UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

NATURAL RESOURCES DEFENSE COUNCIL, INC., *et al.*

Plaintiffs,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION, *et al.*,

Defendants.

11 Civ. 3562 (THK)
ECF Case

DECLARATION OF WILLIAM T. FLYNN, D.V.M., M.S.

I, William T. Flynn, D.V.M., M.S., declare as follows:

1. I am the Deputy Director for Science Policy for FDA's Center for Veterinary Medicine ("CVM"). I have held this position since February 2011. Previously, I was the Senior Advisor for Science Policy at CVM from July 2008 through January 2011, and Director of CVM's Policy and Regulations Staff from 2003 through 2008. From 2001 to 2003, I served as a special assistant to the CVM Deputy Center Director. I also served from 1993 to 2001 in various capacities in CVM's Office of New Animal Drug Evaluation, including as a drug application reviewer and acting Team Leader. Prior to joining FDA, I was in private veterinary practice in Maryland from 1991 to 1993.

2. In my capacity as Deputy Director for Science Policy, I am responsible for advising CVM's Center Director on science and policy issues related to CVM's mission, which is to protect human and animal health. CVM accomplishes its mission by, among other things, approving safe and effective products for animals and by enforcing applicable provisions of, among other laws, the Federal Food, Drug, and Cosmetic Act (the "Act").

3. I received the degrees of Doctor of Veterinary Medicine in 1991, and Master of Science in Veterinary Preventative Medicine in 1987 from the Ohio State University. I am a member of the American Veterinary Medical Association.

4. I am familiar with FDA's regulation and enforcement program for animal drugs, and with the procedures for approving new animal drugs and withdrawing such approvals. The statements in this declaration are based on my personal knowledge and belief, and on my background, training, education, and experience as an FDA official.

FDA's Proposed Schedule For Penicillin and Tetracycline Withdrawal Proceedings

5. I am aware of this Court's order that FDA re-initiate withdrawal proceedings ("Withdrawal Proceedings") for the approximately 73 penicillin and tetracycline drug products currently approved for use in animal feed for growth promotion and feed efficiency indications (the "NOOH Products"). FDA had originally proposed to withdraw the NOOH Products pursuant to two NOOHs issued in 1977 (the "1977 NOOHs") because of concerns about antimicrobial resistance. Following the issuance of the 1977 NOOHs, various manufacturers of the NOOH Products (often called "sponsors") requested hearings, as permitted by the Act, 21 U.S.C. § 360b(e)(1). The Commissioner of Food and Drugs ("Commissioner") granted these requests, but the Agency did not hold the hearings after Congress requested that FDA study this issue further. Because the hearings were requested by the sponsors, but never held, FDA could not, under the Act, withdraw approvals for the NOOH Products. Moreover, before this Court's recent ruling, FDA did not consider itself to be under any legal obligation to proceed to hearings under the 1977 NOOHs.

6. Pursuant to the Court's order, CVM conducted an analysis to estimate the time and resources that would be required to complete the Withdrawal Proceedings. 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. As discussed below, CVM's best projection at this time is that the Withdrawal Proceedings, including one hearing, would take approximately five and a half years, and would require the involvement of more than one dozen FDA employees, many of whom would need to devote substantial effort on this project, taking them away from other duties, including drug review, scientific research, policy and guidance development, antimicrobial resistance surveillance activities, and post-approval monitoring activities. To the best of my knowledge, CVM has never convened hearings to withdraw so many animal drug products at a single time, and therefore these estimates are highly speculative. Moreover, to the extent that multiple hearings are required, CVM estimates that substantially more time will be required.

7. Even for the involuntary withdrawal of a single animal drug product, it is impossible to predict with certainty how long the proceedings will take. This is because CVM does not know whether the drug sponsor will request a hearing, whether the request for a hearing will have merit and be granted, or the complexity of the scientific and legal issues that the sponsor may raise. Moreover, to the extent that a drug sponsor requests and is granted a hearing on a proposed withdrawal, the schedule for such hearings will not be determined by CVM, but rather will be controlled primarily by the Presiding Officer (most likely an Administrative Law Judge ("ALJ")).

Timeline For Re-Issuance of NOOHs For Penicillins and Tetracyclines

8. The first step in the Withdrawal Proceedings would be to update and re-issue the 1977 NOOHs. The 1977 NOOHs must be updated because the FDA is legally required to provide drug sponsors with notice of the bases for a proposed withdrawal prior to a hearing. 21

C.F.R. § 12.21(b). Because the scientific knowledge surrounding antimicrobial resistance has evolved over the past 35 years, CVM believes that it is obligated to consider the more recent science since the 1977 NOOHs were originally published.

