IN THE UNITED STATES DISTRICT COURT
FOR THE 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,	)	11 CIV 3562 (THK)
	)	ECF Case
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.	)	

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

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INTRODUCTION

The Government's response to this lawsuit is striking for what it omits: not once has the U.S. Food and Drug Administration (FDA) recanted or even cast doubt upon its own 1977 findings that subtherapeutic uses of penicillin and tetracyclines in animal feed are not shown to be safe for human health. It has not done so in the papers filed in this Court, nor in the notice the agency published in the Federal Register last month, withdrawing its 1977 notices of opportunity for a hearing. On the contrary, consistent with its repeated pronouncements over the last three decades, FDA continues to highlight the human health risks posed by nontherapeutic uses of medically important antibiotics in farm animals.

FDA's unrecanted findings trigger mandatory actions under the Federal Food, Drug, and Cosmetics Act (Food and Drug Act) to protect public health. FDA must withdraw approval for drug uses not shown to be safe unless a drug sponsor proves at a hearing that the uses are safe. FDA asserts that its findings do not compel agency action because they were made before, not after, a hearing, and not by a particular official. This litigation position defies the plain meaning of the Food and Drug Act and contradicts FDA's own implementing regulations.

The question at the core of the case is this: Can FDA, over the course of more than three decades, repeatedly express serious concerns about the safety of previously approved drugs, and yet allow those drugs to remain on the market all that time, without ever requiring the drug sponsors to prove their safety? For the reasons set forth in Plaintiffs' opening brief and below, the answer is no. Plaintiffs request an order directing FDA to withdraw approval for penicillin and tetracyclines in animal feed within one year, unless the agency's findings are overturned in formal hearings.

ARGUMENT

I. FDA Is Required to Withdraw Approval for Penicillin and Tetracyclines Unless the Agency's 1977 Findings Are Reversed in Administrative Hearings

The Food and Drug Act mandates that FDA "*shall*, after due notice and opportunity for hearing to the applicant, issue an order withdrawing approval" of a previously approved animal drug if the agency "finds . . . that new evidence . . . shows that such drug is not shown to be safe." 21 U.S.C. § 360b(e)(1)(B) (emphasis added). The Government admits that if FDA makes the finding contemplated by the statute, then it is "*required* to withdraw approval" for the drug not shown to be safe. Mem. in Supp. of the Government's Mot. for Summ. J. and in Opp'n to Pls.' Mot. for Summ. J. (Gov't Opp'n Br.) 19 (Dkt. 41) (emphasis added); *see Rhone-Poulenc, Inc. v. FDA*, 636 F.2d 750, 752 (D.C. Cir. 1980); *cf. Cutler v. Hayes*, 818 F.2d 879, 893 n.116 (D.C. Cir. 1987). The only question, then, is whether FDA has made the requisite findings with respect to penicillin and tetracyclines in animal feed. It has. *See* Tetracycline (Chlortetracycline and Oxytetracycline)-Containing Premixes (Tetracyclines Notice), 42 Fed. Reg. 56,264, 56,288 (Oct. 21, 1977) (proposing, with limited exceptions, to "withdraw all approvals for tetracycline-containing premix products [i.e., feed supplements] intended for subtherapeutic uses in animal feed . . . on the grounds that they have not been shown to be safe"), Ex. B to Decl. of Jennifer A. Sorenson, Oct. 5, 2011 (Sorenson Decl.) (Dkt. 33-2); Penicillin-Containing Premixes (Penicillin Notice), 42 Fed. Reg. 43,772, 43,772 (Aug. 30, 1977) (proposing to withdraw approvals for "all penicillin-containing premixes intended for use in animal feed on the grounds that . . . new evidence shows that the penicillin-containing products have not been shown to [be] safe for subtherapeutic use"), Sorenson Decl. Ex. A (Dkt. 33-1).

The Government contends that the statute mandates withdrawal only on a finding by the Commissioner of Food and Drugs, made *after* the drug sponsor has been provided with notice

and opportunity for a hearing. Because FDA's 1977 findings on penicillin and tetracyclines were made by the Director of the Bureau of Veterinary Medicine (BVM, now known as the Center for Veterinary Medicine or CVM), and because hearings were never held on the agency's proposal to withdraw approval for penicillin and tetracyclines, the Government argues that FDA is free to leave the drugs on the market.

Plaintiffs recognize that the law requires FDA to provide notice and opportunity for a hearing so that a drug sponsor can try to prove the safety of a drug FDA has proposed to prohibit. But that procedural requirement does not diminish FDA's statutory obligation to withdraw approval for a drug that is not shown to be safe. Rather, a "not shown to be safe" finding has two procedural consequences: it sets in motion mandatory withdrawal proceedings, and it shifts to the drug sponsor the burden of proving the drug's safety. If the drug sponsor fails to carry its burden in a formal administrative hearing, then FDA must withdraw approval for the drug.

