substantial merit." Order at 19.

Central to the Court's holding that Sanofi demonstrated that Apotex' substantial question of invalidity vis-à-vis anticipation lacked substantial merit, was the Court's belief that deriving clopidogrel bisulfate from the '596 patent's disclosure would be like finding a needle in a haystack. Particularly, the Court found that the '596 claimed a genus which included potentially hundreds of thousands, if not millions of various species, including clopidogrel bisulfate. Thus, although clopidogrel bisulfate is one possible embodiment of the invention claimed in the '596 patent, the Court found that the patent includes too many possibilities for a person skilled in the art to arrive at clopidogrel absent undue experimentation. Apotex respectfully disagrees.

According to the Court, the potential hundreds of thousands, if not millions of potential embodiments of the genus claimed in the '596 patent renders the '596 patent a nonanticipatory reference as to one of those single embodiments. This is simply not true. The potential likely embodiments which a person of ordinary skill in the art (POSA) would pursue based on the disclosure in the '596 patent, are, in fact, very few. First, PCR 4099, which is covered by the '596 patent, was known to have anti platelet aggregating characteristics. Based on evidence presented to the Court, it was well known in the art (for decades prior to the patent-in-suit) that separate enantiomers of a racemate could have different properties. In the context of undue experimentation, it is irrelevant whether the enantiomers would definitely have different properties and whether a POSA could predict what exactly the differences would be. A racemate has only two enantiomers – the levorotatory enantiomer and the dextrorotatory enantiomer. A POSA has two choices in enantiomers of the claimed PCR 4099. This is certainly not an overwhelming number of choices. Apotex presented evidence establishing that a POSA was well versed, decades prior to the patent-in-suit, in methods of separating a racemate into its individual enantiomers. Moreover, as a United States patent, the '596 patent is presumed to be enabling (otherwise it would be invalid). Thus, there is a legal presumption that a POSA would have understood from the '596 patent how to separate PCR 4099 into its constituent enantiomers. Since the '596 patent covers the racemate PCR 4099, its enantiomers and its mixtures, it most certainly "describes" clopidogrel, i.e. the dextrorotatory enantiomer of PCR 4099.

Furthermore, although the court noted that Sanofi's expert, Dr. Davies said that there are 50 pharmaceutically acceptable salts (Order at p. 16, n. 1), this estimate means that a POSA would at most potentially experiment with two enantiomers of PCR 4099 and 50 salts, rendering a total of 100 possible combinations, as opposed to millions. That alone would not require undue experimentation. Moreover, only three salts are specifically disclosed in the examples given in the specification of the '596 patent, including the bisulfate. Thus, a POSA faced with seeking out an improved anticlotting drug based on PCR 4099 as disclosed in the '596 patent would, in all likelihood, experiment with two enantiomers and three different salts, i.e. a total of six different realistic choices. This would not, by any stretch, be considered "undue experimentation."

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Respectfully, the court's decision does not cite controlling case law. The court's decision does not cite or discuss:

In re Adamson, 275 F.2d 952, 954 (C.C.P.A. 1960) ("In view of the teaching of Karrer we feel that one of ordinary skill in the stereoisomer and pharmaceutical arts would recognize that the Adamson compounds exist as racemates, hence the fact that no reference to stereoisomerism is made in the Adamson references themselves is of no moment").

See *In re Petering*, 301 F.2d 676, 682 (C.C.P.A. 1962) (holding that when a reference references a discrete class of readily identified members, that reference "has described to those with ordinary skill in this art each of the various permutations ... as fully as if he had drawn each structural formula or had written each name"); see also *In re Schaumann*, 575 F.2d 312, (C.C.P.A. 1978) (reaffirming *Petering*, and finding that "the reference provides a description of those compounds just as surely as if they were identified in the reference by name").

"[I]t is well known to those skilled in the art that racemic mixtures are potentially separable, for Karrer teaches that racemates may be resolved into their laevo- and dextro-isomers by one of several methods including the specific method utilized, though not claimed, by appellants." *Adamson*, 275 F.2d 954.

Apotex urges this Court to reconsider its analysis regarding the '596 patent's enablement of clopidogrel bisulfate, and consider the probabilities of a POSA formulating clopidogrel bisulfate based on the '596 patent's disclosure of PCR 4099. It is incorrect to assume that every possibility would be tried without any rhyme or reason. Apotex presented sufficient evidence to show that a POSA would be logically limited to a finite number of possibilities, based on the examples specifically shown in the '596 patent.

An analogy may be helpful. Suppose a person wished to find a phone number of a bookstore in the vicinity of a certain geographic location. This person has a county phone book. The phone book contains hundreds of thousands of entries. Thus, the person could potentially read each of the hundreds of thousands of entries before finding the entry for the store. This absurd result is based on an assumption that the person does not realize that the phone book is organized alphabetically as well as by subject matter. Obviously, if the person recognizes the logic underlying the organization of the phone book, the potential difficulty in locating the desired phonebook entry is reduced exponentially. Similarly, it is faulty to assume that a POSA would unduly experiment with potentially hundreds of thousands or even millions of permutations of the genus claimed in the '596 patent. The actual combinations which a POSA would be likely to try (including clopidogrel bisulfate) based on the specification, does not amount to undue experimentation.

The Court of Appeals for the Federal Circuit recently explained: "In resisting a preliminary injunction ... one need not make out a case of actual invalidity. *Vulnerability* is the issue at the preliminary injunction stage, while validity is the issue at trial. The showing of a substantial question as to invalidity thus requires less proof than the clear and convincing

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showing necessary to establish invalidity itself." *Abbott Labs.*, 452 F.3d at 1335 (quoting *Amazon.com, Inc.*, 239 F.3d at 1359) (emphasis added).

In light of the above analysis, as well as all of the evidence of record, Apotex has clearly demonstrated the "vulnerability" of the patent-in-suit to a potential finding of invalidity. Apotex therefore respectfully requests that this Court reconsider its ruling regarding anticipation and find that Apotex has raised a substantial question of validity warranting a stay of the preliminary injunction.

Furthermore, in view of the foregoing, the Court is urged to reconsider its finding regarding irreparable harm. Absent the finding on likelihood of success, Sanofi would not have successfully demonstrated irreparable harm, as Apotex presented sufficient evidence that Sanofi's potential harm was calculable in monetary terms. Based upon the clear irreparable harm to Apotex by reason of the loss of the six month exclusivity and the harm to the public, it is respectfully submitted that a stay is appropriate.

Respectfully, the Court's decision on the prospect of Sanofi's suffering irreparable harm from irreversible price erosion caused by ongoing sales is unsupported by the evidence and testimony. The court did not cite evidence of record on the issue of on-going harm proffered by defendant's expert.

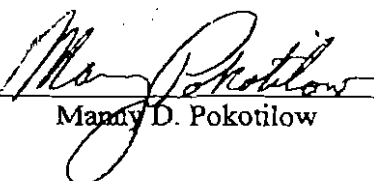
Conclusion

For all the foregoing reasons and those set forth in Apotex' Opposition to Plaintiffs' Motion for a Preliminary Injunction, Apotex respectfully requests that the Court stay the injunction.

Apotex' counsel is available to discuss this matter at the court's earliest convenience and may be reached at 215-498-1894 if the Court is unable to reach counsel at their offices.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.

By 
Manny D. Pokotilow

MDP/tc

cc: Evan Chesler, Esq. (via facsimile and Federal Express – Saturday Delivery)
Robert Baechtold, Esq. (via facsimile and Federal Express – Saturday Delivery)
Karen J. Bernstein, Esq. (via facsimile and Federal Express)