9. To update the scientific evidence would involve conducting a thorough analysis of the available evidence to determine whether any new information has emerged over the past 35 years that could bear on FDA's original analysis. Failing to update the 1977 NOOHs to take into account the current state of scientific understanding would result in presentations in the Withdrawal Proceedings that would be incomplete, lack scientific rigor, and would be subject to challenge.

10. According to precedent, CVM must first satisfy the initial burden of producing evidence that provides a legally sufficient basis for initiating withdrawal proceedings before the burden shifts to the drug sponsor to show that its product is safe. Given the significance of this initial showing by the Agency, it is critically important that the evidence presented in the NOOH be complete and scientifically rigorous. It would be imprudent for CVM to issue an NOOH that did not include an examination of the scientific developments of the past 35 years, as this could obviously put the Agency at greater risk of not meeting its burden of proof at a hearing.

11. CVM has attempted to identify the specific tasks required to re-issue the NOOHs, and has estimated the time and personnel commitments associated with each of these tasks. As noted above, because these proceedings could be substantially more complex than any in CVM's history, these projections are speculative. *First,* CVM will need to search its official files for relevant information. Under 21 C.F.R. § 12.85(a)(2), prior to a hearing, CVM is required to provide "all documents in the director's files containing factual information, whether favorable or unfavorable to the director's position, which relate to the issues involved in the hearing."

CVM would collect all such documents at the outset so they are available to prepare for an NOOH and an administrative hearing. Because antimicrobial resistance has been the subject of research and concern for more than 40 years, this search for documents will be a substantial undertaking. CVM estimates that the search will take a team of 10 to 14 Agency employees (3 to 5 from CVM's Office of New Animal Drug Evaluation, 3 to 5 from CVM's Office of Research, 2 from CVM's Office of the Director, and 2 from CVM's Office of Surveillance and Compliance) approximately 60 days, although more time may be required depending on the location and condition of FDA's older files. These employees would need to devote substantial time to this document search, taking them away from their day-to-day public health protection activities, including pre-approval drug safety review, policy and guidance development, post-approval monitoring activities, and enforcement efforts.

12. *Second*, CVM would need to conduct an in-depth search for publicly available literature and other information (*e.g.*, scientific reports) on the scientific topics that would be addressed at the hearings. In addition to requiring submission of all documents in the Director's files, FDA regulations require CVM to submit "[a]ll other documentary data and information relied upon." 21 C.F.R. § 12.85(a)(3). Because CVM has a large amount of information in hand already, and given that CVM should be able to assign multiple research teams to cover separate subjects simultaneously, CVM estimates that a team of six to ten Agency employees (3 to 5 from CVM's Office of New Animal Drug Evaluation, and 3 to 5 from CVM's Office of Research) will be able to complete the necessary literature search in 90 days.

13. *Third*, as the information in CVM's files and the publicly-available information and literature is compiled, CVM estimates that it will require a team of six to ten Agency employees (3 to 5 from CVM's Office of New Animal Drug Evaluation, and 3 to 5 from CVM's

Office of Research), including several senior scientists spending substantial amounts of time, 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. This task involves reviewing the documents retrieved in CVM's files and through a literature search of publicly available information, analyzing the materials, understanding how the materials relate to each other, and evaluating the reliability and accuracy of the information. After the information and literature has been fully reviewed, CVM estimates that it will take a team of eight to twelve Agency employees (3 to 5 from CVM's Office of New Animal Drug Evaluation, 3 to 5 from CVM's Office of Research, 1 from CVM's Office of the Director, and 1 from the Office of Chief Counsel), including several senior scientists spending substantial amounts of time, approximately 60 days to identify whether the available scientific data supports the withdrawal of the NOOH Products, and to frame the legal and scientific arguments that may be included in re-issued NOOHs.

14. *Fourth,* CVM expects that it will take a team of ten to fourteen Agency employees (3 to 5 from CVM's Office of New Animal Drug Evaluation, 3 to 5 from CVM's Office of Research, 2 from CVM's Office of the Director, and 2 from the Office of Chief Counsel) approximately 60 days to draft the revised NOOHs.

15. *Fifth*, CVM anticipates that it will take approximately 60 days for senior Agency management and FDA's Office of Chief Counsel to review and clear the revised NOOHs, and for the revised NOOHs to be edited and published in the Federal Register.