FDA's own regulations and rulings support Plaintiffs' understanding of the procedures prescribed by law. The agency's regulations also demonstrate that BVM was authorized to make findings triggering the agency's duty to act. Moreover, the history of FDA's pronouncements on penicillin and tetracyclines in animal feed reveals that the Commissioner himself endorsed BVM's findings that the drugs were not shown to be safe. To this day, the agency's statements continue to reinforce the conclusion that approval for the drugs must be withdrawn, absent proof of safety.

A. The Government's Interpretation Strains the Text and Logic of the Statute

Statutory construction must take into account the "structure and grammar" of a provision. *Bloate v. United States*, 130 S. Ct. 1345, 1354 (2010). The Food and Drug Act directs that "[t]he Secretary shall, *after due notice and opportunity for hearing to the applicant*, issue an order withdrawing approval of an [animal drug] . . . if the Secretary finds . . . that new evidence . . .

shows that such drug is not shown to be safe . . . .” 21 U.S.C. § 360b(e)(1)(B) (emphasis added). The plain meaning of the provision is this: If FDA finds that a drug is not shown to be safe, it must withdraw its approval for the drug. Before it can issue the withdrawal order, the agency must provide notice and opportunity for a hearing. Unless FDA’s findings are reversed in a hearing, the withdrawal order must issue. The Government’s contention that FDA’s duty to withdraw approval for a drug not shown to be safe is triggered only by a finding made *after* a hearing strains both the text and logic of the statute.

“The position of the words in a sentence is the principal means of showing their relationship. . . . Modifiers should come, if possible, next to the word they modify.” William Strunk, Jr. & E.B. White, *The Elements of Style* 22, 24 (Macmillan Paperbacks ed. 1962). Here, Congress interposed the phrase “after due notice and opportunity for hearing to the applicant” between the words “shall” and “issue an order,” indicating that the phrase modifies these words. That is, the event that may take place only after notice and opportunity for a hearing is the issuance of an order withdrawing approval for a drug.

Congress could have placed the phrase “after due notice and opportunity for hearing” after the words “if the Secretary finds,” like so: “The Secretary shall issue an order withdrawing approval of an [animal drug] . . . if the Secretary finds, *after due notice and opportunity for hearing to the applicant*, . . . that new evidence . . . shows that such drug is not shown to be safe . . . .” That would have indicated that the agency could not make a finding compelling withdrawal until after notice and opportunity for a hearing. Or, if Congress had intended the phrase “after due notice and opportunity for hearing” to modify the entire provision, it could have put those words at the beginning of the sentence: “*After due notice and opportunity for hearing to the applicant*, the Secretary shall issue an order withdrawing approval of an [animal

drug] . . . if the Secretary finds . . . that new evidence . . . shows that such drug is not shown to be safe . . . .” But Congress did neither of these things. Instead, it placed the phrase “after due notice and opportunity for hearing” as close as possible to the words “shall issue an order,” even interrupting a compound verb to do so. This drafting decision supports Plaintiffs’ natural reading of the provision.

Far from dispensing with the procedural requirement of providing notice and opportunity for a hearing, *see* Gov’t Opp’n Br. 13-15, Plaintiffs’ reading explains when FDA must issue a notice of opportunity for a hearing in the first place. Unlike the Government’s interpretation, this reading also accounts for the situation in which a drug sponsor receives notice of opportunity for a hearing and *waives* a hearing. In that case, there would be no hearing and necessarily no post-hearing findings. But surely FDA would still have both the authority and the obligation to withdraw approval for the drug, based on the agency’s pre-hearing findings that the drug was not shown to be safe.

B. The Government’s Interpretation Contradicts FDA’s Own Regulations

The interpretation of the withdrawal provision advanced by the Government in this litigation contradicts FDA’s own regulations implementing that provision. The Government all but concedes this contradiction, acknowledging that “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 id.* at 18 n.16. The regulation states: “The Commissioner *shall* notify in writing the person holding an [animal drug] application approved pursuant to [21 U.S.C. § 360b(c)] and afford an opportunity for a hearing on a proposal to withdraw approval of such application if he finds . . . [t]hat . . . [n]ew evidence . . . shows that such drug *is not shown to be safe* . . . .” 21 C.F.R. § 514.115(b)(3)(ii) (emphasis added).

The "not shown to be safe" finding is the legal predicate to the notice. Once the Commissioner finds that a drug is not shown to be safe, she is *required* to initiate the statutorily mandated withdrawal proceedings by providing notice and opportunity for a hearing on a proposal to withdraw approval for the drug. *See id.* Unless the drug sponsor proves the drug's safety, these proceedings must end in withdrawal. *See* 21 U.S.C. § 360b(e)(1)(B). As discussed in Part II, below, FDA cannot avoid its duty to withdraw approval for penicillin and tetracyclines in animal feed by withdrawing its notices of opportunity for a hearing, when it has not recanted the findings themselves.

