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HOW FDA ANNOUNCES DRUG APPROVAL DECISIONS: A BROKEN FDA "SYSTEM" THAT MUST BE FIXED

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Introduction

FDA is often called upon to make difficult decisions when a blockbuster drug is about to go off patent protection. These decisions generally fit into three categories. Often, the question is whether a brand-name drug company is entitled to extended exclusivity (perhaps due to an assertion that a provision of the Federal Food, Drug, and Cosmetic Act (FDC Act) confers marketing exclusivity beyond the life of a patent). In other instances, the brand-name drug company will argue that a generic drug should not be approved because that drug does not meet the FDC Act's requirements for approval of an Abbreviated New Drug Application (ANDA). Finally, a generic company sometimes argues that it is entitled to 180-day generic drug marketing exclusivity, or another generic company will argue that there is no exclusivity under the FDC Act.

Companies that want FDA to take action in one of these situations often file Citizen Petitions seeking a particular result. Although FDA has acknowledged that the Agency is not legally required to couple its decision on the Citizen Petition with a decision to approve a generic drug, or grant (or not grant) 180-day exclusivity, FDA's practice for many years has been to simultaneously announce both decisions. See 81 Fed. Reg. 78,500 at 78,504 (Nov. 8, 2016).

The larger the sales volume of a drug, the greater the chance that some company or companies will challenge FDA's decision in court. Pleadings are drafted by: (1) companies that anticipate filing a lawsuit against FDA; (2) companies and others that may want to intervene on the side of the plaintiff; and (3) companies and others that may want to intervene on the side of defending FDA's decision. Of course, until FDA renders a decision, no one knows whether FDA's decision will be acceptable to any particular company or person. Thus, companies often need to prepare alternative pleadings, including affidavits, in anticipation of an uncertain FDA decision. We have even seen cases where FDA is sued by more than one company, in different judicial districts, over one approval decision.

FDA and industry have been dealing with these challenges and uncertainties since passage of the 1984 Hatch-Waxman Amendments. One would expect that by

now, FDA would have established a system to bring order and certainty to a complicated drug approval process. That has not happened. Instead, FDA insists on announcing approval decisions when ***the Agency*** wants to do so, with no advance notice to potential litigants, courts, or the public regarding when the Agency will make a decision, let alone what that decision will be.

As a result of this FDA "process," which is really no process at all, FDA has succeeded in irritating and frustrating federal judges, brand-name drug companies, generic drug companies, the investment community, the public at large, and even FDA's own attorneys at the Department of Justice (DOJ).

Our firm has been on both sides of these battles. We have represented companies that have sued FDA to challenge one of these decisions, and we have represented companies that defend FDA's decision in a case filed by another company. We thus have a perspective that may not be unique, but that qualifies us to express our views on the way that FDA handles these matters. We address two of those cases below.

The Hi-Tech Case

In 2008, our firm filed an action in the United States District Court for the District of Columbia against FDA. Hi-Tech Pharmacal Co., Inc., v. United States Food and Drug Administration, No. 08-01495 (JDB). Hi-Tech's Complaint asserted that it was entitled to 180-day marketing exclusivity for the generic version of the drug COSOPT (dorzolamide hydrochloride-timolol maleate ophthalmic solution). Hi-Tech filed a "Motion For Expedited Preliminary Injunction Relief," asserting that Hi-Tech expected that its ANDA would be approved on October 28, 2008. Concerned that FDA might not give Hi-Tech the 180-day exclusivity that it believed it was entitled to, Hi-Tech asked FDA to issue a ruling well before that date. FDA rejected that request, responding that it would not render an exclusivity decision before October 28, 2008, at the earliest. If FDA ruled that Hi-Tech was not entitled to exclusivity, FDA would presumably approve another company's ANDA on October 28th, giving Hi-Tech no opportunity to challenge FDA's approval in court before the other company started marketing its product on the same date Hi-Tech would start marketing.

Hi-Tech argued that FDA had both the legal right and responsibility to inform Hi-Tech well before October 28th if it was entitled to 180-day exclusivity. Hi-Tech's brief cited five instances where FDA had announced decisions to approve drugs days and even years before FDA actually approved the drugs.

FDA responded by arguing that the court did not have jurisdiction over the case because FDA had not rendered a decision. FDA acknowledged what it called its "general practice" of making exclusivity decisions at the same time as an ANDA

is given final approval. Of course, that is exactly why Hi-Tech wanted FDA to do something before Hi-Tech filed the lawsuit. Apotex, which opposed Hi-Tech's argument that it was entitled to exclusivity, actually agreed with Hi-Tech that FDA should be compelled to rule on the issues before October 28th.

