UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

NATURAL RESOURCES DEFENSE COUNCIL, INC.; CENTER FOR SCIENCE IN THE PUBLIC INTEREST; FOOD ANIMAL CONCERNS TRUST; PUBLIC CITIZEN, INC.; and UNION OF CONCERNED SCIENTISTS, INC.,

Plaintiffs,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION; MARGARET HAMBURG, in her official capacity as Commissioner, United States Food and Drug Administration; CENTER FOR VETERINARY MEDICINE; BERNADETTE DUNHAM, in her official capacity as Director, Center for Veterinary Medicine; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; and KATHLEEN SEBELIUS, in her official capacity as Secretary, United States Department of Health and Human Services,

Defendants.

11 Civ. 3562 (THK)
ECF Case

MEMORANDUM OF LAW IN SUPPORT OF THE GOVERNMENT'S' MOTION FOR SUMMARY JUDGMENT AND IN OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

PREET BHARARA
United States Attorney for the
Southern District of New York
Attorney for Defendant
86 Chambers Street, 5th Floor
New York, New York 10007
Tel.: (212) 637-2716

AMY A. BARCELO
Assistant United States Attorney
– Of Counsel

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The above-captioned defendants (hereafter, the "Government"), by their attorney, Preet Bharara, United States Attorney for the Southern District of New York, respectfully submit this memorandum of law in support of their motion for summary judgment pursuant to Federal Rules of Civil Procedure 56 and in opposition to Plaintiffs' motion for summary judgment dated October 6, 2011 ("Plfs' Br.").

PRELIMINARY STATEMENT

Summary judgment should be awarded to the Government and Plaintiffs' summary judgment motion should be denied, because Plaintiffs' claim in this lawsuit is based on a demonstrably incorrect premise and is wholly without legal support. Plaintiffs' action is brought under section 706(1) of the Administrative Procedure Act ("APA"), 5 U.S.C. § 501 *et seq.*, and the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 301 *et seq.*, and seeks to compel the United States Food and Drug Administration ("FDA" or the "Agency") to ban the use of penicillin and tetracycline antibiotics in animal feed (such animal feed products the "NOOH Products").[1] As explained below, FDA would be statutorily authorized to withdraw approval for the contested antibiotic use only after the Commissioner of Food and Drugs ("Commissioner") makes appropriate "findings" following a hearing. No such findings exist.

The Court should reject Plaintiffs' arguments to the contrary. Plaintiffs' first claim is that FDA is required by statute to withdraw approval of the NOOH Products based on two notices of opportunity for hearing that FDA's Bureau of Veterinary Medicine ("BVM") issued in 1977 regarding the potential withdrawal of the NOOH Products (the "1977 NOOHs"). Plaintiffs' argument is based on a faulty premise—that the 1977 NOOHs contained "findings" by the Commissioner compelling such withdrawal—whereas the 1977 NOOOHs actually were issued

[1] As used herein, the term "NOOH Products" does not refer to penicillin and tetracycline drugs in connection with other approved uses.

by a subsidiary FDA bureau that did not have authority to make the required findings in this case. Indeed, the plain language of the FDCA provides that such "findings" may be made only after an opportunity for a hearing has been provided on the subject of the potential withdrawals. *See* 21 U.S.C. § 360b(e)(1). In this case, although FDA found that hearings were necessary before it could withdraw approvals for the NOOH Products, such hearings were never held, and the Commissioner never made any "findings." The Government is therefore entitled to judgment on the first claim as a matter of law.

To the extent that Plaintiffs seek any further relief with respect to the 1977 NOOHs, such claims would be moot, because on December 16, 2011, FDA withdrew the 1977 NOOHs. Thus, any such claims should be dismissed for lack of subject matter jurisdiction.

Plaintiffs concede that the Court lacks subject matter jurisdiction over their second claim—that FDA unreasonably delayed in responding to Citizen Petitions submitted by certain Plaintiffs in 1999 and 2005 requesting that the agency withdraw approval of certain uses of antibiotics in livestock. Indeed, on November 7, 2011, FDA responded to those Citizen Petitions, and the Court has since "so-ordered" a stipulation executed by the parties dismissing that claim as moot. Dkt. No. 37.

BACKGROUND

A. The FDA's Regulation of New Animal Drugs and Statutory Provisions Governing Withdrawals of Drug Use Approvals

The FDCA prohibits the introduction into interstate commerce of any new animal drug,[2] unless it is the subject of an approved new animal drug application ("NADA"), or, with respect

[2] A new animal drug is defined, in part, as any drug intended for use in animals other than man, including any drug intended for use in animal feed but not including the animal feed, the composition of which is such that the drug is not generally recognized as safe and effective for

to generic animal drugs, an abbreviated NADA ("ANADA"). 21 U.S.C. § 360b(a)(1)(A).[3] Drug companies that submit NADAs or ANADAs are typically referred to as "applicants" or "sponsors." There is no dispute that the drugs at issue in this litigation are new animal drugs that are currently sold lawfully pursuant to NADAs or ANADAs. (For simplicity, the term NADA will be used herein to refer to both NADAs and ANADAs.)

The FDCA also establishes procedures whereby the FDA can withdraw an approved NADA. Under 21 U.S.C. § 360b(e)(1), "the [Commissioner][4] shall, after due notice and opportunity for hearing to the applicant, issue an order withdrawing approval of an [NADA] with respect to any new animal drug if the [Commissioner] finds" that any of the conditions or events enumerated in 21 U.S.C. § 360b(e)(1)(A) through (F) are shown to have occurred. Two of these six subsections are relevant here. First, 21 U.S.C. § 360b(e)(1)(A) provides for withdrawal if "experience or scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved . . . ." Second, 21 U.S.C. § 360b(e)(1)(B) provides for withdrawal if "new evidence not contained in [an NADA] or not available to the [Commissioner] until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated

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the use under the conditions prescribed, recommended, or suggest in the labeling of the drug. *See* 21 U.S.C. § 321(v).

[3] A new animal drug may also be introduced into interstate commerce if there is a conditional approval in effect pursuant to 21 U.S.C. § 360ccc or there is an index listing in effect pursuant to 21 USC § 360ccc-1. Neither of these provisions are relevant here.