C. FDA's 1977 Findings Are Sufficient to Compel Withdrawal

The Government attempts to explain away the contradiction between its statutory interpretation and FDA's own regulations by inventing a distinction between so-called "preliminary," pre-hearing findings and "final," post-hearing findings that a drug is not shown to be safe. Gov't Opp'n Br. 12. The Government argues that BVM's 1977 findings that penicillin and tetracyclines have not been shown to be safe are insufficient to compel withdrawal because BVM was authorized only to make preliminary findings, which do not obligate FDA to take any action. *See* Gov't Opp'n Br. 15-18. These arguments fail for three reasons: First, neither the statute nor the implementing regulations mention, much less require, two sets of findings meeting two different standards. Second, BVM was authorized to make findings compelling withdrawal of approval for animal drugs not shown to be safe. Third, the Commissioner of Food and Drugs has endorsed BVM's 1977 findings that penicillin and tetracyclines in animal feed have not been shown to be safe.

1. Once FDA Finds that a Drug Is Not Shown to Be Safe, the Burden Shifts to the Drug Sponsor to Prove Safety

The Government misreads several of FDA's own administrative adjudications to suggest that the agency must meet a higher standard of proof when it actually withdraws approval for a drug, *after* a hearing, than when it proposes to withdraw approval for a drug, *before* a hearing. Gov't Opp'n Br. 17-18. An attentive reading of these adjudications, and the case law on which they rely, demonstrates that FDA bears only an initial burden of showing that a drug is not shown to be safe. It is the drug sponsor, not FDA, who carries the burden of persuasion. Once FDA has found that a drug is not shown to be safe, the burden shifts to the drug sponsor to prove otherwise. If the drug sponsor fails to do so, then FDA must withdraw approval for the drug.

In the Enrofloxacin Decision, on which the Government primarily relies, the Commissioner explains that the withdrawal of approval for an animal drug involves a two-step inquiry: "CVM, as the proponent of withdrawal of approval of [the drug], has the burden of making the first showing; in other words, CVM has the initial burden of production." Enrofloxacin in Poultry (Enrofloxacin Decision), No. 2000N-1571, at 7 (FDA July 27, 2005), Ex. N to Decl. of Amy A. Barcelo, Jan. 9, 2012 (Barcelo Decl.) (Dkt. 44-14). To meet this burden, CVM "must provide a reasonable basis from which serious questions about the ultimate safety of [the drug] . . . may be inferred." *Id.* (alteration in original; internal quotation marks omitted). "If CVM carries its burden of production, . . . the drug's sponsor[] has the burden of persuasion on the ultimate question of whether [the drug] is shown to be safe." *Id.* at 9. That is, the drug sponsor "must come forward with evidence that is sufficient to address CVM's safety questions." *Id.* at 8. As the "fact finder," the Commissioner determines whether the drug sponsor has carried its burden of proving the drug's safety. *Id.* at 9. If not, CVM's findings stand, and approval for the drug must be withdrawn.

Without analysis, the Government asserts that the "serious questions" 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.'" Gov't Opp'n Br. 17. But the Enrofloxacin Decision makes clear that the "serious questions" standard *is the same as* the "not shown to be safe" standard: the Commissioner explains that "the relevant statutory question is whether the animal drug 'has been shown to be safe,' 21 U.S.C. § 360b(e)(1), which, as explained earlier, has been interpreted to require that CVM show that there are serious questions about the safety of [the drug]." Enrofloxacin Decision 45. In other words, FDA has concluded that a drug is "not shown to be safe" when there are "serious questions" about its safety.

Once FDA has found that a drug is not shown to be safe—that is, that there are "serious questions" about the drug's safety—it is up to the drug sponsor to prove otherwise. If the drug sponsor fails to do so, then the inquiry is over, and approval for the drug must be withdrawn. There is no statutory or regulatory requirement that FDA make an additional, "final" finding meeting some higher standard.

The administrative adjudications cited by the Government confirm this two-step sequence. Like the Enrofloxacin Decision, the Nitrofurans Decision explains that "[t]he proponent of withdrawal, [CVM], has the burden of making the first showing (*i.e., that the drug is no longer shown to be safe*). . . . Once the limited threshold burden has been satisfied, of course, the burden passes to the sponsors to demonstrate safety." Nitrofurans (Nitrofurans Decision), 56 Fed. Reg. 41,902, 41,903 (Aug. 23, 1991), Ex. A to Supplemental Decl. of Jennifer A. Sorenson, Jan. 31, 2012 (emphasis added). Similarly, the DES Decision states, "Because the Bureaus are the proponents of withdrawal, . . . they have the burden of proving that the first

'showing' (i.e., a showing that the drug is no longer shown to be safe) has been made . . . . In other words, the Bureaus must provide a reasonable basis from which serious questions about the ultimate safety of [the drug] . . . may be inferred." Diethylstilbestrol (DES Decision), 44 Fed. Reg. 54,852, 54,861 (Sept. 21, 1979), Barcelo Decl. Ex. P (Dkt. 44-16) (internal quotation marks omitted). In both cases, the Commissioner ordered withdrawal after concluding that CVM/BVM had carried its burden and the drug sponsors had not carried theirs. Nitrofurans Decision, 56 Fed. Reg. at 41,911-12; DES Decision, 44 Fed. Reg. at 54,900.

