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

**BRIEF IN SUPPORT OF THE GOVERNMENT'S**
**POSITION ON THE ISSUE OF TIMING**

PREET BHARARA
United States Attorney for the
Southern District of New York
Attorney for Defendants
86 Chambers Street, 5th Floor
New York, New York 10007
Tel.: (212) 637-2716/2737

AMY A. BARCELO
ELLEN LONDON
Assistant United States Attorneys
– Of Counsel –

## TABLE OF CONTENTS

PRELIMINARY STATEMENT .....1

BACKGROUND .....2

A. 1977 Hearing Notices and Ensuing Congressional and Regulatory Actions, and Time and Resources for One Representative Withdrawal Proceeding .....2

B. This Litigation .....5

ARGUMENT .....6

POINT I. THE COURT SHOULD NOT SET A SCHEDULE FOR FDA'S WITHDRAWAL PROCEEDINGS .....6

A. A Court-Imposed Deadline On Agency Action is an Extraordinary Remedy .....6

B. There Is No Basis to Conclude That FDA Will Not Appropriately Conduct and Complete The Withdrawal Proceedings .....8

POINT II. ANY TIMELINE SHOULD ALLOW SUFFICIENT TIME FOR ORDERLY PREPARATION AND PROCEEDINGS .....10

A. Re-Issuance of the NOOHs .....11

B. Timing of Hearings .....13

C. Allocation of Resources Away From Other FDA Programs .....15

CONCLUSION .....17

## TABLE OF AUTHORITIES

**CASES** **PAGES**

*In re Barr Laboratories, Inc.*,
930 F.2d 72 (D.C. Cir. 1991) ..... 9

*Baystate Medical Ctr. v. Leavitt*,
587 F. Supp. 2d 37 (D.D.C. 2008) ..... 8

*Board of Trade v. SEC*,
883 F.2d 525 (7th Cir. 1989) ..... 9

*Cobell v. Norton*,
240 F.3d 1081 (D.C. Cir. 2001) ..... 9

*Cutler v. Hayes*,
818 F.2d 879 (D.C. Cir. 1987) ..... 9

*Electric Workers Insurance Fund v. Sebelius*,
No. 08 Civ. 14738, 2010 WL 728934 (E.D. Mich. Feb. 25, 2010) ..... 10

*FCC v. Pottsville Broadcasting Co.*,
309 U.S. 134 (1940) ..... 7

*FPC v. Transcontinental Gas Pipe Line Corp.*,
423 U.S. 326 (1976) ..... 7

*International Union, United Mine Workers of America v. Department of Labor & Mine Safety & Health Adm'n*,
554 F.3d 150 (D.C. Cir. 2009) ..... 8

*Nat. Resources Defense Counsel v. Environmental Protection Agency*, ,
489 F.3d 1364 (D.C. Cir. 2007) ..... 10

*Qwest Commc'ns Intern., Inc. v. FCC*,
398 F.3d 1222 (10th Cir. 2005) ..... 6

*Sierra Club v. U.S. Army Corps. of Engineers*,
701 F.2d 1011 (2d Cir. 1983) ..... 7

*Vermont Yankee Nuclear Power Corp. v. NRDC*,
435 U.S. 519 (1978) ..... 9

**STATUTES**

21 C.F.R. § 12.21(b) ..... 11

21 C.F.R. § 12.70 ..... 14

21 C.F.R. § 12.92 ..... 10

21 C.F.R. § 514.121(c) ..... 13

21 U.S.C. § 360b(e)(1)(B) ..... 3,6

**RULES AND REGULATIONS**

42 Fed. Reg. 43772, 43773 (Aug. 30, 1977) ..... 2

42 Fed. Reg. 56264, 56266 (Oct. 21, 1977) ..... 2

70 Fed. Reg. 44105 (August 1, 2005) ..... *passim*

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 brief to address "the issue of a timeline for holding a hearing and issuing a final decision" as to penicillin and tetracycline animal drug applications ("Withdrawal Proceedings"), as requested by the Court in its March 22, 2012 Order (the "March 22 Order"). *See Natural Resources Defense Council, Inc., et al. v. United States Food & Drug Adm'n, et al.*, *slip op.* at 55 n.19.