[4] Delegations of authority from the Secretary of Health and Human Services to the Commissioner, and subsequent subdelegations, are reflected in §1410.10 of the FDA Staff Manual Guides, relevant excerpts of which are attached as Exhibit A to Declaration of Amy A. Barcelo dated January 9, 2012 ("Barcelo Decl."). Pursuant to § 1410.10(1)(A)(1) of the Staff Manual Guides, the Secretary delegated to the Commissioner, among other things, the "[f]unctions vested in the Secretary under the [FDCA], as amended." *Id.* at 1.

together with the evidence available to the [Commissioner] when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved."

B. Factual Background

1. The History of Research Regarding Antimicrobial Resistance and the Use of Antibiotic Drugs in Livestock

Antimicrobial drugs[5] have been approved to promote the growth of food producing animals since the early 1950s. These uses are generally referred to as "production uses" and by some (but not currently by FDA) as "subtherapeutic uses." *See* FDA Draft Guidance #209, *The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals* (2010) ("Draft Guidance 209"), at 4, attached as Exhibit C to Barcelo Decl. In accordance with the FDCA at that time, FDA approved the use of penicillin, tetracycline, and some other animal drugs, for use in promoting the growth of food producing animals. Many of these approvals remain in effect. *See, e.g.*, 21 C.F.R. §§ 558.128; 558.145; 558.155; 558.450; 558.455; and 558.460, (reflecting FDA's approval of penicillins and tetracyclines for growth promotion and feed efficiency indications).

Although antimicrobial drugs kill bacteria, they also promote "antimicrobial resistance" (*i.e.*, a decreased susceptibility of bacteria to an antimicrobial drug). *See* Draft Guidance Q&A at 1. Antimicrobial resistance occurs after bacteria are exposed to an antimicrobial drug and continue to survive in the drug's presence. *Id.* Once bacteria become resistant to a drug, the

[5] "Antimicrobial drugs" are drugs that work against a variety of microorganisms, such as bacteria, viruses, fungi, and parasites. Antimicrobial drugs that work specifically against bacteria are called "antibacterial drugs" or "antibiotics." *See* Questions and Answers on FDA's Draft Guidance on the Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals ("Draft Guidance Q&A") at 1, attached as Exhibit B to Barcelo Decl.

continued use of that drug may increase the number of resistant bacteria. *Id.* The use of any antimicrobial drug, including in animals and humans, can add to antimicrobial resistance. *Id.*

In the mid-1960s, FDA became concerned about the safety to humans and animals of production uses of antibiotics, and began to study the effects of giving low-levels of antibiotics to animals. *See* Penicillin-Containing Premixes; Opportunity for Hearing, 42 Fed. Reg. 43772, 43773 (Aug. 30, 1977) ("Penicillin NOOH"), attached as Exhibit D to the Barcelo Decl.; Tetracycline (Chlortetracycline and Oxytetracycline)-Containing Premixes; Opportunity for Hearing ("Tetracycline NOOH"), 42 Fed. Reg. 56264, 56266 (Oct. 21, 1977), attached as Exhibit E to the Barcelo Decl. In April 1970, the Commissioner established a scientific task force to review the use of antibiotic drugs in animal feeds. In 1972, that task force published a report acknowledging that the use of antimicrobials in food-producing animals was associated with the development of antimicrobial-resistant bacteria. *See* Antibiotic and Sulfonamide Drugs in Animal Feeds; Proposed Statement of Policy, 37 Fed. Reg. 2444, 2445 (Feb. 1, 1972), attached as Exhibit F to Barcelo Decl.; *see also* Draft Guidance 209 at 5.

Following the task force's report, FDA initiated a process through which drug companies were required to submit evidence on the safety and effectiveness of antibiotics in animal feeds. *See* 37 Fed. Reg. at 2445.[6] After reviewing the information submitted in response to the notice, BVM[7] issued the 1977 NOOHs, which proposed to withdraw approval of the NOOH Products in animal feed because of safety concerns related to those uses, subject to interested parties' right to

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[6] The resulting regulations are now codified at 21 C.F.R. § 558.15.

[7] In 1984, the BVM became known as the Center for Veterinary Medicine ("CVM"), as it is known today.

request hearings on the proposal. *See* Penicillin NOOH, 42 Fed. Reg. 43772, Tetracycline NOOH, 42 Fed. Reg. 56264. [8]

In response to the 1977 NOOHs, approximately 20 parties requested hearings on BVM's proposal, including some NADA sponsors. *See* Penicillin and Tetracycline in Animal Feeds Hearing, 43 Fed. Reg. 53827, 53827 (Nov. 17, 1978), attached as Exhibit G to the Barcelo Decl. On November 9, 1978, the Commissioner granted these requests, announcing that "there w[ould] be a formal evidentiary public hearing on these proposals," and that a date for the hearing would be set "as soon as practicable." *Id.* at 53827-28.

The 1977 NOOHs received substantial criticism on the ground that the data were not adequate to show that bacteria of animal origin were commonly transmitted to humans and caused serious illness. *See* FDA Draft Guidance at 6. In light of these concerns, in the late 1970s and early 1980s, Congress requested that FDA conduct further studies and hold in abeyance the implementation of the 1977 NOOHs pending the outcome of these studies. *See id.* at 6; s*ee also* H.R. Rep. No. 95-1290, at 99-100 (1978) (report by the House Committee on Appropriations "recommend[ing]" that FDA conduct research regarding "whether or not the continued subtherapeutic use of [the NOOH Products] would result in any significant human health risk" before revoking such approval); H.R. Rep. No. 96-1095, at 105-06 (1980) (report by the House Committee on Appropriations requesting FDA to "hold in abeyance any implementation" of the proposed revocation pending further research); S. Rep. No. 97-248, at 79 (1981) (report by the Senate Committee on Appropriations making the same request).

[8] The Tetracycline Notice included a series of important exceptions, through which the use of tetracycline feeds would remain approved for certain "subtherapeutic conditions of use." 42 Fed. Reg. at 56287.