The case law cited in these adjudications likewise demonstrates that once FDA has found that a drug is not shown to be safe, the burden shifts to the drug sponsor to prove safety. Evaluating a finding made by the Commissioner *after* a hearing, the D.C. Circuit held that "the Commissioner has met his *initial* burden of coming forward with some evidence of the relationship between the residue and safety . . . . This evidence is sufficient to shift the burden of showing the safety of DES to the manufacturers." *Rhone-Poulenc*, 636 F.2d at 753 (emphasis added) (internal citations and quotation marks omitted). The Court referred to FDA's burden as "initial" *not* because the agency was later required to meet some higher standard, but because the *only* burden FDA bore was an initial one: once it had been met, the burden shifted to the drug sponsors to prove safety. Because the Commissioner's determination that the drug sponsors "had not sustained their burden" was supported by substantial evidence, the Court upheld FDA's withdrawal of approval for DES. *Id.*

This interpretation of FDA's burden is the only sensible one. The Food and Drug Act places squarely on drug sponsors the burden of proving that a drug is safe: they must prove safety if a drug is to be approved in the first instance, 21 U.S.C. §§ 360b(b)(1)(A), (c)(1) & (d)(1)(A), and if serious questions later arise about the safety of a previously approved drug, they

must put those questions to rest. FDA cannot evade its statutory duty to protect the public from potentially unsafe drugs by labeling its 1977 findings "preliminary." Once FDA has found that a drug has "not been shown to be safe," Tetracyclines Notice, 42 Fed. Reg. at 56,288; Penicillin Notice, 42 Fed. Reg. at 43,772, it is both illegal and irresponsible for the agency to allow the drug to remain on the market indefinitely, without ever requiring the drug sponsor to prove its safety. That is what FDA is doing here.

2. BVM Was Authorized to Make Findings Requiring Withdrawal

The Government's contention that BVM was not authorized to make findings requiring withdrawal is baseless. FDA's own regulations provide that "[t]he Commissioner shall notify in writing the person holding an application approved pursuant to [21 U.S.C. § 360b(c)] and afford an opportunity for a hearing on a proposal to withdraw approval of such application if he finds . . . [t]hat . . . [n]ew evidence . . . shows that such drug is not shown to be safe." 21 C.F.R. § 514.115(b)(3)(ii). The Commissioner has delegated this duty to BVM (and now CVM): as of 1977, the Director of BVM was "authorized to issue notices of an opportunity for a hearing on proposals . . . to withdraw approval of new animal drug applications." 21 C.F.R. § 5.84 (1977), Barcelo Decl. Ex. M (Dkt. 44-13); *see also* FDA, Staff Manual Guides § 1410.503 (2011), Barcelo Decl. Ex. A (Dkt. 44-1).

The delegation to "issue notices of an opportunity for a hearing on proposals . . . to withdraw approval of new animal drug applications" necessarily encompasses the authority to make findings that an animal drug is not shown to be safe. The notice could not issue absent such a finding. Any notice issued must "specify the grounds upon which" the proposal is based. 21 C.F.R. § 514.200(a). If, upon receiving notice, a drug sponsor elects to waive its opportunity for a hearing, then the Commissioner never gets involved at all: BVM is authorized to issue an order withdrawing approval of the drug. 21 C.F.R. § 5.84 (1977); *see also* FDA, Staff Manual

Guides § 1410.503, ¶ 1.A.2 (2011). Thus, BVM must have the authority to issue a finding sufficient to compel withdrawal under 21 U.S.C. § 360b(e)(1).

If the sponsor requests a hearing, then FDA's formal hearing procedures come into play. *See* 21 C.F.R. §§ 514.200, 514.201 & pt. 12. The officer presiding over the hearing makes an initial decision as to whether the drug sponsor has proved the drug's safety; if the sponsor appeals, the Commissioner makes a final decision. *Id.* §§ 12.120-.130. But the involvement of the Commissioner does not diminish the legal significance of BVM's findings. These findings still trigger the statutorily mandated withdrawal proceedings, which must end in withdrawal if the drug sponsor cannot prove the drug safe. Moreover, as explained in the administrative adjudications discussed in the previous section, it is BVM, as the "proponent of withdrawal," that makes the showing that a drug is not shown to be safe or, in other words, that there are "serious questions" about the drug's safety. Enrofloxacin Decision 7; Nitrofurans Decision, 56 Fed. Reg. at 41,903; DES Decision, 44 Fed. Reg. at 54,861. Nothing about this scheme suggests that BVM lacks the authority to make findings compelling withdrawal under the Food and Drug Act.

3. The Commissioner of Food and Drugs Has Endorsed BVM's 1977 Findings

In this case, the question whether BVM, rather than the Commissioner, was authorized to make findings compelling withdrawal is academic. As the history of FDA's statements on penicillin and tetracyclines in animal feed shows, the Commissioner of Food and Drugs has endorsed BVM's 1977 findings. Moreover, those findings were not written on a blank slate: the drug sponsors had already submitted data to FDA that failed to prove the drugs' safety.