The court held a hearing on Hi-Tech's motion on October 2, 2008. Judge John Bates noted his concern that FDA would be making a decision on exclusivity without either company having the ability to challenge that decision before facing irreparable harm. Judge Bates asked why FDA thought that its "process" was good, in contrast to the fact that neither of the competing companies thought that FDA's system for announcing decisions made sense. "The public doesn't think it's good, I don't think. You're not doing anything for the public except what you're going to say in terms of FDA fulfilling its obligations responsibly." Tr. at 9, Oct. 2, 2008. "I'm asking why it makes sense to FDA to wind up in a situation on October 28 when it has this chaos to deal with in terms of an attempt to challenge the exclusivity decision, if indeed a meaningful challenge can even be brought." Id. at 10.

The DOJ lawyer explained that "there are a lot of drug companies and lawyers who would like to see these things for their own convenience come out early. On the other hand, the Food and Drug Administration has a finite amount of resources to devote toward doing its job. . . . And it's up to the agency to decide what its priorities are." Id. at 11. The judge responded that "all the reasons that the FDA has put forward for not deciding these exclusivity issues before the ANDA decision date, they don't really have much weight here, do they? They don't really exist here." Id. at 12. After then acknowledging the policies that DOJ argued were present with regard to FDA, Judge Bates stated "I think there's a possibility on October 28 of a mess that we're all going to have to deal with." Id. at 14.

On October 10, 2008, the court denied Hi-Tech's motion. It ruled that FDA had not taken "final agency action" that would make the matter subject to judicial review. The court noted however, that "despite reasonable requests by both Hi-Tech and Apotex—***now echoed by this Court***—that the FDA determine Hi-Tech's entitlement to exclusivity in advance of October 28, 2008, the FDA has refused." Slip Op. at 19 (emphasis added). The court then took the extraordinary step to "request" FDA to make a determination before that date. Id. at 20.

FDA rejected the court's request. Instead, the Agency informed the court on October 24, 2008, that FDA intended to issue its exclusivity decision and any ANDAs **in court** on October 28, 2008. FDA stated that "FDA will not make a decision on whether Hi-Tech has forfeited generic exclusivity in advance of the decisions on approval of the pending ANDAs." Federal Def.'s Status Report at 1.

Coming just four days before FDA announced its decisions, FDA had obviously already made those decisions.

This led to what can only be characterized as an extraordinary hearing on October 28, 2008. The hearing began with the companies present not knowing what FDA's decision would be. With regard to scheduling, the government stated that it "will do whatever the Court wants." Tr. at 7, Oct. 28, 2008. Judge Bates responded "You're kidding. The FDA is saying it will do whatever the Court wants?" The Court then closed the courtroom to the public, refused to let the parties leave the courtroom to announce the decision to the relevant business people at the companies involved, and asked FDA to hand out its decision to give the parties one hour to digest the decision and decide how they wanted to proceed. In the meantime, none of the parties could act (such as distribute products). Judge Bates then stated "I'm not going to try to make sense out of this idiotic process that the FDA—not requires, but given the statutory structure and the way it does business, allows to happen. It is, from my perspective, insane what we're going through." Id. at 13.

These and earlier comments from Judge Bates, led to a highly unusual appearance from a high level DOJ official. He stated in court that:

"I want to let you know we've heard the criticism of the FDA, heard your frustration with the process. . . . understand the frustration that parties and the Court has had, and we'll revisit the way that we handle [these cases]." Id. at 21. Judge Bates responded: "I appreciate that, and even more importantly, I'm sure that those in the marketplace would appreciate that." Id.

As best as we can tell, FDA's experience in this case, including hearing Judge Bates' critical comments and promises made by a high level DOJ official, resulted in ***no*** change to the way that FDA handles these decisions.

The AstraZeneca Pharmaceuticals LP Case

On June 27, 2016, AstraZeneca filed an action against FDA in the United States District Court for the District of Columbia, AstraZeneca Pharmaceuticals LP v. Burwell, No. 16-cv-1336 (RDM). AstraZeneca sought to block what it alleged was FDA's imminent approval of some ANDAs involving the blockbuster drug Crestor. Our firm represented an interested party in the case.

Judge Randolph D. Moss heard oral argument on AstraZeneca's Motion for a Temporary Restraining Order on July 7, 2016. Like Judge Bates, Judge Moss struggled with how to deal with the timing of approval issues that FDA had created..