In the years following these Congressional requests, FDA contracted with the National Academy of Science, the Seattle-King County Health Department, and the Institute of Medicine to conduct research on this topic. *See* Draft Guidance 209 at 6-7. Although the results of the studies produced by these three institutions did not conclusively determine whether the use of antibiotics for growth promotion in animals resulted in harm to the public health, one did conclude that *Campylobacter jejuni* bacteria "does appear to flow from chickens to man via consumption of poultry products." *Id.* at 7. The studies also noted a considerable body of indirect evidence implicating both subtherapeutic and therapeutic use of antimicrobials as a potential human health hazard, and recommended further study of the issue. *Id.* at 6-7.

A series of additional studies were conducted by other government agencies and non-governmental organizations during the 1990s, all of which generally supported FDA's concerns regarding the public health threat posed by antimicrobial resistance. *See* Draft Guidance 209 at 7-9. In 2003, FDA recommended a new approach for evaluating antimicrobial resistance associated with the use of antimicrobial new animal drugs in food-producing animals, by issuing Guidance for Industry #152, *Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to their Microbiological Effects on Bacteria of Human Health Concern* (2003) ("GFI 152"), attached as Ex. H to the Barcelo Decl. GFI 152 is generally premised on the concept that the risk of generating resistance to those antimicrobial drugs is increased as the exposure of bacterial populations to antimicrobial drugs increases. *See generally* GFI 152. The guidance also recommended measures for mitigating such risk, such as restricting use of such drugs to use by or on the order of a veterinarian. *See id.* at 22.

2. FDA's Current Thinking on Antimicrobial Resistance

Since publishing GFI 152 in 2003, FDA has not approved any new antimicrobial drugs for use in animal feed. To mitigate potential risks posed by the use of antimicrobial drugs approved before 2003 in food producing animals, on June 28, 2010, FDA published a draft guidance titled, *The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals*, draft Guidance for Industry #209. *See* Draft Guidance 209, attached as Exhibit to the Barcelo Decl. Draft Guidance 209 explains that "the continued availability of effective antimicrobial drugs is critically important for combating infectious disease in both humans and animals" (Draft Guidance 209 at 15), and recommends two principles regarding the appropriate or judicious use of medically important antimicrobial drugs in food-producing animals. First, "the use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that are considered necessary for assuring animal health." *See* Draft Guidance 209 at 16. FDA elaborated that it considers "uses that are associated with the treatment, control, or prevention of specific diseases, including administration through feed and water, to be uses that are necessary for assuring the health of food-producing animals" and, accordingly, "some prevention indications are necessary and judicious." *Id*. However, FDA also made clear that it considers the use of antimicrobial drugs to promote growth or improve feed efficiency to represent an injudicious use. *Id*.

Second, Draft Guidance 209 provides that: "[t]he use of medically important antimicrobial drugs in food-producing animals should be limited to those uses that include veterinary oversight or consultation." Draft Guidance 209 at 17. The Draft Guidance recognized that this limitation represented a significant change from current practice, as most antimicrobial drugs approved for subtherapeutic use are available now "over-the-counter." *Id.* FDA

concluded that requiring the involvement of a veterinarian in connection with the use of antimicrobial drugs would provide an "important mechanism for helping to assure appropriate use" of antimicrobial drugs. *Id.*

FDA is now working with sponsors to voluntarily change the status of medically important antimicrobial drugs currently approved for use in feed from "over the counter" to "veterinary feed directive" ("VFD") status.[9] *See* November 7, 2011 FDA Final Response to Citizen Petition New Docket No. FDA-1999-P-1286 to Sarah Klein ("Klein Citizen Petition Response") at 4, attached as Barcelo Decl. Ex. I; November 7, 2011 FDA Final Response to Citizen Petition New Docket No. FDA-2005-P-0007 to Andrew Maguire ("Maguire Citizen Petition Response") at 3, attached as Barcelo Decl. Ex. J. In March 2010, anticipating voluntary transitions of products to VFD status, FDA issued an advance notice of proposed rulemaking seeking public comment on whether improvements in the current VFD regulation, codified at 21 C.F.R. § 558.6, are needed. *See* Advance Notice of Proposed Rulemaking, 75 Fed. Reg. 15387 (March 29, 2010), Ex. K to Barcelo Decl. FDA has received and is considering numerous comments on how to improve and revise the VFD rule. *See* Klein Citizen Petition Response at 4; Maguire Citizen Petition Resp. at 3-4. Once the revised rule is finalized, FDA expects to begin the process of converting the antimicrobial drugs currently approved for use in feed from over-the-counter to VFD status. When this is accomplished, FDA anticipates that the VFD

[9] A VFD drug is a drug intended for use in or on animal feed that is limited by its approval or index listing to use under the professional supervision of a licensed veterinarian. *See* 21 U.S.C. § 354(a)(1). The VFD classification was established pursuant to the Animal Drug Availability Act of 1996 ("ADAA") (*See* Pub. L. 104-250, § 504, 110 Stat. 3151 (1996)) and is "critical to reducing unnecessary use of [] drugs in animals and to slowing or preventing any potential for the development of bacterial resistance to antimicrobial drugs." *See* Final Rule, 65 Fed. Reg. 76924 (December 8, 2000).

antimicrobials will be allowed only under the direct supervision of a licensed veterinarian. *See* Klein Citizen Petition Response at 4; Maguire Citizen Petition Resp. at 3.

C. Plaintiffs' Claims in This Action

Plaintiffs began this action by filing a complaint on May 25, 2011, which they then amended on July 7, 2011 (the "Amended Complaint" or "Am. Compl."). Dkt. No. 11. The amended complaint contains two APA claims under 5 U.S.C. § 706(1), seeking to "compel agency action unlawfully withheld or unreasonably delayed." First, the Amended Complaint alleges that the Government has "unlawfully withheld or unreasonably delayed" taking action that it is allegedly required to take because it has failed to withdraw approval for subtherapeutic uses of penicillin and tetracyclines in animals feed since BVM issued the 1977 NOOHs. Am. Compl. ¶ 98. Plaintiffs' second claim, that the Government has "delayed unreasonably" in issuing a final response to Citizen Petitions submitted by certain Plaintiffs in 1999 and 2005 requesting that the agency withdraw approval of certain uses of antibiotics in livestock, Am. Compl. ¶ 101, has been dismissed because it is now moot. Dkt. No. 37.