In 1970, the Commissioner established a Task Force to evaluate the potential human health threats posed by the long-term use of antibiotics in animals. *See* Antibiotic and

Sulfonamide Drugs in Animal Feeds, 37 Fed. Reg. 2444, 2444 (Feb. 1, 1972), Sorenson Decl. Ex. C (Dkt. 33-3). The Commissioner concluded that the Task Force's findings raised "sufficient question" about potential human health hazards to require drug sponsors to prove that the drugs were safe. Antibiotic and Sulfonamide Drugs in the Feed of Animals, 38 Fed. Reg. 9811, 9813 (Apr. 20, 1973), Sorenson Decl. Ex. D (Dkt. 33-4). He ordered drug sponsors and other interested parties to submit data within the next two years "which resolve conclusively the issues concerning [the drugs'] safety to man and animals . . . under specific criteria" established by FDA, or the agency would propose to withdraw all approvals for subtherapeutic uses of antibiotics in animal feed. *Id.* (codified at former 21 C.F.R. § 135.109; renumbered as 21 C.F.R. § 558.15).

Evaluating the information submitted by drug sponsors and others, the Director of BVM concluded that "the affected parties have failed to answer the safety questions raised" about penicillin, Penicillin Notice, 42 Fed. Reg. at 43,774, and "the affected parties have failed to show that extensive subtherapeutic use of the tetracyclines is safe." Tetracyclines Notice, 42 Fed. Reg. at 56,267. Finding that the drugs had "not been shown to be safe" for the uses for which they were approved, the Director issued notices of opportunity for a hearing on proposals to withdraw all subtherapeutic uses of penicillin and most subtherapeutic uses of tetracyclines in animal feed. Penicillin Notice, 42 Fed. Reg. at 43,772; Tetracyclines Notice, 42 Fed. Reg. at 56,288.

In 1983, the Commissioner denied a request by drug sponsors that FDA withdraw the notices of opportunity for a hearing regarding penicillin and tetracyclines. The Commissioner explained that "[t]he Director [of BVM] has not changed his earlier conclusion that the available scientific information warrants the proposed actions. . . . The notices of opportunity for hearing represent the Director's formal position that use of the drugs is not shown to be safe." Penicillin

and Tetracycline in Animal Feeds, 48 Fed. Reg. 4554, 4555-56 (Feb. 1, 1983), Sorenson Decl. Ex. DD (Dkt. 33-30). For these reasons, the Director did not wish to withdraw the notices of opportunity for a hearing. The Commissioner stated that he had "reviewed the Director's decision and concur[red] with it." *Id.* at 4556. The sole regulatory basis for the notices, and thus for the Commissioner's concurrence, was the substantive finding that the animal drug uses were not shown to be safe.

Recent statements by FDA continue to confirm the substance of the agency's 1977 findings. It is undisputed that in 2010, FDA concluded that "the overall weight of evidence available to date supports the conclusion that using medically important antimicrobial drugs for production purposes [in livestock] is not in the interest of protecting and promoting the public health." Gov't Resp. to Pls.' Statement of Facts ¶ 33 (Dkt. 45) (alterations in original) (internal quotation marks omitted). FDA reached that conclusion after reviewing forty years' worth of scientific reports issued by leading authorities around the world. *See* FDA, Draft Guidance No. 209, *The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals* 4-13 (2010), Sorenson Decl. Ex. O (Dkt. 33-15). In its review, FDA quoted the 2004 comments of its parent agency, the Department of Health and Human Services (HHS): "'We believe that there is a preponderance of evidence that the use of antimicrobials in food-producing animals has adverse human consequences. . . . There is little evidence to the contrary.'" *Id.* at 12. Since FDA published its review, the Centers for Disease Control and Prevention, another division of HHS, has stated that there is "strong scientific evidence of a link between antibiotic use in food animals and antibiotic resistance in humans," resulting in "adverse human health consequences." Gov't Resp. to Pls.' Statement of Facts ¶ 38 (internal quotation marks omitted). Last month, in withdrawing the 1977 notices of opportunity for a hearing, FDA reiterated that it "remains

concerned about" antimicrobial resistance and "continues to view [it] as a significant public health issue." Withdrawal of Notices of Opportunity for a Hearing, 76 Fed. Reg. 79,697, 79,698, 79,700 (Dec. 22, 2011), Barcelo Decl. Ex. L (Dkt. 44-12).

Against this backdrop, the Government's contention that BVM lacked authority to make findings compelling withdrawal is specious. FDA has repeatedly identified serious questions about the safety of penicillin and tetracyclines in animal feed, and has made formal findings that the drugs "have not been shown to be safe." The Food and Drug Act dictates what the agency must do in this situation: it must withdraw approval for the drugs, after notice and opportunity for a hearing. FDA has made clear that it has no intention of complying with this statutory mandate. It is up to this Court to enforce the law.