**PRELIMINARY STATEMENT**

The Government understands the Court's request for briefing on "the issue of a timeline" as calling both for information about how much time Withdrawal Proceedings are likely to consume, and for argument concerning whether the Court can and should impose any deadline or schedule to govern the Withdrawal Proceedings. The Court should decline to impose a deadline on the United States Food and Drug Administration ("FDA" or the "Agency") to complete the Withdrawal Proceedings. As numerous courts have recognized, the judicial imposition of a deadline for agency action is an extraordinary remedy that should be granted sparingly. As a general matter, agencies are entitled to considerable deference in how they discharge their responsibilities, and courts should be reticent to direct the internal operations of agencies.

Courts generally impose deadlines on agency action only in cases in which there has been a judicial finding of unreasonable delay, a failure to comply with a statutory deadline, or agency intransigence in complying with court orders. None of these circumstances is present here. Before the March 22 Order, FDA believed it had no legal duty to proceed with hearings. Since the Court's ruling, the Agency has ascertained the numerous tasks that would be required to complete the Withdrawal Proceedings, and, subject to any future direction by the appellate

courts, it intends to abide by the orders of the Court. There is no basis to assume that there will be any unreasonable delay going forward.

If the Court does decide to impose a deadline notwithstanding these considerations, any such deadline should be crafted to ensure that the Withdrawal Proceedings do not detract from other Agency programs that are important to protect the public health. The Agency has provided evidence in the accompanying declaration from the Deputy Director of Science Policy at FDA's Center for Veterinary Medicine ("CVM"), Dr. William T. Flynn ("Flynn Decl."), describing FDA's rough but conservative estimation of the tasks needed to complete the Withdrawal Proceedings. As discussed below, FDA estimates that issuing new notices of opportunity for hearing ("NOOHs") will take between 11 and 17 months, and completing the hearing process, including agency appeals, could take about four more years, although that time period is extremely difficult to predict at this point.[1]

## BACKGROUND

### A. 1977 Hearing Notices and Ensuing Congressional and Regulatory Actions, and Time and Resources for One Representative Withdrawal Proceeding

In 1977, CVM published two NOOHs proposing to withdraw the approval of penicillins and tetracyclines in animal feeds for certain "nontherapeutic" uses (the "1977 NOOHs") because of concerns about antimicrobial resistance. 42 Fed. Reg. 43772, 43773 (Aug. 30, 1977), attached as Exhibit D to the Declaration of Amy A. Barcelo dated January 9, 2012 ("Jan. Barcelo Decl."); 42 Fed. Reg. 56264, 56266 (Oct. 21, 1977), Jan. Barcelo Decl. Ex. E. In response to the 1977

[1] While the Government indicated in Court during the May 10 hearing that FDA expected the process to take approximately four and one half years to complete, this reflected a preliminary projection that assumed that reissuing both NOOHs would necessarily take only 11 months, and that failed to account for an eight-month period between the re-issuance of the NOOHs and, assuming hearings are requested and granted, the issuance of the notice announcing actual hearings.

NOOHs, numerous manufacturers (also known as "sponsors") of products subject to the notices (the "NOOH Products") requested hearings pursuant to the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. § 360b(e)(1), to contest the proposed withdrawals. 43 Fed. Reg. 53827, 53828 (Nov. 17, 1978), attached as Ex. G to the Jan. Barcelo Decl. FDA granted the requests for hearings, but soon after, FDA's Congressional appropriators requested that the Agency abstain from holding hearings and instead study the issue of antimicrobial resistance in more depth. *Slip op.* at 13. There is no dispute that, unless the requested hearings were held, FDA would not have been lawfully permitted to withdraw approvals for the NOOH Products. *E.g.*, Plaintiffs' Brief in Opposition to the Government's Motion for Summary Judgment at 3 (Dkt. No. 50).

FDA proceeded to study the issue in more depth, Defendants' Brief in Support of the Government's Motion for Summary Judgment at 2 (Dkt. No. 41), and although the withdrawal hearings for the NOOH Products were never convened, FDA withdrew approval for another class of antimicrobial drugs (fluoroquinolones) for use in poultry because of concerns about antimicrobial resistance. 70 Fed. Reg. 44105 (August 1, 2005). In that case, although only one drug sponsor (Bayer) requested a hearing to contest the proposed withdrawals with regard to a single new animal drug application ("NADA") for its product called Baytril, the hearing process consumed a significant amount of Agency resources (over five years and $3.3 million dollars). Jan. Barcelo Decl. Ex. N at 4; Jan. Barcelo Decl. Ex. I at 3 & Ex. J at 3.