D. FDA Withdraws the 1977 NOOHs

On December 16, 2011, FDA withdrew the 1977 NOOHs for three principal reasons. *See* Withdrawal of Notices of Opportunity for a Hearing; Penicillin and Tetracycline used in Animal Feed, 76 Fed. Reg. 79697 (Dec. 22, 2011), attached as Exhibit L to the Barcelo Decl. First, FDA concluded that continuing the implementation of other regulatory strategies developed since 1977 was the quickest and most efficient way to achieve FDA's goals regarding the judicious use of antibiotics in livestock. *Id.* at 79698-700. Second, the 34-year-old 1977 NOOHs rested on outdated data and information and therefore could not serve as the basis for further regulatory action without updating. *Id.* at 79700. FDA therefore explained that if, in the future, it proposes

to withdraw approvals for the NOOH Products pursuant to 21 U.S.C. § 360b(e)(1)(B), a new, updated notice of opportunity for hearing would be issued at that time. *Id.* Third, if and when FDA decides to seek the withdrawal of any antimicrobial drugs for use in animals, FDA would need to prioritize which drugs to focus on first. 76 Fed. Reg. at 79700. As FDA's December 16, 2011 withdrawal of the 1977 NOOHs makes clear, its current approach leaves open the possibility of pursuing withdrawal proceedings at a later time if FDA's proposed strategy does not yield satisfactory results. *Id.* at 79700-01.

ARGUMENT

I. PLAINTIFFS ARE NOT ENTITLED TO A COURT ORDER "REQUIRING" FDA TO WITHDRAW APPROVAL FOR SUBTHERAPEAUTIC USES OF PENICILLLIN AND TETRACYCLINES IN ANIMAL FEED

A. Plaintiffs Can Compel Agency Action Only If That Action Is Required

Where, as here, an APA action is brought to "compel agency action unlawfully withheld," 5 U.S.C. § 706(1), that claim "can proceed only where a plaintiff asserts that an agency failed to take a *discrete* agency action that it is *required to take*."[10] *Norton v. Southern Utah Wilderness Alliance*, 542 U.S. 55, 64 (2004) (emphasis in original); *see also* Plfs' Br. 10-11. Where, as here, an agency is not "legally required" to undertake certain action, a court cannot compel it to undertake that action. *Id.* at 63 (emphasis in original); *see also Benzman v. Whitman*, 523 F.3d 119, 130-31 (2d Cir. 2008) (no remedy available to plaintiffs under section 706(1) of the APA where they could not point to any statute or regulation that "required" agency to undertake action that formed the basis for plaintiffs' claims); *Sadler v. Mineta*, 3:05-CV-1189 (MRK), 2006 WL 2772699, at *7 (D. Conn. Sept. 26, 2006) (same).

[10] The APA provides a cause of action for a plaintiff who is "suffering legal wrong because of agency action, or adversely affected or aggrieved by agency action within the meaning of a relevant statute." 5 U.S.C. § 702. In the context of this provision, "agency action" includes an agency's "failure to act." 5 U.S.C. § 551(13).

B. The Government Is Not Required to Withdraw Approval for the NOOH Products

Contrary to Plaintiffs' assertions, FDA is not required to withdraw approval of the NOOH Products simply because it took the preliminary step of issuing the 1977 NOOHs. Plfs' Br. at 9-10. Specifically, Plaintiffs' argument that BVM's issuance of the 1977 NOOHs now "require[s] that FDA] withdraw approval for certain subtherapeutic uses of penicillin and tetracyclines in animal feed," Plfs' Br. at 9, incorrectly conflates: (1) *BVM's* preliminary determination that served as the basis for FDA's decision to issue the 1977 NOOHs, with (2) the final finding, by the *Commissioner* herself, that one of the conditions or events enumerated in 21 U.S.C. § 360b(e)(1)(A) through (F) have been established. Contrary to Plaintiffs' interpretation, the FDCA explicitly requires that such a finding by the Commissioner is a precondition to withdrawal, and such finding can only be made after the applicant has had the opportunity for a hearing on the proposed withdrawal. Because those requirements have not been met in this case, Plaintiffs are not entitled to any relief with respect to the NOOH Claim.

1. Standards of Statutory Interpretation and Deference Due to FDA's Interpretation in Relevant Statutory Text

In interpreting a statute, a court will first look to its plain meaning. *See Benzman*, 523 F.3d at 130-31; *see also Sadler*, 2006 WL 2772699, at * 8. If a statute does not specifically speak on a particular question, so-called *Chevron* deference to an agency's reasonable statutory interpretation applies where, as here, "Congress delegated authority to the agency generally to make rules carrying the force of law, and that the agency interpretation claiming deference was promulgated in exercise of that authority." *United States v. Mead Corp.*, 533 U.S. 218, 226-27 (2001). "Delegation of such authority may be shown in a variety of ways." *Id.* at 227. With the FDCA, Congress has authorized FDA to decide what drugs may lawfully enter the marketplace, and when and how they may enter. *See, e.g.*, 21 U.S.C. §§ 360b(c), 360b(d), 360b(e), 360b(f),

360b(j); *see also* 21 U.S.C. § 371(a) (vesting the Secretary of the Department of Health and Human Services (the "Secretary") with authority to promulgate regulations under the FDCA). Further, the Supreme Court has explained that *Chevron* deference is appropriate when "the interstitial nature of the legal question, the related expertise of the Agency, the importance of the question to administration of the statute, the complexity of that administration, and the careful consideration the Agency has given the question over a long period of time all indicate that *Chevron* provides the appropriate legal lens through which to view the legality of the Agency interpretation here at issue." *Barnhart v. Walton*, 535 U.S. 212, 222 (2002). Thus, deference is appropriate in the drug approval context because of "the complexity of the statutory regime" and "FDA's expertise." *Wyeth Holdings Corp. v. Sebelius*, 603 F.3d 1291, 1296 (Fed. Cir. 2010) (according *Chevron* deference to FDA's interpretation of FDCA); *United States v. Genendo Pharmaceutical, N.V.*, 485 F.3d 958, 963 (7th Cir. 2007) (same); *Mylan Laboratories, Inc. v. Thompson*, 389 F.3d 1272, 1280 (D.C. Cir. 2004) (same).