D. The Government's Litigation Position Is Not Entitled to *Chevron* Deference

The Government contends that its interpretation of the withdrawal provision, 21 U.S.C. § 360b(e)(1), is "long-standing" and therefore entitled to *Chevron* deference. Gov't Opp'n Br. 16. Where, as here, the statutory language is "unambiguous," the Court "must give effect to the unambiguously expressed intent of Congress." *Clark v. Astrue*, 602 F.3d 140, 147 (2d Cir. 2010) (internal quotation marks omitted). Even if the withdrawal provision were ambiguous, however, the Government's claim for deference would fail, because the agency documents it offers in support of its position do not embody the statutory interpretation it advances in this litigation. Courts do not defer to "agency litigating positions that are wholly unsupported by regulations, rulings, or administrative practice." *Bowen v. Georgetown Univ. Hosp.*, 488 U.S. 204, 212 (1988).

As evidence of its "consistent[]" interpretation of the withdrawal provision, the Government points to two sources: the Commissioner's delegations of authority to the Director of BVM, and FDA's administrative adjudications in the Enrofloxacin, Nitrofurans, and DES

cases. Gov't Opp'n Br. 16-17. None of these documents explicitly states that only a post-hearing finding that a drug is not shown to be safe requires FDA to withdraw approval for the drug. The Government contends, instead, that the documents *imply* that position by drawing a distinction between preliminary findings by BVM, meeting a "lower . . . standard" of proof, and final findings by the Commissioner, meeting the "high standard of section 360b(e)(1)." Gov't Opp'n Br. 17-18. As demonstrated in the previous sections, however, the documents do not draw any such distinction. *See supra* pp. 7-11. The Commissioner's delegations authorized the Director of BVM to make findings legally sufficient to compel withdrawal under 21 U.S.C. § 360b(e)(1). And FDA's administrative adjudications make clear that FDA is not required to make two separate showings, meeting two separate standards. These agency documents support Plaintiffs' reading of the withdrawal provision, rather than the interpretation now advanced by the Government.

If this Court defers to FDA at all, it should defer to FDA's own regulation implementing the withdrawal provision, on which, notably, the Government does *not* rely. *See* 21 C.F.R. § 514.115(b)(3)(ii). As discussed above, this regulation makes clear that a *pre-hearing* finding by FDA that a drug is "not shown to be safe" obligates the agency to pursue withdrawal proceedings. *Id.* The Government argues that this regulation does not mean what it says, and for support it points again to FDA's administrative adjudications. *See* Gov't Opp'n Br. 18 n.16. Again, the Court should not credit this litigation position.

Deference to an agency's interpretation of its own regulation "is warranted only when the language of the regulation is ambiguous." *Christensen v. Harris County*, 529 U.S. 576, 588 (2000). The Government concedes that the language of the regulation is plain: it "*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." Gov't Opp'n Br. 18 n.16 (emphasis added). Moreover, as demonstrated above, the administrative adjudications cited by the Government cannot bear the reading the Government now imposes on them. *See supra* pp. 7-10. This Court should read the implementing regulation as it is written and defer to it, rather than to a Government position "newly minted, it seems, for this lawsuit." *NRDC v. Abraham*, 355 F.3d 179, 201 (2d Cir. 2004) (quoting *Defenders of Wildlife v. Norton*, 258 F.3d 1136, 1145-46 n.11 (9th Cir. 2001)).

II. FDA's Withdrawal of the 1977 Notices of Opportunity for a Hearing Does Not Alter Its Statutory Duty to Act on Its Unrecanted Findings

A. Withdrawal of the Notices of Opportunity for a Hearing Does Not Moot Plaintiffs' Claim that FDA Has Unlawfully Withheld Agency Action

Contrary to the Government's representation when it requested and received an extension of the briefing schedule, *see* Letter from Amy A. Barcelo to the Hon. Theodore H. Katz, at 2 (Nov. 7, 2011), the Government does not now argue that FDA's recent withdrawal of the 1977 notices of opportunity for a hearing moots Plaintiffs' claim that FDA has unlawfully withheld agency action. Plaintiffs' claim cannot be moot because FDA has never recanted its findings that penicillin and tetracyclines in animal feed are not shown to be safe for human health. In fact, FDA's notice withdrawing the 1977 notices *reinforces* the science underlying the agency's earlier findings, lending additional support to Plaintiffs' claim.

FDA's December 22, 2011, notice acknowledges that the agency "remains concerned about" antimicrobial resistance and "continues to view [it] as a significant public health issue." Withdrawal of Notices of Opportunity for a Hearing, 76 Fed. Reg. at 79,698, 79,700. The notice explicitly states that the withdrawal of the 1977 notices "should not be interpreted as a sign that FDA no longer has safety concerns about the use of medically important antibiotics in food producing animals or that FDA will not consider re-proposing withdrawal proceedings in the future." *Id.* at 79,700-01. FDA also acknowledges that the scientific evidence supporting

withdrawal of approval of penicillin and tetracyclines has increased since 1977: the agency explains that, were it to re-propose withdrawal proceedings, it would issue new notices of opportunity for a hearing because "the body of scientific information relevant to the use of penicillins and tetracyclines in animal feeds has grown since 1977," and "FDA would need to provide notice to the sponsors that the information available since 1977 would be used to support the proposal to withdraw the approved uses of the drugs." *Id.* at 79,700.

