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

REPLY BRIEF IN SUPPORT OF
THE GOVERNMENT'S POSITION ON TIMING

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The above-captioned defendants (the "Government"), by their attorney, Preet Bharara, United States Attorney for the Southern District of New York, respectfully submit this reply brief in further support of their position on timing as set forth in their brief dated May 15, 2012 ("Opening Brief") (Dkt. No. 85).

PRELIMINARY STATEMENT

There is no basis for imposing a deadline on FDA to complete the Withdrawal Proceedings.[1] Although Plaintiffs express skepticism that the Agency will abide by the Court's order in a timely fashion, and even wrongly allege that FDA is ignoring the public health issue regarding antimicrobial resistance, there is no indication that FDA will not comply with the Court's order[2] or will unreasonably delay in so doing. In short, there are no compelling circumstances that could justify the extraordinary remedy of a deadline in this case.

If the Court nevertheless does impose a schedule, it should give credence to the Agency's testimony regarding what is reasonable. FDA has set out in detail the time it believes would be required to complete what is likely to be the most complex regulatory action in CVM's history, within approximately the same amount of time it took to withdraw a single drug in 2005 because of similar concerns about antimicrobial resistance. Plaintiffs have failed to rebut this explanation. Moreover, the Court should reject Plaintiffs' proposal for an unreasonably short schedule; in fact, that schedule would actually be harmful to the parties' shared goal of eliminating the use of all Medically Important Antimicrobials for growth promotion in food producing animals.

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[1] The defined terms in this brief have the same meaning as in the Opening Brief.

[2] The Government filed a notice of appeal of the Court's March 22 Order on May 21, 2012 (Dkt. No. 88) and a motion to stay the Order on June 1, 2012 (Dkt. No. 92).

I. This Court Should Not Impose a Deadline on the Withdrawal Proceedings

Plaintiffs' argument that CVM should be required to complete what may be the most complex drug withdrawal proceedings in its history, *see* First Flynn Decl. ¶ 6,[3] on an unreasonable timeline is based on Plaintiffs' prediction that the Agency will refuse to abide by this Court's order in a timely manner, *see* Plfs' Br. at 10-13. This argument cannot justify the extraordinary remedy that Plaintiffs now seek in the form of a court-imposed deadline to comply with the March 22 Order. As discussed in the Government's Opening Brief, courts avoid interfering with the internal operations of administrative agencies except in "the most extraordinary circumstances." *Sierra Club v. U.S. Army Corps. of Eng'rs*, 701 F.2d 1011, 1042 (2d Cir. 1983); Opening Br. at 6-7. Here, FDA has not ignored a court order, and has not given any indication that it will ignore or unreasonably delay taking the actions ordered by the Court on March 22, unless the Order is stayed or reversed. Moreover, there is no statutory deadline for completing the Withdrawal Proceedings.

Plaintiffs' principal argument is that FDA has failed to take adequate action to protect the public from the dangers of antimicrobial resistance in the past, and that this asserted failure portends future delays. Plfs' Br. at 8. However, the record shows that FDA has been working toward the same goals as Plaintiffs: the withdrawal of Medically Important Antimicrobials for growth promotion uses. Prior to this case, FDA did not believe it was under a legal obligation to initiate Withdrawal Proceedings. Opening Br. at 8. Instead, FDA was developing a regulatory approach intended to stop the use of all Medically Important Antimicrobials (not just penicillins

[3] The "First Flynn Decl." refers to the Declaration of William T. Flynn, D.V.M., M.S., dated May 15, 2012 and submitted in support of the Government's Opening Brief (Dkt. No. 86).

and tetracyclines) sooner than through involuntary withdrawal proceedings.[4] *Id.* at 4. Indeed, FDA recently finalized GFI 209 and published Draft GFI 213, crystallizing its plan to attack the problem first by encouraging the voluntary elimination of growth promotion uses for all Medically Important Antimicrobials. *Id.* The Court held in the March 22 Order that FDA's current strategy to initially encourage voluntary compliance does not substitute for Withdrawal Proceedings; however, this holding with respect to penicillins and tetracyclines does not, despite Plaintiffs' suggestion to the contrary, Plfs' Br. at 12-13, prohibit FDA from implementing its strategy with regard to other classes of drugs (even if, as required by the March 22 Order, FDA must work simultaneously to decide whether these other classes of drugs are shown to be safe, *slip op.* at 52-53). FDA's continued commitment to these efforts is an exercise of its judgment as to how best to address the issue, not intransigence.