Furthermore, under the doctrine of *Skidmore* deference, agency interpretations that are not entitled to deference under *Chevron* can still "influence courts facing questions the agencies have already answered." *Mead Corp.*, 533 U.S. at 226-27. The "fair measure of deference to an agency administering its own statute has been understood to vary with circumstances, and courts have looked to the degree of the agency's care, its consistency, formality, and relative expertness, and to the persuasiveness of the agency's position." *Id.* at 228.

2. Applicants Must Have an Opportunity for Hearing Before Withdrawal Can Be Ordered

As the plain language of section 360b(e)(1) sets forth, any "finding" by the Commissioner that could compel the withdrawal of an animal drug under section 360b(e)(1) can only be made "*after*" the applicant has been granted "due notice and opportunity for [a] hearing."

See 21 U.S.C. § 360b(e)(1). (providing that "the [Commissioner] shall, after due notice and opportunity for hearing to the applicant, issue an order withdrawing approval of an [NADA] with respect to any new animal drug if the [Commissioner] finds" that any of the conditions or events enumerated in 21 U.S.C. § 360b(e)(1)(A) through (F) are shown to have occurred). Here, because such a hearing was never provided and the Commissioner never made the statutorily prescribed finding, section 360b(e)(1) does not provide a basis to "require" the withdrawal of any drug approval.

Indeed, courts have consistently held that withdrawals under section 360b(e)(1) may only proceed after the FDA has provided all of the sponsor's procedural rights.[11] *See Hess & Clark v. FDA*, 495 F.2d 975, 994-95 (D.C. Cir. 1974) (holding that FDA had "failed to carry its statutory burden[] under section . . . 360b(e)(1)(B)" where it revoked approval for animal drugs without holding a hearing); *Chemetron Corp. v. Dep't of Health, Educ. & Welfare*, 495 F.2d 995, 999 (D.C. Cir. 1974) (same); *see also Weinberger v. Hynson, Wescott and Dunning, Inc.*, 412 U.S. 609, 620-21 (1973) (a withdrawal under 21 U.S.C. § 360b(e)(1) cannot proceed without a hearing unless the Commissioner finds that a sponsor's request for a hearing raises no "genuine and substantial issue of fact").[12] In this case, the Commissioner initially granted the requests of approximately 20 parties to hold hearings to present evidence (s*ee* 43 Fed. Reg. 53827 (Nov. 17, 1978), Barcelo Decl. Ex. G)), but such hearings were never held because Congress requested that

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[11] Case law has also recognized that the issuance of an NOOH is fundamentally different from a ruling by the Commissioner that a drug should be withdrawn because the drug is *actually* unsafe or has not been shown to be safe. *Cf. Sterling Drug, Inc. v. Weinberger*, 384 F. Supp. 557, 561 (S.D.N.Y. 1974), *affd.* 509 F.2d 1236 (2d Cir. 1975) (issuance of NOOH is not an appealable agency decision; appeal to federal court may be taken from the Commissioner's final decision).

[12] *See also John D. Copanos and Sons, Inc. v. FDA*, 854 F.2d 510, 518 (D.C. Cir. 1988) (considering whether issues of fact necessitated hearing); *Masti-Kure Products Co., Inc. v. Califano*, 587 F.2d 1099, 1102-03 (D.C. Cir. 1978) (same).

FDA hold the 1977 NOOHs in abeyance pending further research (*see supra* Background at p. 6). As a result, the prerequisite for withdrawal under section 360b(e)(1) that that a sponsor receive "due notice and opportunity for hearing" *prior* to withdrawal plainly was never satisfied.

3. FDA's Bureau of Veterinary Medicine Was Not Authorized to Make Findings Sufficient to Compel Withdrawal of the NOOH Products

In addition to the absence of the statutorily-required opportunity for a hearing, there has been no finding by the Commissioner that one of the conditions or events enumerated in 21 U.S.C. § 360b(e)(1)(A) through (F) has transpired. Plaintiffs are incorrect in contending that the "finding" requirement was satisfied when BVM issued the 1977 NOOHs. Plfs' Br. at 9-10

It was BVM, not the Commissioner, who issued the 1977 NOOHs, and the Commissioner had not delegated to BVM the delegated authority to make any findings or taken any other action in 1977 to withdraw the NOOH Products on behalf of the Commissioner. When FDA issued the 1977 NOOHs, the Commissioner had delegated to BVM the authority to "issue notices of an opportunity for a hearing on proposals to refuse approval or to withdraw approval of new animal drug applications." 21 C.F.R. § 5.84 (1977). BVM did not, however, have authority to issue an actual "notice of withdrawal of approval" unless the "opportunity for hearing ha[d] been waived." *Id.* This authority to withdraw approvals was reserved to the Commissioner. Today, the Commissioner has made the same limited delegation of authority to CVM, and still has not delegated authority to withdraw approval where a hearing has been requested. *Compare* FDA, Staff Manual Guides § 1410.503(1)(A)(1) (reflecting delegation of authority to CVM to "issue notices of opportunity for a hearing on proposals to . . . withdraw approval of new animal drug applications . . . .") *with id.* at § 1410.503(1)(A)(2) (reflecting delegation of authority to CVM to "issue notices . . . withdrawing approval [for a new animal drug] when opportunity for hearing has been waived. . . . "), attached as Exhibit A to the Barcelo Decl. In this case, because

hearings were both requested and granted, BVM in 1977 did not have the authority to order withdrawals without subsequent findings by the Commissioner that the NOOH Products were "unsafe" or "not shown to be safe." For the same reasons, CVM does not have such authority today. Thus, there has been no previous finding by FDA that "requires" FDA to now withdraw the NOOH Products.

4. To the Extent That Section 360b(e)(1) Contains Any Ambiguity, the Court Should Defer to FDA's Interpretation of the Statute

In line with the plain language of section 360b(e)(1), FDA has consistently interpreted that section to provide that the decision to issue an NOOH is a preliminary finding that is both separate and distinct from the ultimate finding that forms the basis for a decision to revoke approval, and does not form basis to revoke approval where, as here, the sponsors' procedural rights under section 360b(e)(1) have not been satisfied. To the extent that this Court finds any ambiguity in section 360b(e)(1), it should defer to FDA's reasonable and long-standing interpretation of that provision. *See, e.g.*, *Mylan*, 389 F.3d at 1280.