As the Court knows, in light of FDA's experience with the fluoroquinolone withdrawals, and the time and expense required to withdraw just one drug approval, the Agency concluded that it would not be practical to immediately seek involuntarily to withdraw the remaining 161 individual approved applications covering the nontherapeutic uses (*i.e.,* "growth promotion"

uses) for antimicrobial drugs that are considered important to human medicine ("Medically Important Antibiotics"). Jan. Barcelo Decl. Ex. B at 13-17; Jan. Barcelo Decl. Ex. I at 3-4, Jan. Barcelo Decl. Ex. J at 2-4; Exhibit A to the Declaration of Amy A. Barcelo dated April 16, 2012 ("Third Barcelo Decl.") at 18-22. FDA therefore formulated an alternate regulatory strategy that would focus first on eliminating the injudicious use of such drugs voluntarily, with the potential for more forceful regulatory action later, if needed. Jan. Barcelo Ex. I at 4; Jan. Barcelo Decl. Ex. J at 4; *see also* Third Barcelo Ex. C at 7. FDA publicly announced its new plan in 2010 when it published a draft guidance titled *The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals*, draft Guidance for Industry #209 ("Draft GFI 209"). Based on Draft GFI 209, FDA began working with sponsors to voluntarily withdraw approvals for growth-promotion uses, and also to make labeling changes sufficient to require that Medically Important Antibiotics may be used for therapeutic purposes only under the direction of a veterinarian. Jan. Barcelo Decl. Ex. B at 17. (FDA believes that the involvement of a veterinarian is critically important in reducing the misuse and overuse of Medically Important Antibiotics.) On April 11, 2012, FDA took another important step to implement its strategy by publishing finalized Draft GFI 209, and published Draft Guidance for Industry 213 ("Draft GFI 213"), which describes the Agency's plan to encourage the withdrawal of growth-promotion indications and transition the remaining therapeutic indications to veterinarian oversight. Third Barcelo Decl. Exs. A & C.

FDA intended to apply its new regulatory strategy to all 161 Medically Important Antibiotics, including the 73 NOOH Products. By implementing this strategy, FDA believed that it could most quickly and efficiently reduce the misuse and overuse of antibiotics in animals that are contributing to the development of antimicrobial resistance. FDA is optimistic that the

draft guidance will result in the withdrawal of growth promotion indications within a three-year period after Draft GFI 213 is finalized. When FDA chose to pursue this new regulatory strategy, it believed that it was not under any legal obligation to hold hearings pursuant to the 1977 NOOHs.

**B. This Litigation**

Plaintiffs disagreed with FDA's new regulatory strategy, and in 2011, filed the instant action to, *inter alia*, compel the Agency to hold the withdrawal proceedings that had been proposed thirty-four years earlier. But FDA no longer viewed the 1977 NOOHs as having any continuing significance, and to ensure that there was no confusion about its regulatory strategy going forward (*i.e.,* that it intended to proceed along the path first articulated in 2010 in Draft GFI 209), FDA withdrew both NOOHs on December 16, 2011. *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 Jan. Barcelo Decl.[2]

Following cross-motions for summary judgment, on March 22, 2012, this Court rejected FDA's long-held belief that the 34-year-old 1977 NOOHs did not constitute "findings" and so did not require FDA to conduct withdrawal proceedings. Rather, the Court held that, prior to issuing the 1977 NOOHs, FDA had made "findings" that the NOOH Products had not been "shown to be safe," and that the Agency was under a continuing obligation to convene the

[2] FDA stated three reasons for withdrawing the 1977 NOOHs. 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.

Withdrawal Proceedings pursuant to 21 U.S.C. § 360b(e)(1). *Slip. op.* at 46-47. Moreover, this Court found that FDA's pursuit of its new regulatory strategy could not substitute for Withdrawal Proceedings because the Court concluded that the findings relating to the NOOH Products had never been withdrawn. *Slip op.* at 50-53.