16. Altogether, 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. To 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. It is also important to note that, in addition to the tasks identified above, there is other work that CVM will need to accomplish during this time period. For instance, in preparation for submitting documents to the hearing docket in accordance with 21 C.F.R. § 12.85, it will likely take 2 CVM employees about 30 days to develop an index of files and other relevant documents to be submitted. 21 C.F.R. § 12.85. Because documents in the record will be available to the public, 21 C.F.R. § 12.105, FDA would have to redact the documents to remove confidential commercial and trade secret information that FDA is obligated by law to protect. It would likely take 2 Agency employees (1 from CVM's Office of the Director, and 1 from the Office of Chief Counsel) about 60 days to redact these documents. Likewise, as is often done in cases involving complex and disputed scientific issues, CVM would interview and retain outside expert witnesses to testify on its behalf at a hearing. Although CVM could proceed to a hearing using only witnesses who are FDA employees, FDA believes that the use of independent outside experts may be warranted depending on the issues identified for hearing.

Timeline for Hearings

17. As discussed above, 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 the hearings would take. However, based upon prior experience with other hearings to withdraw approval of new animal drug applications, most recently enrofloxacin in poultry, CVM's estimate of the time and personnel needed for the hearing is as follows.

18. *First*, following the publication of revised NOOHs, drug sponsors would be given 30 days to respond and request hearings. *See* 21 C.F.R. § 12.22(b)(1); 21 C.F.R. § 514.200(a)(1). As part of their submissions, the sponsors would be required to submit specific data and information to support the continued approval of their products. 21 C.F.R. § 514.200(c).

19. *Second*, any requests for hearings would need to be reviewed carefully by the Agency. We would expect such review to take approximately 90 days, and CVM estimates that it would involve from between nine and thirteen Agency employees (2 from CVM's Office of the Director, 3 to 5 from CVM's Office of Research, 3 to 5 from CVM's Office of New Animal Drug Evaluation, and 1 from the Office of Chief Counsel).

20. *Third*, a team of four Agency employees (2 from CVM, 1 from the Office of Chief Counsel, and 1 from the Office of Foods) 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).

21. *Fourth,* if the Commissioner does not grant summary determinations in favor of CVM, the Commissioner would decide which disputed issues need to be resolved through a hearing and, as required by 21 C.F.R. § 12.35, publish a Federal Register notice announcing hearings and describing the issues in dispute. We anticipate this would occur within approximately 60 days from the recommendation to the Commissioner on whether to grant a hearing. In sum, we anticipate that a notice of hearing in the Federal Register would be published approximately 8 months after the publication of the NOOHs.

22. Although the Commissioner has the authority to serve as the presiding officer at a withdrawal hearing, the Commissioner has historically designated an ALJ as the hearing officer.

See 21 C.F.R. § 12.60. Once designated, the ALJ would have substantial control over the timing and nature of the remaining proceedings, and scheduling issues would be largely left to his or her discretion. 21 C.F.R. § 12.70.

23. Based on prior experience in the recent withdrawal of enrofloxacin for use in poultry, CVM estimates a hearing schedule as follows. This estimate is for one hearing, and assumes that it would involve a limited number of sponsors. If a significant number of sponsors request hearings, or if two or more separate hearings are required to be held, substantially more time and personnel may be required to complete the hearings. Also, this projection assumes that approximately 11 to 15 Agency employees will be substantially committed to supporting the Withdrawal Proceedings.

- *Submission of Information by CVM.* CVM must submit relevant documents to the docket, along with a statement on the factual issues in the Notice of Hearing and the type of supporting evidence the Center Director intends to introduce at the hearing. 21 C.F.R. § 12.85(a) This information must be submitted before publication of the Notice of Hearing.

- *Notice of Participation.* Notices of participation would need to be filed within **30 days** after publication of the Notice of Hearing.

- *Motions to Modify Issues for Hearing.* Motions to modify the issues for hearing would be due approximately three weeks after the Notices of Participation are filed. Responses to such motions would be due approximately one week later.

- *Sponsors/Review by CVM.* Drug sponsors normally have 60 days to submit materials that they intend to rely upon at the hearing. 21 C.F.R. § 12.85(b).

- *Exchange of Witness Lists, Curriculum Vitae, and Prior Written Statements by All Experts on Witness List.* Although 21 C.F.R. § 12.92 anticipates that participants in a hearing will bring their witness lists (along with CVs and prior written statements) to the prehearing conference, in practice, the ALJ may set a schedule that allows CVM and the other hearing participants to exchange witness lists, CVs, and all prior written statements by any of the proposed witnesses after the prehearing conference, or the ALJ may issue a scheduling order without having a prehearing conference. CVM anticipates the participants would have to exchange witness lists, CVs and prior

written statements approximately 30 days after the sponsor submits materials they intend to rely on at the hearing.