As a preliminary matter, FDA's interpretation of section 360b(e)(1) is reflected by the Commissioner's limited delegation of authority to BVM in 1977 (and CVM today) to issue withdrawal notices, but *not* to act on such notices unless they go uncontested (discussed *supra* at pp. 15-16). This limited delegation of authority rests on FDA's view that, under section 360b(e)(1), the determination to issue an NOOH is *not* equivalent to a final determination regarding a drug's safety and effectiveness. Rather, those are two distinct determinations, for which two separate delegations of authority apply.[13]

[13] As a regulation promulgated pursuant to 21 U.S.C. § 371(a), the delegation to BVM contained in 21 C.F.R. § 5.84 (1977), is entitled to *Chevron* deference. *E.g.*, *United States v. Genendo Pharmaceutical, N.V.*, 485 F.3d 958, 961-64 (7th Cir. 2007) (according *Chevron* deference to regulations promulgated by FDA); *see also* 5 U.S.C. § 553(a)(2) (rulemaking

FDA's administrative adjudications have also interpreted section 360b(e)(1) as providing that an NOOH should issue before FDA has made any final determination regarding the safety or effectiveness of a drug. As FDA has interpreted section 360b(e)(1), the issuance of an NOOH reflects no more than that BVM's (or more recently CVM's) belief that there is a "reasonable basis from which serious questions about the ultimate safety of [the drug] . . . may be inferred." *See* Final Decision of the Commissioner, Withdrawal of Approval of the New Animal Drug Application for Enrofloxacin in Poultry, at 7, attached as N to Barcelo Decl.[14] (articulating the standard for this issuance of a notice of opportunity for hearing under 21 U.S.C. § 360b(e)(1)); *see also* Nitrofurans; Withdrawal of Approved New Animal Drug Applications (Nitrofurans), 56 Fed. Reg. 41902, 41903 (Aug. 23, 1991) attached as Exhibit O to the Barcelo Decl., (same); *see also* Diethylstilbestrol; Withdrawal of New Animal Drug Applications (DES), 44 Fed. Reg. 54852, 54861 (Sept. 21, 1979), attached as Exhibit P to the Barcelo Decl.[15] This standard is lower than the standard for withdrawal contained in section 360b(e)(1), which requires an actual determination that the drugs at issue are "unsafe" or not "shown to be safe." Thus, *even if* a withdrawal could theoretically be predicated on findings made in 1977 by BVM alone, it remains

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related to "a matter relating to agency management" are not subject to the requirements of notice and comment rulemaking).

[14] FDA announced the availability of its final decision withdrawing approval of Enrofloxacin at 70 Fed. Reg. 44105 (August 1, 2005).

[15] The Commissioner's interpretation of the law in the context of an adjudicative proceeding is accorded *Chevron* deference. *Mylan*, 389 F.3d at 1279-80 (according *Chevron* deference to FDA decision letters revoking approval for a drug); *Das v. HHS*, 17 F.3d 1250, 1254 (9th Cir. 1994) (according *Chevron* deference to Secretary's interpretation of the Social Security Act in adjudication of social security retirement benefits).

true that BVM never *actually made* a finding that could satisfy the high standard of section 360b(e)(1).[16]

Accordingly, if this Court determines that 21 U.S.C. § 360b(e)(1) contains any ambiguity relevant to whether BVM's 34-year-old decision to issue the 1977 NOOHs now "requires" FDA to revoke approval for the NOOH Products, it should defer to FDA's reasonable and long-standing interpretations of the requirements for withdrawal of approval of certain uses of an animal drug. *Wyeth*, 603 F.3d at 1296 (according *Chevron* deference to FDA's interpretation of FDCA); *Genendo Pharmaceutical*, 485 F.3d at 963 (same); *Mylan*, 389 F.3d at 1280 (same).[17]

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[16] Although an FDA regulation appears on its face to predicate the issuance of a notice of opportunity for hearing upon a finding that a drug is unsafe or not shown to be safe (*see* 21 C.F.R. § 514.115(b)(3)(ii)), FDA has consistently regulated in accordance with the view that the standard for issuing a withdrawal notice is that there exists a "reasonable basis from which serious questions about the ultimate safety of [the drug] . . . use may be inferred." *See supra* at p. 17. Under the standard established by the Supreme Court in *Auer v. Robbins*, an "agency's interpretations [of its own regulations] are . . . entitled to deference and are 'controlling unless plainly erroneous or inconsistent with the regulation.'" *Llanos-Fernandez v. Mukasey*, 535 F.3d 79, 82 (2d Cir. 2008) (*quoting Auer v. Robbins*, 519 U.S. 452, 461 (1997)); s*ee also Bah v. Mukasey*, 529 F.3d 99, 110-11 (2d Cir. 2008) ("[W]e give 'substantial deference' to [agency] decisions interpreting [its] regulations . . . , unless an interpretation is 'plainly erroneous or inconsistent with the regulation.'") (citations omitted). It is "axiomatic that the [agency's] interpretation need not be the best or most natural one by grammatical or other standards . . . . Rather, the [agency's] view need be only reasonable to warrant deference." *Pauley v. BethEnergy Mines, Inc*., 501 U.S. 680, 702 (1991); *see also Wangchuck v. Dep't of Homeland Sec*., 448 F.3d 524, 528 (2d Cir. 2006) ("We review [the agency's] interpretations of [its] regulations with 'substantial deference'. . . .").

[17] Even if FDA were not entitled to *Chevron* deference (although it is) this Court should still accord substantial deference to FDA's reasoned interpretation of section 360b(e)(1) in light of Congress's delegation of authority to FDA to promulgate regulations and carry out the objectives of the FDCA, as well as FDA's consistent and persuasive interpretation of section 360b(e)(1) as requiring that the finding that forms the basis to issue an NOOH is not equivalent to the finding that forms the basis to withdraw approval for drugs. *Wong v. Doar*, 571 F.3d 247, 255-65 (2d Cir. 2009) (according *Skidmore* deference and deferring to the Department of Health and Human Service's persuasive interpretation of the Medicaid Act where).