As discussed further below in response to the question posed in the Court's March 22 ruling, *see infra* at § II, FDA's current estimate is that the Withdrawal Proceedings will require the efforts of more than a dozen FDA employees, and will take a significant amount of time to complete. Specifically FDA estimates that it will take approximately 11 to 17 months to reissue NOOHs, and that hearings could take about four years to complete (totaling from between about five to five and a half years to complete). Although FDA has ascertained the steps required by the Withdrawal Proceedings, and is prepared to move forward with them, the Government also is evaluating its potential defenses and appeal rights in this action.

## ARGUMENT

### I. THE COURT SHOULD NOT SET A SCHEDULE FOR FDA'S WITHDRAWAL PROCEEDINGS

#### A. A Court-Imposed Deadline On Agency Action is an Extraordinary Remedy

First, both applicable law and the facts of this case show that the Court should not mandate any particular schedule for the completion of the Withdrawal Proceedings that the Court has directed FDA to commence. The imposition of a court-imposed deadline for agency action on remand is an extraordinary remedy that should be imposed only in rare circumstances that are not present here. *See Qwest Commc'ns Intern., Inc. v. FCC*, 398 F.3d 1222, 1238-39 (10th Cir. 2005) ("[I]t is clear that a court-imposed deadline for agency action constitutes an extraordinary remedy."). As recognized by the Second Circuit, "the Supreme Court has ruled repeatedly that, except in the most extraordinary circumstances, the courts may not control the internal

operations of federal administrative agencies." *Sierra Club v. U.S. Army Corps. of Eng'rs*, 701 F.2d 1011, 1042 (2d Cir. 1983). The Supreme Court has noted that its decisions "could hardly be more explicit" that, "[a]bsent constitutional constraints or extremely compelling circumstances[,] the administrative agencies should be free to fashion their own rules of procedure and to pursue methods of inquiry capable of permitting them to discharge their multitudinous duties." *Vermont Yankee Nuclear Power Corp. v. NRDC*, 435 U.S. 519, 543-44 (1978) (internal quotations omitted). Accordingly, even where a court remands a matter to an agency for further proceedings, it should not dictate "the time dimension of the needed inquiry" without "substantial justification." *Id.* at 544-45. Otherwise, the court risks intruding "into the domain which Congress has set aside exclusively for the administrative agency." *Id*. *See also FPC v. Transcon. Gas Pipe Line Corp*., 423 U.S. 326, 333 (1976) (following a remand, an agency should be allowed to "exercise its administrative discretion in deciding how, in light of internal organization considerations, it may best proceed to develop the needed evidence . . . .").

*Sierra Club* illustrates the high bar that courts apply before asserting control over internal agency procedures on remand. In that case, the district judge set aside an agency decision and appointed a special master to ensure prompt compliance with the court's order. *Sierra Club*, 701 F.2d at 1044. In reversing, the Second Circuit held that "the timing concerns expressed by the district court simply are not the 'extremely compelling circumstances' needed to justify judicial control of administrative agency proceedings." *Id.* Even though the district court in *Sierra Club* found that the agency had failed to carry out its responsibilities, the Second Circuit held that there was no reason to believe that the agency would not faithfully discharge its duties on remand. *Id.* at 1048 (citing *FCC v. Pottsville Broadcasting Co.*, 309 U.S. 134, 146 (1940)

("[C]ourts are not charged with general guardianship against all potential mischief in the complicated tasks of government.")).

### B. There Is No Basis to Conclude That FDA Will Not Appropriately Conduct and Complete The Withdrawal Proceedings

Although this Court may retain jurisdiction to monitor the Withdrawal Proceedings, this "is typically reserved for cases alleging unreasonable delay of agency action or failure to comply with a statutory deadline, or for cases involving a history of agency noncompliance with court orders or resistance to fulfillment of legal duties." *Baystate Medical Ctr. v. Leavitt*, 587 F. Supp. 2d 37, 41 (D.D.C. 2008). Here there is no relevant statutory deadline, no history of noncompliance with court orders, and no resistance to fulfillment of legal duties that were known to or understood by FDA.