Similarly, Plaintiffs argue that the need for a schedule is demonstrated by the Agency's "complain[t] that withdrawal proceedings will divert resources from other agency work, including responses to hypothetical emergencies," but this contention ignores the reality that FDA cannot disregard its wide-ranging public-health responsibilities. Plfs' Br. at 12. As important as the issue of antimicrobial resistance may be, it is only one of countless issues that FDA must address, and trying to find a solution to this problem is only one of FDA's myriad responsibilities. First Flynn Decl. at ¶¶ 2, 26, 27. FDA's recognition of its need to strike a balance among its many competing responsibilities reflects the reality of managing a scientific regulatory agency with extensive and complex public health responsibilities.

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[4] FDA's approach was guided by its experience withdrawing Baytril (enrofloxacin) for use in poultry; because of the extensive time and resources that it expended on the Baytril withdrawal (*i.e.,* over five years at a cost of more than $3.3 million), FDA concluded that it might not be realistic to withdraw approvals of nontherapeutic uses for the approximately 161 remaining approved applications for Medically Important Antimicrobials within a reasonable amount of time. Opening Br. at 3-4.

Plaintiffs' remaining arguments as to why FDA is intransigent are similarly without merit. First, FDA is not "relitigat[ing] the merits" by saying that it needs time to update its assessment of the current science and to decide whether currently available scientific evidence still supports involuntary withdrawals. Plfs' Br. 5-6. If FDA is to initiate administrative proceedings to withdraw drug approvals under the FDCA, it would not be enough to offer testimony at a hearing that, in 1977, the standard for withdrawal was satisfied. The probative value of such testimony would at least be questioned by the ALJ or federal court on review. FDA's witnesses must be able to testify, under oath, that the applicable standards for withdrawal are satisfied now for each of the applicable drug products, and they must be permitted an adequate opportunity to reach and substantiate that conclusion on their own. Indeed, this Court's March 22 Order recognized that FDA has the discretion to update the science related to the 1977 NOOHs. *Slip op.* at 51 n.16, 54.

Furthermore, although FDA has indeed concluded that "the weight of the scientific evidence" supports the general proposition that the misuse and overuse of Medically Important Antimicrobials is not in the interest of public health, GFI 209, Third Barcelo Decl. Ex. A at 17, the Agency must conduct an analysis to determine whether the use of any particular drug product in accordance with its approved conditions of use may be unsafe or not shown to be safe. Before reissuing NOOHs, FDA scientists must be provided the opportunity to confirm that their general concerns about Medically Important Antimicrobials apply to each specific drug product. FDA's desire to give its scientists adequate time to do their work is not intransigence, and Plaintiffs' counterargument, that FDA witnesses effectively should be bound to the Agency's earlier beliefs and conclusions and deprived of an opportunity to formulate their own answers, Plfs' Br. 20, should be rejected.

Finally, Plaintiffs argue, incorrectly and without citing any support, that FDA should be subjected to a schedule as a result of its actions in this litigation. Plfs' Br. at 11-13. Specifically, the Court should reject Plaintiffs' assertion that FDA's conduct in this litigation has been "marked by evasion and delay," and that FDA's decision to withdraw the almost 35-year-old NOOHs was a "disingenuous, last-ditch attempt to avoid adjudication of plaintiffs' claims for relief," as well as Plaintiffs' contention that FDA's conduct in this case shows that it needs ongoing court oversight. *Id.* at 11-12. Contrary to these assertions, the NOOH withdrawals accurately reflected FDA's decision not to hold the withdrawal proceedings—at least not yet. Despite Plaintiffs' argument to the contrary, Plfs' Br. at 12, the Government's statement in its brief that FDA withdrew the notices "to ensure that there was no confusion about its regulatory strategy going forward" is and was entirely true, and not indicative of intransigence or bad faith. *See* Opening Br. at 5.

None of the cases that Plaintiffs cite in their opposition changes the validity of the Government's arguments; indeed, these cases further demonstrate the lack of any valid basis to impose a schedule. Plfs' Br. at 6-7 (citing cases). Plaintiffs' cases merely stand for the undisputed proposition that, although courts do have discretion to impose deadlines on administrative agencies, they exercise this authority in limited circumstances. First, as Plaintiffs' cases show, courts impose deadlines when agencies ignore judicial orders. *See In re Core Commc'ns*, 531 F.3d 849, 861-62 (D.C. Cir. 2008) (imposing a deadline for the FCC after the agency had failed to respond to the court's prior order); *Farmworker Justice Fund v. Brock*, 811 F.2d 613, 633 (D.C. Cir. 1987), *vacated as moot* 817 F.2d 890 (D.C. Cir. 1987) (imposing a deadline for completing a rulemaking twelve years after the district court's order to initiate the rulemaking); *Potomac Elec. Power Co. v. ICC,* 702 F.2d 1026, 1035 (D.C. Cir. 1983) (imposing