Indeed, even if FDA had not previously articulated the position it takes in this brief (as explained above, it has), its interpretation of section 360b(1)(e) would nevertheless still be entitled to *Skidmore* deference in light of FDA's expertise in administering the FDCA, the

5. Plaintiffs' Authorities are Inapposite

The FDA's longstanding and sound position is not undermined by the authority that Plaintiffs cite, none of which provide support for their claim that the Government is currently "required" to revoke approval for the NOOH Products. Plaintiffs' reliance on *Rhone-Poulenc, Inc. v. FDA*, 636 F.2d 750 (D.C. Cir. 1980), *see* Plfs' Br. at 8, is misplaced because that case stands for the unremarkable proposition that *after* the Commissioner has fulfilled its obligation to provide sponsors with notice and opportunity for hearing regarding a drug's safety, and if the "Commissioner" then finds that the drugs are "unsafe" or not "shown to be safe," FDA is, only at that point, required to withdraw approval for that drug. 636 F.2d at 752. Indeed, the court in *Rhone-Poulenc* expressly noted that section 360b(e)(1) would have prohibited FDA from withdrawing an approval had it not held the required "evidentiary hearing" on the proposed withdrawal. *Id.* at 751.

Plaintiffs' reliance on *dicta* from one of the 188 footnotes in the D.C. Circuit's opinion in *Cutler v. Hayes*, 818 F.2d 879, 893 (D.C. Cir. 1987) *see* Plfs.' Br. at 8, *citing Cutler*, 818 F.2d at 893 n. 116, also does not support their claim. Although that footnote described 21 U.S.C. § 355(e) (containing language similar to 21 U.S.C. § 360b(e)) as providing "an enforceable statutory directive," that footnote (and, for that matter the rest of the court's opinion) do not suggest that the court purported to negate the express statutory requirements for drug withdrawals contained in section 360b(e)(1), which include notice and opportunity for hearing, and a finding by the Commissioner. Rather, this footnote *dicta* appears intended to communicate

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persuasiveness of its position, and the substantial length of time over which FDA has acted consistently with its interpretation of section 360b(e)(1). *In re: New Times Sec. Serv., Inc.*, 371 F.3d 68, 81-88 (2d Cir. 2004) (according *Skidmore* deference to SEC's interpretation of Securities Investor Protection act of 1970, although the SEC that had not previously articulated that position "in *any* form") (emphasis in original).

the court's assumption that FDA would withdraw drug approvals *after* the Commissioner—*following* a hearing if one has been granted—has made the requisite finding that the drugs are unsafe or have not be shown to be safe. Accordingly, this case is no more helpful to Plaintiffs than *Rhone-Poulenc*.

Plaintiffs also rely on a 39-year-old case from another district, *American Public Health Ass'n v. Veneman*, 349 F. Supp. 1311 (D.D.C. 1972), *see* Plfs' Br. at 12, but that decision likewise does not support their position. The plaintiffs in *American Public Health Ass'n* sued FDA, alleging that FDA was required to expedite the review and withdrawal of over-the-counter drugs subject to what is commonly referred to as the "DESI" review process. *Id.* at 1313-15. Specifically, the plaintiffs challenged: (1) FDA's practice of extending the deadlines by which sponsors of drugs subject to the DESI review process were required to submit evidence beyond the time frame set forth in FDA regulations, and (2) the procedures FDA followed in withdrawing approval for such drugs. The court held that FDA's decision regarding the timing of the DESI process were subject to judicial review,[18] found that those extensions violated specific DESI-related regulations, and held that FDA's regulations required a "hearing on withdrawal of a new drug application . . . to be scheduled as soon as practicable." *Id.* at 1313-16. This holding is inapposite because the NOOH Products are not subject to the DESI review process. Unlike in *American Public Health Ass'n*, FDA's regulations impose no deadlines with respect to the 1977 NOOHs (indeed, Plaintiffs do not argue that FDA has not met any specifically mandated deadlines). More fundamentally, like all other authority interpreting 21

[18] This holding that FDA's action was subject to judicial review has arguably been overruled. Specifically, although the *American Public Health Ass'n* held that FDA's actions in that case were subject to judicial review because they were not committed to agency discretion, 349, F. Supp. at 1315, thirteen years later, in *Heckler v. Chaney*, 470 U.S. 821 (1985), the Supreme Court clarified (and arguably expanded) the law regarding when a statute "can be taken to have 'committed' the decisionmaking to the agency's judgment absolutely." 470 U.S. at 830.

U.S.C. §§ 355(e) and 360b(e)(1), this case *recognizes* the express statutory requirement that the opportunity for a hearing must be provided to sponsors before FDA may withdraw an approval pursuant to section 360b(e)(1). 349 F. Supp. at 1314 (the FDCA "require[s] that there be an opportunity for a hearing").

The legislative history that Plaintiffs cite for 21 U.S.C. § 355(e), *see* Plfs.' Br. at 11—a provision of the FDCA similar to section 360b(e)—is similarly not relevant to the issues before this Court. FDA agrees with Plaintiffs that the 1962 amendments to the FDCA changed the standard for withdrawing approval for human drugs, and that Congress expressed its intention to establish "procedures" that could lead to "prompt" withdrawal of human drugs that "should not have been cleared for safety in the first instance." S. Rep. No. 87-1744, at 8 (1962), *reprinted in* 1962 U.S.C.C.A.N 2884, 2885-86. Congress's explicit reference to such procedures, however, contradicts, rather than supports, Plaintiffs' argument that a Court can order withdrawal of approval where, as here, those procedures have not been followed and the Commissioner has not made the statutorily prescribed finding.

Accordingly, the Government is entitled to judgment as a matter of law that FDA's issuance of the 1977 NOOHs does not "require" it to now withdraw approval for the NOOH Products.