FDA did not abstain from holding withdrawal hearings because of indifference or intentional disregard of law, but because of its belief that it was not under a legal duty to proceed with hearings. Had FDA believed it was under a duty to convene a hearing following the issuance of the 1977 NOOHs, it would have done so long ago. Accordingly, the Court has "no reason to assume that [FDA] will not proceed expeditiously." *Int'l Union, United Mine Workers of Am. v. Dep't of Labor & Mine Safety & Health Adm'n*, 554 F.3d 150, 155 (D.C. Cir. 2009). In *United Mine Workers*, as here, the actions required to comply with the Court's order on remand "obviously, have not yet been delayed," and the court thus "decline[d] to impose a scheduling order or to retain jurisdiction." *Id.* Similarly, this Court should decline to impose a scheduling order for the Withdrawal Proceedings.

Furthermore, any hard deadlines necessarily would interfere with FDA's discretion and ability best to manage the Withdrawal Proceedings in the context of its other duties. FDA "is in a unique—and authoritative—position to view its projects as a whole, estimate the prospects for

each, and allocate its resources in the optimal way," and the Court should allow FDA the flexibility needed to pursue all of its projects simultaneously. *In re Barr Labs., Inc.* 930 F.2d 72, 76 (D.C. Cir. 1991). *See also Cutler v. Hayes*, 818 F.2d 879, 896 (D.C. Cir. 1987) ("Any discussion of the standards relevant to the issue of delay must begin with recognition that an administrative agency is entitled to considerable deference in establishing a timetable for completing its proceedings."); *Cobell v. Norton*, 240 F.3d 1081, 1096 (D.C. Cir. 2001) ("An agency's own timetable for performing its duties in the absence of a statutory deadline is due 'considerable deference.'"). Thus, while the Court's holding that FDA has a statutory duty to pursue Withdrawal Proceedings could logically support an order that FDA do so, any such order should not—before the FDA has even had a chance to comply based on its independent assessment of how appropriately to do so—impose a mandatory schedule controlling the resulting administrative action.

Practical real-world considerations support this consideration. As the D.C. Circuit has recognized, a premature reordering of the agency's priorities could cause the agency to shortchange other important work. *See In re Barr Labs, Inc.*, 930 F.2d at 75 ("Assuming constant resources . . . , a judicial order putting Barr at the head of the queue simply moves all others back one space and produces no net gain. Agency officials not working on Barr's matters presumably have not just been 'twiddl[ing] their thumbs.'") (citing *Board of Trade v. SEC*, 883 F.2d 525, 531 (7th Cir. 1989)). The imposition now of a time table would not be in the interest of public health or assist the Agency in discharging its "multitudinous duties." *Vermont Yankee,* 435 U.S. at 543.

Moreover, FDA is far from certain about the accuracy of its estimated timeline given that significant parts of the withdrawal process will be largely outside of CVM's and FDA's control.

For instance, the timing of hearings will depend on, *inter alia*, how many sponsors request hearings, the complexity of the issues they may raise, and the number of witnesses each party calls. Moreover, the Administrative Law Judge ("ALJ"), not CVM or the Commissioner, sets the hearing schedule, and it is not advisable for this Court to cabin the ALJ's scheduling discretion in advance. *See* 21 C.F.R. § 12.92 ("The presiding officer shall issue . . . a prehearing order reciting the actions taken at the prehearing conference and setting forth the schedule for the hearing.").

Finally, there is no harm to Plaintiffs if the Court does not set a schedule for remand at this time. If and when Plaintiffs believe that FDA's pace in holding hearings is too slow, they can seek relief from the Court. *See Nat. Resources Defense Counsel v. Envtl. Prot. Agency*, 489 F.3d 1364, 1375 (D.C. Cir. 2007) (declining to set a time limit on remand due to the availability of a future remedy for any undue delay); *Elec. Workers Ins. Fund v. Sebelius*, No. 08 Civ. 14738, 2010 WL 728934 at *4 (E.D. Mich. Feb. 25, 2010) (same).

Accordingly, the Court should allow the agency to proceed on remand with the necessary discretion to prepare for and conduct the Withdrawal Proceedings.