a deadline on the ICC to issue a new order on remand five years after the D.C. Circuit ordered a remand in the first instance). Second, courts may impose deadlines in cases of unreasonable delay. *See In re Am. Rivers & Idaho Rivers United,* 372 F.3d 413, 418-20 (D.C. Cir. 2004) (imposing deadline upon finding of unreasonable delay); *Barnett v. Califano*, 580 F.2d 28, 32-33 (2d Cir. 1978) (same); *White v. Matthews*, 559 F.2d 852, 859-60 (2d Cir. 1977) (same). Finally, Plaintiffs' cases demonstrate that courts may impose a schedule when—unlike here—the relevant statute mandates a particular schedule or deadline. *See Ass'n of Am. R.R. v. Costle*, 562 F.2d 1310, 1321-22 (D.C. Cir. 1977) (imposing a deadline based on the statute); *Natural Res. Def. Council v. Train*, 545 F.2d 320, 327-28 (2d Cir. 1976) (same).

Moreover, Plaintiffs' cases show that, even when courts impose deadlines, the courts may defer to the agencies' view of an appropriate schedule.[5] *See In re Int'l Chem. Workers Union*, 958 F.2d 1144, 1150 (D.C. Cir. 1992) (although the court imposed a deadline six years after it first ordered OSHA to initiate a rulemaking, it acceded to the agency's proposed schedule); *Pub. Citizen Health Rsrch. Grp. v. Brock*, 823 F.2d 626, 629 (D.C. Cir. 1987) (imposing a deadline five years after it ordered OSHA to initiate a rulemaking, and again acceding to OSHA's proposed schedule).

Plaintiffs' cases underscore the judicial reluctance to impose deadlines on administrative agencies except in certain limited circumstances, none of which are present here. While it is

[5] Moreover, in some of Plaintiffs' cases, courts held that, in light of the totality of the circumstances, deadlines to complete *rulemakings* would be imposed after long delays. *See Families for Freedom v. Napolitano*, 628 F. Supp. 2d 535, 541 (S.D.N.Y. 2009) (establishing a deadline for responding to a petition for a rulemaking); *Pub. Citizen Health Rsrch. Grp. v. FDA*, 724 F. Supp 1013, 1023 (D.D.C. 1989) (same); *Pub. Citizen v. Heckler*, 602 F. Supp. 611, 614 (D.D.C. 1985) (same). As discussed above, here there has been no delay in complying with this Court's order. Moreover, it is much different for a court to order a deadline to complete a notice and comment rulemaking than to set a deadline for multiple adversarial proceedings to withdraw numerous drug licenses, which, as discussed *infra*, are procedurally and scientifically complex and difficult to plan for in advance.

clear that FDA and Plaintiffs continue to have significant disagreements over applicable law and policy, Plaintiffs' efforts to paint FDA as intransigent are without merit. Plaintiffs have failed to justify the imposition of any schedule, much less the abbreviated schedule described in their brief, which is discussed in further detail below.

II. If the Court Imposes a Schedule, FDA's Proposal Is Reasonable and Should Be Adopted

Plaintiffs are wrong that the schedule proposed by FDA is "leisurely." Plfs' Br. at 14. To the contrary, FDA has proposed an aggressive schedule in which it would withdraw approximately 77 individual drug approvals in about the same amount of time it took to withdraw Baytril's approval in 2005 because of concerns about antimicrobial resistance. Indeed, the Withdrawal Proceedings required by the March 22 Order likely would be the most complex and wide-ranging set of drug approval withdrawals in CVM's history, *see* First Flynn Decl. ¶ 6, and the Agency should be given the necessary amount to time to prepare for and complete them.

The proceedings regarding Baytril resulted in a 126-page Final Decision of the Commissioner and demonstrated the complexity and scope of a drug withdrawal proceeding. *See* Jan. Barcelo Decl. N. The Baytril decision capped years of heavily contested administrative litigation over the safety of a single antimicrobial drug product. The decision's 68-page factual discussion reflects a complex analysis covering, among other things, extensive microbiologic and epidemiological data, as well as FDA's careful preparation and years-long commitment of significant agency resources. *Id.* at 17-85.