First, Judge Moss stated that "all fair-minded people would say that the best state of affairs would be a world in which the Court has the opportunity to actually review the FDA's actual decision and actual reasoning in this case." Tr. at 40. He asked if FDA could issue a decision on the Citizen Petition that AstraZeneca had earlier filed and wait another day or two to act on the pending ANDAs, in order to give the court an opportunity to review the Citizen Petition decision ***before*** it became operative in terms of actual approvals. The government acknowledged that no regulation specifically prohibited FDA from proceeding as Judge Moss suggested. Id. at 42. Judge Moss later stated that FDA's decision on the pending Citizen Petition was "not necessarily tied to the approval of the ANDAs." Id. at 50. Government counsel, citing 21 U.S.C. 355(q)(2)(A), asserted that once FDA issues a decision on a Citizen Petition, the Agency is legally ***prohibited*** from delaying approval of an ANDA that is relevant to the Citizen Petition decision. Id. at 60. Judge Moss immediately questioned the accuracy of that assertion. Id. He then asked the parties to confer to see if they could reach agreement on a mechanism whereby the court could review an FDA decision in a manner that would not cause anyone prejudice, but would also not foreclose judicial review. Id. at 78.

The very next day, the parties filed a status report regarding the court's request to reach an agreement on the timing of announcing FDA's decision. Plaintiffs asked the court to require FDA to give 48 hours advance notice before rendering a decision on the Citizen Petition. FDA and the companies that intervened on FDA's side opposed that suggestion.

The parties also presented different views regarding whether there should be a "review period" between issuance of FDA's decision on the Citizen Petition and FDA approval of ANDAs if the Citizen Petition was denied. Plaintiffs proposed a 48-hour review period between the two actions to permit review of the Citizen Petition decision and allow for further briefing. FDA opposed that review period, asserting that, under 21 U.S.C. § 355(j)(4) and (q)(2)(B), FDA cannot delay an ANDA approval once the agency determines that an ANDA has met the legal requirements for approval. FDA cited the approach that three other courts had taken in earlier cases to provide for court review of final action taken on an ANDA being approved. FDA was willing to give the court and only the court notice that a decision on a Citizen Petition was imminent. Some of the intervenors who were hoping for approval of their ANDAs agreed with FDA. Others proposed that FDA issue a decision on the Citizen Petition in the early morning, and defer approval of all ANDAs until later that same day to permit judicial review.

Just as Judge Bates did in the Hi-Tech case, Judge Moss thoroughly deliberated how to handle this "mess." On July 11, 2016, he issued a twelve page

Memorandum and Order. Clearly, he intended his order to be precedent for how future courts would handle the same issues.

First, he ruled that AstraZeneca should have ***some*** opportunity to present its arguments to the court before it suffers an irretrievable loss of six months or more of exclusivity. The court noted that the law favors the availability of judicial review of agency action and that, unless AstraZeneca had an opportunity to get such review, up to a half-dozen manufacturers could ship a supply of six months or more of the generic form of Crestor into the marketplace before AstraZeneca had an opportunity to be heard on the legality of the Agency's action in approving the ANDAs.

However, he concluded that that mechanism should ***not*** deprive the intervenors of their right to market generic versions of Crestor as soon as lawfully allowed to do so. He concluded that the court should not unnecessarily or unduly interfere with the usual operation of the administrative process.

Judge Moss rejected AstraZeneca's 48-hour delay proposal. However, he required that FDA provide the court, but not the parties, with 24 hours notice before issuing its decision on AstraZeneca's Citizen Petition, to allow the court to schedule a ***closed*** hearing where FDA would issue FDA's decision on the Citizen Petition and any decision that it may have reached on any of the ANDAs to the parties. He required that even though FDA had not signaled when it would be issuing its decision on the Citizen Petition, lead counsel for all parties had to be prepared to appear in Court on two hours' notice.

He also rejected some parties' proposal that FDA be compelled to issue its decision on the Citizen Petition before it rendered a decision on the pending ANDAs. He noted that FDA had represented that it lacks statutory authority to agree to this approach; however, Judge Moss noted that FDA did not suggest that ***the court*** lacked authority to order the Agency to proceed in this manner. Nevertheless, Judge Moss decided not to so compel FDA, ruling that doing so would constitute a substantial break with FDA practice.

On July 19, 2016, the procedures set forth above were followed. FDA denied AstraZeneca's Citizen Petition and FDA approved a number of ANDAs during the closed court hearing. Judge Moss heard arguments on AstraZeneca's Motion for a Temporary Restraining Order and then denied the Motion.