FDA's December 2011 notice demonstrates why this Court must compel FDA to act by withdrawing approval for penicillin and tetracyclines in animal feed, unless the agency's findings are reversed in a hearing. For more than three decades, the agency has acknowledged that it has serious concerns about the safety of these drugs. The December notice reiterates these concerns. Yet FDA continues to shirk its statutory and regulatory duty to remove the drugs from the market absent proof of safety. The Court should compel FDA to withdraw the approvals unless the drug sponsors can prove in a hearing that the drug uses are safe.

B. FDA's Stated Reasons for Withdrawing the Notices of Opportunity for a Hearing Do Not Excuse FDA's Failure to Act

In its December 2011 notice, FDA offered three justifications for withdrawing the 1977 notices of opportunity for a hearing. First, the agency would prefer to address the mounting problem of antibiotic resistance by "promoting voluntary reform and the judicious use of antimicrobials." *Id.* at 79,701. Second, if FDA were to withdraw approval for penicillin and tetracyclines in animal feed, it would "update" the notices of opportunity for a hearing "to reflect current data, information, and policies." *Id.* Third, if FDA were to withdraw approval for any animal drugs, it would need to prioritize the withdrawal proceedings to "take into account which withdrawal(s) would likely have the most significant impact on the public health." *Id.* None of

these justifications relieves FDA of its statutory duty to withdraw approval of penicillin and tetracyclines in animal feed.

1. Nonbinding Recommendations Cannot Substitute for Withdrawal

Rather than withdraw approval for penicillin and tetracyclines in animal feed, FDA has issued a nonbinding, draft guidance document that discourages the use of medically important antibiotics in livestock for "production" purposes, such as "promoting faster weight gain or improving feed efficiency." *Id.* at 79,699 (discussing Draft Guidance No. 209). The agency "believes" that Draft Guidance No. 209 "represents another pathway to achieving the same goals contemplated by the 1977 [notices of opportunity for a hearing]." *Id.* In lieu of evidence that a nonbinding guidance will protect human health, the agency offers its "*belie[f]* that the animal pharmaceutical industry is *generally responsive* to the *prospect* of working cooperatively with the Agency," and says it "intends to work with sponsors *who approach FDA* and are interested in working cooperatively with the Agency to phase out production uses of medically important antimicrobials." *Id.* (emphasis added). FDA "believes" that by pursuing voluntary reform, "it will achieve its goal of promoting the judicious use of antimicrobial drugs in a more timely and resource-efficient manner than could be accomplished otherwise." *Id.* at 79,699-700. FDA has presented not a scrap of evidence (in the notice or to this Court) to support its counterintuitive belief in the efficacy of voluntary measures, and the degree of equivocation in the agency's own language effectively refutes any professed confidence in such measures.

Moreover, as a matter of law, FDA's issuance of nonbinding recommendations cannot excuse its failure to withdraw approval for animal drugs that are not shown to be safe. "[A]n agency ordered by Congress to promulgate binding regulatory requirements may not issue a non-binding policy statement that encourages but does not compel action." *Pub. Citizen, Inc. v. Nat'l Highway Traffic Safety Admin.*, 374 F.3d 1251, 1261 (D.C. Cir. 2004) (summarizing the holding

of *Pub. Citizen v. Nuclear Reg. Comm'n*, 901 F.2d 147, 157 (D.C. Cir. 1990)). As the D.C. Circuit has explained, for example, when Congress provided that the Secretary of Labor "shall establish minimum requirements" for firefighting equipment in coal mines, "[o]ne would hardly surmise . . . that Congress wanted the Secretary merely to exhort coal mine operators to have minimally suitable firefighting equipment on hand." *Pub. Citizen v. Nuclear Reg. Comm'n*, 901 F.2d at 155. Similarly, where the Environmental Protection Agency (EPA) had made *de facto* findings that certain chemicals were subject to a mandatory testing regime under the Toxic Substances Control Act, the court rejected EPA's "negotiation and acceptance of voluntary testing agreements by the manufacturers." *NRDC v. EPA*, 595 F. Supp. 1255, 1261 (S.D.N.Y. 1984). Finding "no support for EPA's decision to utilize negotiated testing agreements instead of the statutorily-prescribed initiation of rulemaking proceedings either on the face of the statute or based on some vague assertion of agency discretion," the court explained that "[t]he agency charged with implementing the statute is not free to evade the unambiguous directions of the law merely for administrative convenience." *Id.* (internal quotation marks omitted).

Here, the Food and Drug Act commands FDA to take binding action if a previously approved animal drug is no longer shown to be safe: the agency must "issue an order withdrawing approval" for the drug. 21 U.S.C. § 360b(e)(1). FDA is not free to substitute an improvised, unenforceable program for the mandatory regime devised by Congress. The agency "is not in the business of reaching consensus with the 'stakeholders' it regulates." *W. Harlem Envtl. Action v. EPA*, 380 F. Supp. 2d 289, 296 (S.D.N.Y. 2005). FDA does not point to any statutory authorization for its voluntary approach, nor is there any. The agency must withdraw approval for penicillin and tetracyclines in animal feed, as the Food and Drug Act requires, unless the drug sponsors can prove that the drug uses are safe.