Contrary to Plaintiffs' arguments, CVM cannot realistically be expected to initiate administrative proceedings with respect to 77 individual drug approvals within the 125 day period that Plaintiffs propose, Plfs' Br. at 14-20, as contrasted with Dr. Flynn's estimate that it will take 11 to 17 months to reissue and update the NOOHs, First Flynn Decl. ¶ 16. If FDA is

required to initiate administrative proceedings to withdraw the 77 individual drug approvals within 125 days, this could result in the issuance of NOOHs that are incomplete and lack scientific rigor, putting the Agency at greater risk of not meeting its initial burden of proof in a hearing. First Flynn Decl. ¶ 10. This would be in neither party's interests, nor would it serve the public interest.

Plaintiffs' arguments that revised NOOHs for 77 drugs can be reissued in 125 days amount to little more than speculation about the level of preparation that it takes to initiate a complex set of drug withdrawal proceedings. For instance, the argument that FDA should be allotted no more than 14 days to search its regulatory files for information spanning more than four decades is baseless. *See* Plfs' Br. 14-15. The assertion that FDA should be allotted two weeks to conduct a search of the scientific literature fares no better. *Id.* at 16-17. If FDA is to be forced to attempt to engage in significant and technically complex adversarial administrative litigation, it will need the amount of time to collect information and prepare as described by Dr. Flynn.

Plaintiffs' argument that CVM should be able to reissue NOOHs in little or no time is based on its faulty assertion that the work required is largely complete. Plfs' Br. at 15, 17, 19. Although FDA has done prior work to assess available information relevant to the risks posed by the misuse and overuse of penicillins and tetracyclines, this prior work would need to be updated. Moreover, additional work would be needed to tailor this analysis to the specific goal of initiating involuntary withdrawal proceedings for individual products. And, as stated by Dr. Flynn, unless sufficient time is allotted for FDA to prepare revised NOOHs, FDA's case in the Withdrawal Proceedings "would be incomplete, lack scientific rigor, and would be subject to challenge." First Flynn Decl. ¶ 9. FDA has never asserted that it will be starting from scratch in

reissuing the NOOHs; obviously FDA has had a head start in many respects. But it is this head start that should permit FDA to reissue NOOHs that would apply to 77 individual drug products in just 11 to 17 months, instead of much longer.

Furthermore, Dr. Flynn's projection is intended to appropriately balance resources devoted to Withdrawal Proceedings, which will necessarily be substantial, with resources required for CVM's myriad other responsibilities. *See* First Flynn Decl. ¶¶ 26-29. CVM must continue to discharge all of its statutory duties, and, while FDA would certainly treat the Withdrawal Proceedings as a high-priority project, it cannot disregard its other responsibilities. Accordingly, Plaintiffs' criticism that Dr. Flynn's declaration does not specify the number of hours to be devoted by each employee to Withdrawal Proceedings is misplaced. Plfs' Br. at 14. Some employees will work nearly full time for periods, others will work in supervisory or consultative capacities, but each employee's commitment will need to be balanced with his or her responsibilities to CVM's other important public health programs. As emphasized by Dr. Flynn, given the many uncertainties inherent in the process, it is difficult to provide a more specific prediction. First Flynn Decl. ¶ 6.

Nor is there any foundation for Plaintiffs' contention that, after revised NOOHs are issued, hearings necessarily could be completed within approximately 21 months. Plfs' Br. 21-24. Plaintiffs have no way of knowing this; even FDA can only speculate about how long hearings will take. That is because there is no way to know how many parties will request hearings, how many issues may be raised, or how complex such issues may be. Opening Br. at 14. It is certainly in FDA's interests to proceed expeditiously with a hearing, but the pace of a hearing can only be evaluated when the full complexity of the issues becomes known.

One reason why the hearing process can be lengthy is that, as part of their request for a hearing following the issuance of an NOOH, sponsors may submit new clinical and/or safety data to the Agency in support of their applications. 21 C.F.R. § 12.22. Depending on the nature and volume of the information submitted, FDA's review may take time. In other cases, no new data is submitted, or only immaterial data that the Agency can digest quickly. But there is no basis for Plaintiffs' prediction that the Agency should necessarily be able to review and decide requests for hearings within 60 days, Plfs' Br. 24, because this will depend on the nature and volume of sponsors' submissions. Likewise, depending on the complexity and nature of the issues, the ALJ may need more or less time to render an initial decision, and the Commissioner may need more or less time to render a final decision. All that can be expected of FDA now is that it proceed with reasonable promptness in light of the circumstances as they develop, and this FDA already is obligated to do.

CONCLUSION

For the foregoing reasons, and as and set forth in the Government's Opening Brief, no schedule to complete Withdrawal Proceedings should be imposed, and if a schedule is required, FDA's proposal should be adopted.

Dated: New York, New York
June 6, 2012

Respectfully submitted,

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