Nevertheless, even though its patents had expired on July 8th, AstraZeneca had been able to delay generic competition for eleven days. Blame for this occurring falls squarely on FDA. After all, it almost surely delayed issuing the ANDAs for

that period for one reason--a desire to couple issuance of the ANDAs with a decision on a Citizen Petition that had been submitted less than sixty days earlier.

As noted above, FDA has cited 21 U.S.C. § 355(j)(4) and (q)(2)(B) as the reason why it claims it is legally required to issue ANDAs once the Agency has decided that the products meet the legal requirements for approval. In fact, there is nothing in either provision that deals with the ***timing*** for approval of ANDAs or indeed, how that approval is or is not tied to a decision on a Citizen Petition. Moreover, exactly when does FDA decide when a product meets all approval requirements? Is it only when the approval letter is issued? How about when it is signed? What if FDA officials write internal memos indicating that a yet to be approved drug will indeed be approved?

In contrast, 21 U.S.C. § 355(q)(1)(A) reflects a determination by Congress that the Secretary shall ***not*** delay approval of an ANDA based on a Citizen Petition unless FDA ***determines*** that a delay is necessary to protect the public health.

So who benefits from the current "system"? Both brand-name and generic drug companies are suffering from the uncertainty of knowing when products will enter the market and whether there will be competition in situations where FDA is facing an approval "deadline." It is virtually impossible for those companies to plan manufacturing, distribution, or contractual arrangements with potential customers when the FDA approval process follows the current FDA procedures.

Their counsel are brought into virtual "fire-drills" that jack-up legal fees unnecessarily. Even though few people may have much sympathy for lawyers in these situations, there is no question that FDA's approval process is incredibly disruptive. In the AstraZeneca case, at least one lawyer who is not based in Washington was forced to stay in Washington for an entire week to be ready for the hearing that could be scheduled at any time based on the court's "two hour notice" ruling. We do not suggest that Judge Moss either erred or was insensitive to the needs of the lawyers involved in the case. He tried his best to manage a quagmire that FDA created, not him!

Does DOJ, which represents FDA in court, or the FDA lawyers who are involved in those proceedings benefit? In one sense they do. They have a leg up on the other litigants because presumably the government lawyers get advance notice of FDA's decision and can be a step ahead of the other litigants in terms of writing a brief before the other litigants know what the decision will be. However, this advantage is counterbalanced by criticisms that these lawyers have received from federal judges who ask those lawyers to defend FDA's "process" for announcing approval decisions.

In sum, the current FDA system to announce these hotly contested decisions is broken. As we see it, FDA's "system" pleases no one and does not appear to be legally mandated. Moreover, whatever advantage FDA may think it is getting from hiding the ball from the world on the timing and substance of these decisions is more than overcome by the criticism the Agency has received from judges. After all, it is one thing for FDA to keep litigants on their toes by working nights and weekends to prepare emergency pleadings that may need to be filed within minutes of an FDA approval decision. However, the companies and others need to foot the bill for this uncertainty. Lawyer and client inconvenience do not seem to weigh heavily on FDA.

FDA's decisions are generally subject to judicial review in a federal district court. District Court judges and their staffs have lives outside of their jobs. They get paid nothing extra for having to work overtime to deal with emergency pleadings filed by litigants in one of these cases simply because FDA is unwilling to alter the current "system." Even worse, these judges have many other cases to deal with in addition to an emergency lawsuit filed against FDA. Because FDA creates uncertainty regarding the timing and substance of approval decisions, FDA burdens litigants in those other cases who may find their cases bumped from the docket when FDA finally gets around to making a decision.

FDA has badly hurt its own credibility with judges—the very people who decide those cases—by refusing to inform potential litigants or even judges regarding either the timing or substance of an approval decision.

This broken approval system must be fixed. There appears to be ample authority conferred on FDA to make changes without the need for additional legislation to be enacted. If legislation is needed, we call on FDA to spearhead a legislative fix. Congressional oversight committees may be a sound vehicle to compel FDA to focus on this problem. Perhaps the Department of Health and Human Services may be able to force FDA to change its ways. FDA needs to involve interested stakeholders in this process. We also urge FDA to communicate with the courts, particularly the United States District Courts for the District of Columbia and the District of Maryland to try to get judicial input.

FDA's current system is a quagmire. However, we are not suggesting a specific procedure for how these cases should be handled, and nothing in this blog should suggest otherwise. Indeed, the views expressed in this document represent solely the views of the authors and not any of our clients.