## II. ANY TIMELINE SHOULD ALLOW SUFFICIENT TIME FOR ORDERLY PREPARATION AND PROCEEDINGS

If the Court nevertheless decides to set a timeline for the Withdrawal Proceedings, which it should not, any such timeline should allow FDA sufficient time to develop and present its case, and should not impinge on the ALJ's discretion in setting the schedule for hearings. Failing to do so would give the Agency inadequate time to develop a sound case in favor of withdrawing the NOOH Products; this in turn could yield a rushed process that could render the proceedings to be disorganized and possibly unsuccessful. As set forth in the accompanying Declaration of CVM Deputy Director for Science Policy Dr. William T. Flynn, DVM, FDA estimates that it

should be possible to reissue NOOHs within 11 to 17 months, and that a hearing could take an additional four years or more to complete, including potential administrative appeals. (Flynn Decl. ¶¶ 6, 25.) As noted in Dr. Flynn's declaration, this projection is highly speculative and includes assumptions about events that are beyond FDA's control. (*Id.* ¶¶ 6, 11, 25.)

**A. Re-Issuance of the NOOHs**

As discussed by Dr. Flynn, the first step in the Withdrawal Proceedings would be to update and re-issue the 1977 NOOHs. (*Id.* ¶ 8.) The 1977 NOOHs must be updated because FDA is legally required to provide drug sponsors with the bases for a proposed withdrawal prior to a hearing. (*Id.*; 21 C.F.R. § 12.21(b)). Because the scientific knowledge surrounding antimicrobial resistance has developed and changed over the past 35 years, CVM must evaluate the more recent science since the 1977 NOOHs were originally published "to determine whether any new information has emerged over the past 35 years that could bear on FDA's original analysis." (Flynn Decl. ¶¶ 8, 9.)

As Dr. Flynn states, "[f]ailing to update the 1977 NOOHs to take into account the current state of scientific understanding would result in presentations in the Withdrawal Proceedings that are incomplete, lack scientific rigor, and would be subject to challenge." (*Id.* ¶ 9.) Furthermore, as Dr. Flynn notes, a failure to update the 1977 NOOHs "could obviously put the Agency at greater risk of not meeting its burden of proof at a hearing." (*Id.* ¶ 10.)[3]

CVM estimates that it will take approximately eleven to seventeen months to re-issue the NOOHs. (*Id.* ¶ 16.) This estimate is based on an evaluation of the complexity of the scientific

[3] "At a withdrawal hearing, CVM must first satisfy its burden of production by making out a prima facie case for withdrawal." *See* Jan. Barcelo Decl. Ex. N at 7; 70 Fed. Reg. 44105 (August 1, 2005). According to precedent, CVM satisfies its burden and shifts the burden to the drug sponsors by establishing a "reasonable basis from which serious questions about the ultimate safety of [the drug] . . . may be inferred." *Id.*

issues, the number of sponsors and drugs subject to potential withdrawal, and the Agency's experience with prior hearings. (*Id.* ¶¶ 6, 7, 17; *see also id.* at ¶ 6 ("Because CVM anticipates issuing 2 NOOHs and 73 individual drug products are at stake, these proceedings are likely to be more time-intensive and procedurally complex than any prior CVM drug withdrawal proceeding."))

The re-issuance of the NOOHs would require CVM to complete several distinct tasks. *First,* CVM would be required to search its official files for relevant information. (*Id.* ¶ 11.) Because FDA has been studying antimicrobial resistance for more than 40 years, "this search for documents will be a substantial undertaking." (*Id.*) CVM estimates that the search will take a team of 10 to 14 Agency employees approximately 60 days. (*Id.*) *Second*, "CVM would need to conduct an in-depth search for publically available literature and other information (*e.g.,* scientific reports) on the scientific topics that would be addressed at a hearing." (*Id.* ¶ 12.) Over thirty years have passed since CVM published the 1977 NOOHs, and scientific knowledge in this area has continued to accumulate. (*Id.* ¶ 8.) Although the volume and extent of information is enormous, because CVM has a good deal of information collected already, and because it can assign multiple research teams to work simultaneously, it should take six to ten Agency employees only about 90 days to conduct the search. (*Id.* ¶ 12.)