II. ANY REMAINING CLAIMS SHOULD BE DISMISSED AS MOOT

A. Applicable Legal Standards

The mootness doctrine, which is derived from the "case or controversy" requirement of Article III of the United States Constitution, dictates that federal courts lack jurisdiction to adjudicate a matter if the issues presented are no longer live or the parties lack a legally cognizable interest in the outcome. *See United States v. City of New York*, 972 F.2d 464, 469-70

(2d Cir. 1992) ("[T]he existence of a real case or controversy is an irreducible minimum of the jurisdiction of the federal courts.") (citing *Valley Forge Christian Coll. v. Americans United for Separation of Church & State*, 454 U.S. 464, 471 (1982)). The jurisdictional requirement of a live case or controversy remains "'extant at all stages of review, not merely at the time the complaint is filed.'" *Conn. Office of Prot. & Advocacy for Persons with Disabilities v. Hartford Bd. of Educ.*, 464 F.3d 229, 237 (2d Cir. 2006) (*quoting Steffel v. Thompson*, 415 U.S. 452, 459 n.10 (1974)). Agency action "is one type of subsequent development that can moot a previously justiciable issue." *Natural Res. Def. Counsel, Inc. v. U.S. Nuclear Regulatory Comm'n*, 680 F.2d 810, 814-15 (D.C. Cir. 1982).

B. Any Remaining Claim Plaintiffs May Intend to Assert Is Moot

With respect to Plaintiffs' first claim regarding the 1977 NOOHs, it is not clear that Plaintiffs seek anything in this case other than a court order mandating the outcome of the 1977 NOOHs by compelling FDA to withdraw approval for uses of the NOOH Products in medicated animal feed, *see* Plfs' Br. at 9-13, to which they are not entitled, *see supra* Part I. The Amended Complaint itself, however, only challenges the Agency's *failure* to act, because the Amended Complaint asserts claims only pursuant to section 706(1) and not under the separate provisions of the APA that provide a cause of action to challenge agency action. Thus, the only other claim that Plaintiffs could possibly make would be one of unreasonable delay based on FDA's allegedly improper failure to complete the proceedings initiated by the 1977 NOOHs. *See* 5 U.S.C. § 706(1) (creating a cause of action to "compel agency action unlawfully withheld or unreasonably delayed"). Although Plaintiffs have not explicitly argued that FDA has delayed unreasonably by not completing those proceedings, they have hinted at such a claim. *See* Plfs' Br. at 13 (requesting that the Court compel FDA to "complete the withdrawal proceedings"); *id.*

at 24 (requesting a court order mandating that "statutorily prescribed withdrawal proceedings" with respect to the NOOH Products be complete within one year); *see also* Am. Compl. ¶ 98 (characterizing Plaintiff's NOOH as a claim that FDA has "unlawfully withheld *or* unreasonably delayed") (emphasis added); *id.* Request for Relief ¶ C (requesting, as an alternative to their request for a court order compelling FDA to immediately withdraw approval for subtherapeutic uses of the NOOH Products, that "administrative proceedings" may be warranted with respect to those Products).

Assuming Plaintiffs do intend to bring a claim that the Government has delayed unreasonably by failing to conclude the proceedings it began with the 1977 NOOHs, the sole remedy available to the plaintiff under section 706(1) would be a court order "compelling" the Government to complete that process, without directing the substantive content of the resulting agency decision. *See, e.g.*, *Public Citizen Health Research Group v. FDA*, 740 F.2d 21, 32 (D.C. Cir. 1984) (the court "can order an agency to either act or provide a reasoned explanation for its failure to act"); *cf. S. Utah Wilderness Alliance v. Norton*, 301 F.3d 1217, 1226-27 (10th Cir. 2002) ("[C]ompelling agency action is distinct from ordering a particular outcome."), *rev'd on other grounds*, 542 U.S. 55 (2004).

Because FDA has now resolved the 1977 NOOHs by withdrawing them, there remains no live dispute between the parties regarding FDA's alleged failure to resolve the proceedings, and such claims should properly be dismissed as moot. *See McBryde v. Comm. to Review Circuit Council Conduct and Disability Orders of the Judicial Conference of the United States*, 264 F.3d 52, 55 (D.C. Cir. 2001) ("If events outrun the controversy such that the court can grant no meaningful relief, the case must be dismissed as moot."); *In re Int'l Union, United Mine Workers of Am.*, 231 F.3d 51, 54 (D.C. Cir. 2000) (claim of unreasonable delay in initiating rulemaking is

moot after agency issued proposed rule); *see also Rio Grande Silvery Minnow v. Bureau of Reclamation*, 601 F.3d 1096, 1111-12 (10th Cir. 2010) (challenge to biological opinions of the Bureau of Reclamation and the Army Corps of Engineers moot, where those biological opinions had been superseded); *ALCOA v. Bonneville Power Admin.*, 56 F.3d 1075, 1078 (9th Cir. 1995) (dismissing petition based in part on finding that factual underpinning of biological opinion had been superseded); *Natural Res. Def. Counsel, Inc.*, 680 F.2d at 814-15 (finding a case moot because the court "can hardly order the NRC at this point to do something that it has already done," and refusing to find the agency's earlier complained-of action unlawful because such would be "an advisory opinion which federal courts cannot provide"). Thus any further claims that Plaintiffs intend to bring—which necessarily seek an order compelling the prompt completion of an agency action that in fact has already been completed or terminated—should be dismissed as moot.

CONCLUSION

For the foregoing reasons, the Court should deny Plaintiffs' motion for summary judgment, and grant summary judgment in favor of the Government.

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Respectfully submitted,

PREET BHARARA
United States Attorney
Southern District of New York

/s/ Amy A. Barcelo
By: AMY A. BARCELO
Assistant United States Attorney
86 Chambers Street
New York, New York 10007
Tel.: (212) 637-6559
Fax: (212) 637-2730
Email: amy.barcelo@usdoj.gov

OF COUNSEL:

DAVID J. HOROWITZ
Deputy General Counsel

ELIZABETH H. DICKINSON
Acting Chief Counsel, Food and Drug Division

ERIC M. BLUMBERG
Deputy Chief Counsel, Litigation

THOMAS J. COSGROVE
Associate Chief Counsel

U.S. Department of Health and Human Services
Office of the General Counsel
White Oak 31 Room 4331
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
(Tel): (301) 796-8613