2. Updating the Notices Is Not a Significant Hurdle

The need to update the 1977 notices of opportunity for a hearing to reflect the growing body of scientific knowledge underscoring the dangers of antibiotic resistance does not relieve FDA of its duty to act on its findings that penicillin and tetracyclines in animal feed are not shown to be safe. As discussed above, FDA has confirmed the substance of these findings. If the agency needs to update the notices of opportunity for a hearing to incorporate new scientific information such as "advances in our understanding of the genetics of resistance," then it must do so. Withdrawal of Notices of Opportunity for a Hearing, 76 Fed. Reg. at 79,700. Updating the notices presents no real impediment to FDA's prosecution of withdrawal proceedings for penicillin and tetracyclines. FDA has been actively reviewing the available scientific knowledge on antibiotic resistance, as its Draft Guidance demonstrates. *See* Draft Guidance No. 209, at 4-13. Moreover, it is undisputed that, in 2004, FDA sent letters to several manufacturers of approved animal feed products containing penicillin and tetracyclines, reporting that the agency had conducted a qualitative risk assessment and concluded that the products fell into a "high" risk category. Gov't Resp. to Pls.' Statement of Facts ¶ 65. FDA has had ample time to update the notices with the results of its analyses.

3. The Need to Prioritize the Withdrawal of Approvals Does Not Excuse FDA's Failure to Withdraw *Any* Approvals

FDA's contention that it would need to prioritize which withdrawals to propose, were it to withdraw approval for any animal drugs, is irrelevant. The agency has made clear that it does not intend to pursue *any* withdrawals: "for now, FDA's efforts will focus on promoting voluntary reform and the judicious use of antimicrobials." Withdrawal of Notices of Opportunity for a Hearing, 76 Fed. Reg. at 79,701. Nor is there evidence that FDA has made any attempt to set priorities for the necessary withdrawals. FDA made it known in 1977 that penicillin and

tetracyclines in animal feed are not shown to be safe for human health. For all that time, the agency has been under a statutory obligation to withdraw approval for these drugs. FDA has no excuse for allowing the drugs to linger on the market for more than three decades, when public health is at stake. The Food and Drug Act demands that the agency act.

C. The Court Should Not Countenance FDA's Attempts to Avoid Its Statutory Duty

FDA has not discharged its statutory duty to withdraw approval for subtherapeutic uses of penicillin and tetracyclines in animal feed absent proof of safety. As the existing science required, the agency found in 1977 that these animal drug uses were not shown to be safe. FDA notified the drug sponsors of their opportunity to prove otherwise at a hearing. FDA has never held those hearings or withdrawn the approvals, even though subsequent science has reinforced the validity of the agency's 1977 findings.

When Plaintiffs sued and moved for summary judgment, suddenly FDA withdrew the notices that flowed from the 1977 findings. It did not retract the findings themselves, and could not have done so given the mounting scientific evidence, confirmed by the agency, of the serious threat that antibiotic overuse in animal feed poses to human health. In Plaintiffs' view, FDA's withdrawal of the notices was a litigation maneuver designed to avoid a judicial reckoning with its unlawful conduct. The agency's purported justification for aborting the withdrawal process is an untested voluntary guidance that cannot substitute for the prohibition the statute prescribes.

This is not a game. FDA's principal purpose is to protect public health. For decades it has been clear to FDA that the overuse in animal feed of antibiotics that are also used to treat human infections jeopardizes public health. Yet the agency has refused to act as the law requires. When confronted with that failure, the agency has continued to evade its responsibilities. All the while,

the efficacy of antibiotics to treat human disease diminishes. The Court should not countenance the agency's persistent, harmful refusal to act.

III. Plaintiffs Seek Limited Judicial Relief

Because an updated notice will be required, followed by a hearing if drug sponsors request one, Plaintiffs do not seek an order compelling FDA to withdraw its approval for penicillin and tetracyclines in animal feed immediately. Instead, Plaintiffs request an order directing FDA to withdraw approval for these drug uses within one year, unless the agency's findings are overturned in formal hearings. *See* Am. Compl., Request for Relief ¶ C. This is the primary injunctive relief Plaintiffs seek, not an "alternative" request, as suggested by the Government. Gov't Opp'n Br. 23. It is the appropriate relief if Plaintiffs prevail on their claim that FDA has unlawfully withheld agency action, because it would compel the agency to take the action it is required by statute to take. It is also modest relief: Plaintiffs do not ask this Court to prejudge the outcome of any hearing that FDA may hold. They ask only that this Court enforce the Food and Drug Act by compelling FDA expeditiously to remove from the market drugs that are not shown to be safe, unless the drug sponsors can prove their safety. This is what the Food and Drug Act requires.

CONCLUSION

For these reasons, and those set forth in their opening papers, Plaintiffs respectfully request that this Court grant their motion for summary judgment; deny the Government's motion for summary judgment; and order FDA to withdraw approval for penicillin and tetracyclines in animal feed within one year, unless FDA's findings are reversed in a formal hearing.

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Respectfully submitted,

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