*Third*, it will take a team of six to ten Agency employees, including several senior scientists spending substantial amounts of time on this matter (rather than on other matters), approximately six months to review the information and determine the Agency's current scientific position with regard to the microbial food safety of the NOOH Products. (*Id.* ¶ 13.) Next, it will take a team of 8 to 12 Agency employees, including several senior scientists spending substantial amounts of time, approximately 60 days to decide whether the science still

supports the withdrawal of the NOOH Products, and to frame the legal and scientific arguments accordingly. (*Id.*)

*Fourth,* it will take a team of ten to fourteen FDA employees approximately 60 days to draft the revised NOOHs, and after that, it will take approximately 60 more days for senior management and Agency attorneys to review and clear the revised NOOHs, and for the revised NOOHs to be edited and published in the Federal Register. (*Id.* ¶¶ 14, 15.)

As Dr. Flynn concludes, "[a]ltogether, CVM estimates that it will take approximately 17 months from the beginning of the process to the final publication of the revised NOOHs, although this represents only CVM's best current estimate." (*Id.* ¶ 16.) According to Dr. Flynn, "[t]o the extent that CVM is able to conduct certain of the above tasks simultaneously, or if the tasks take less time than expected, it is possible that the revised NOOHs could be published in as few as 11 months; at this point, CVM believes that the 17 month projection is more realistic." (*Id.*)

**B. Timing of Hearings**

Next, as discussed by Dr. Flynn, "to the extent that drug sponsors request and are granted hearings, the subsequent schedule will be largely controlled by the ALJ and it is impossible to predict with certainty or confidence how long hearings would take." (*Id.* ¶ 17.) But based upon "prior experience with other past hearings to withdraw approval of new animal drug applications, most recently enrofloxacin in poultry" (*id.*), CVM estimates that completing one hearing, including potential appeals to the Commissioner, would take approximately 49 months following the issuance of the revised NOOHs. (*Id.* ¶ 25.)

*First*, drug sponsors would be given 30 days to respond to the revised NOOHs and to request hearings. *See* 21 C.F.R. § 514.121(c). *Second*, any requests for hearings would need to

be reviewed carefully, which may take approximately 90 days and involve from between 9 and 13 Agency employees. (*Id.* ¶ 19.) *Third*, a team of four Agency employees would need approximately 60 days to develop a recommendation to the Commissioner on whether to grant a hearing, or instead grant summary determination in favor of CVM (*i.e.,* withdrawing the drugs without a hearing). (*Id.* ¶ 20.)

*Fourth,* if the Commissioner does not grant summary determinations in favor of CVM, she would decide which disputed issues need to be resolved through a hearing, and a Federal Register notice describing the issues in dispute would be published within approximately 60 days. (*Id.* ¶ 21.) Although the Commissioner has the authority to serve as the presiding officer at a withdrawal hearing, in all or nearly all cases, she designates an ALJ as a hearing officer. *See id.* ¶ 22; *see also* 21 C.F.R. § 12.70.

Once an ALJ is appointed, he or she would have control over the timing and nature of the remaining proceedings. (*Id.*) Based on prior experience, CVM expects that approximately 41 additional months would be required for each hearing. (Flynn Decl. ¶ 25.) This time would be required for, *inter alia*: exchanging information between parties; pre-hearing discovery; resolving objections over witness qualifications; agreeing upon factual stipulations; resolving motions to strike testimony and exhibits; resolving motions to cross-examine witnesses; live witness testimony; and post-hearing briefing. (*Id.* ¶ 40.) It is critical to note that this projection covers only *one* hearing, and assumes that a limited number of sponsors request and/or are granted hearings. (*Id.* ¶ 23.) If a significant number of sponsors request hearings, or if additional hearings are required (*e.g.,* if drugs within the penicillin or tetracycline classes require separate hearings), more time will be required. (*Id.*) CVM's projection further assumes that approximately 11 to 15 FDA employees will be substantially committed to supporting the

Withdrawal Proceedings and that no intervening public health emergencies will occur. (*Id.*) If two or more hearings are ultimately required (*e.g.,* if hearings for both penicillins and tetracyclines are granted, and a separate hearing is held for each),[4] FDA cannot project with any confidence how long the second hearing would take, except to say that it would take substantially more time.

This 41 month period also includes the ALJ's initial decision, which will likely take at least six months, and briefing on the appeal to the Commissioner and her final decision, which would take approximately six to twelve additional months. (*Id.*; *see also* 21 C.F.R. §§ 12.120(f), 12.125(a), 12.125(f)).

Altogether, from issuance of the revised NOOHs to a final decision by the Commissioner, a hearing could take approximately 49 months. (*Id.* ¶ 25.) As discussed above, however, it is impossible to predict exactly how long the hearing process will take.

**C. Allocation of Resources Away From Other FDA Programs**

In his Declaration, Dr. Flynn also discusses the diversion of resources from other important FDA programs as a result of the efforts required for the Withdrawal Proceedings. For instance, CVM's Office of Research helps to run the National Antimicrobial Resistance Monitoring System ("NARMS")," which is a "national public health surveillance system that tracks antibiotic resistance in foodborne bacteria." (*Id.* ¶ 26.) Resources spent on the Withdrawal Proceedings will necessarily detract from those available for NARMS. (*Id.*) Likewise, "the Office of New Animal Drug Evaluation would be required to dedicate substantial

[4] FDA cannot speculate how many hearings will actually be required. It is possible that *no* hearings will be required (*e.g.,* if no hearings are requested or summary determination is granted as to all requestors). If the Commissioner does not grant summary determination on either the revised penicillin or tetracycline NOOH, whether one, two, or more hearings are required will depend in large part on the scientific issues to be determined and on the discretion of the ALJ.

resources to the Withdrawal Proceedings, which could delay CVM's review of pending new animal drug applications. Slowed animal drug application reviews would inevitably delay the approval of important new drug therapies for animals that are currently under review by the Agency." (*Id.* ¶ 27.)

In addition, CVM is concerned that the commitment of resources to Withdrawal Proceedings will detract from FDA's voluntary compliance program set out in Guidance for Industry (GFI) #209. (*Id.* ¶ 28.) "CVM expects that some drug sponsors, in connection with withdrawing their approvals for growth promotion indications, will seek approvals for legitimate new therapeutic indications at the same time. The review of such new applications is expected to require a substantial amount of effort from the CVM scientists who specialize in microbial food safety." (*Id.*) Possible delay of CVM review of these new NADAs may lessen drug sponsors' willingness to engage in the voluntary withdrawal process. (*Id.*)

Perhaps most importantly is that "any schedule for Withdrawal Proceedings, if one is imposed, be flexible enough that CVM can respond to public health and animal health crises as they may arise." (*Id.* ¶ 29.) Dr. Flynn describes current and recent crises that required CVM to redirect substantial resources in a way that could not be anticipated. For example, "FDA is currently monitoring a recall by Diamond Pet Food of nine brands of dry pet food formulas due to Salmonella contamination." (*Id.* ¶ 29.) As of May 11, 2012, CDC has reported 15 human illnesses linked to this pet food, five of which required hospitalization. (*Id.*) Likewise, in 2007, "there was an extensive pet food recall involving melamine and cyanuric acid-contaminated wheat and rice gluten in pet food. Beginning in mid-March 2007, with the report of the deaths of dogs and cats, 60 million individual packages of pet food from approximately 100 companies were recalled. Veterinarians, toxicologists, pathologists, chemists, and other scientists from

CVM and other parts of the Agency collaborated to identify the source of the contamination and the cause of animal deaths." (*Id.* ¶ 29.) Based on CVM's work on the melamine crisis, CVM's Office of Research "developed a method to detect the melamine and related analogs in animal feed and in tissues of animals produced for human consumption. This method was quickly adapted to the testing for these substances in milk and infant formula." (*Id.*) It is critical that CVM retain the flexibility to respond appropriately to any future health crises.

**CONCLUSION**

For the foregoing reasons, this Court should not impose a schedule for FDA to complete the Withdrawal Proceedings. To the extent that the Court decides to impose a schedule, such schedule should provide a reasonable time to complete the proceedings, as set forth above.

Dated: New York, New York
May 15, 2012

Respectfully submitted,

PREET BHARARA
United States Attorney
Southern District of New York

*/s/ Ellen London*
By: AMY A. BARCELO
ELLEN LONDON
Assistant United States Attorneys
86 Chambers Street
New York, New York 10007
Tel.: (212) 637-6559/2737
Fax: (212) 637-2730/2702
Email: amy.barcelo@usdoj.gov
ellen.london@usdoj.gov

OF COUNSEL:

DAVID J. HOROWITZ
Deputy General Counsel

ELIZABETH H. DICKINSON
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