- *Objections to Witness Lists Based on Qualifications.* Objections would be due approximately 30 days after witness lists are exchanged.

- *Discovery.* Discovery, which could include, *e.g.,* written interrogatories and requests for admissions, would begin after witness lists are exchanged and would take approximately 90 days to conduct.

- *Exchange of Proposed Stipulations.* An exchange of proposed stipulations would take place approximately 10 days after the completion of discovery.

- *Joint Stipulations.* Joint stipulations would be due approximately 7 days after the exchange of Proposed Stipulations.

- *Submission of Written Testimony and Exhibits.* Written testimony and exhibits would be due approximately 90 days after submission of Joint Stipulations.

- *Motions to Strike Testimony and Exhibits and Permission to Conduct Cross-Examination.* Motions to Strike Testimony and Exhibits and Permission to Conduct Cross-Examination would be due approximately 45 days after submission of written testimony and exhibits.

- *Responses to Motions to Strike Testimony/Exhibits and Permission to Conduct Cross-Examination.* Responses to Motions to Strike Testimony/Exhibits and Permission to Conduct Cross-Examination would be due approximately 14 days after the Motions to Strike and Motions to Conduct Cross-Examination are submitted.

- *Submission of Proposed Findings of Facts and Conclusions of Law.* Proposed Findings of Fact, with record references, would be due approximately 30 to 45 days after the Responses to Motions to Strike Testimony/Exhibits and Permission to Conduct Cross-Examination are submitted.

- *Submission of Critiques of Other Parties' Proposed Findings of Fact.* Critiques of each party's Proposed Findings of Fact would be due approximately 30 days after the Proposed Findings were submitted.

- *Cross-Examination of Witnesses.* Cross-examination of witnesses during a public hearing would take place as scheduled by the ALJ.

- *Submission of Briefs.* The ALJ will set a schedule for the filing of briefs promptly after the taking of evidence is completed. Ordinarily, briefs are to be filed within 45 days of the close of the hearing. 21 C.F.R. § 12.96(a).

24. Following the completion of post-hearing briefing, the ALJ's initial decision would not likely occur in less than 6 months. The initial decision becomes the final decision of the Commissioner by operation of law unless a participant files exceptions with the Division of Dockets Management under 21 C.F.R. § 12.125(a) or the Commissioner files a notice of review under 21 C.F.R. § 12.125(f). *See* 21 C.F.R. § 12.120(e). In the event the Commissioner reviews the initial decision, we would expect a final decision within 6 to 12 months after the ALJ issues his or her decision.

25. Altogether, the hearing process described above would take approximately 41 months in total. As discussed above, it is impossible to predict exactly how long the hearing process will take. Hearings could take more or less time, depending on factors that are largely out of CVM's control. Assuming the 41-month projection bears out, and if, for instance, CVM were to begin the process of re-issuing the NOOHs on June 1, 2012, CVM's best estimate is that, if a hearing is requested and granted, and if an initial ALJ decision is appealed to the Commissioner, the withdrawal process would not be completed until between June, 2017, and December, 2017. This projection assumes, as discussed above, that the NOOHs will take approximately 11 to 17 months to republish (*see* ¶ 16), and that a notice of hearing would be published in the Federal Register about 8 months after the NOOHs are published (*see* ¶ 21). This projection does not account for any post-hearing appeals to the federal courts. The NOOH Products would remain on the market pending a final decision of the Commissioner.

The Diversion of Resources From Other Programs

26. As discussed above, CVM estimates that the Withdrawal Proceedings will require the efforts of over a dozen of FDA employees and take a minimum of five and one half years to

complete. This will inevitably drain resources from other FDA and CVM programs. CVM has not determined yet precisely how it would reallocate resources in order to hold the hearings, but resources will be diverted from certain important CVM programs because of the Withdrawal Proceedings. For instance, CVM's Office of Research ("OR") employees who would need to be involved in hearing activities work on other important efforts to combat antimicrobial resistance, such as the National Antimicrobial Resistance Monitoring System ("NARMS"). NARMS is a national public health surveillance system that tracks antibiotic resistance in foodborne bacteria. The NARMS program was established in 1996 as a partnership between FDA, the Centers for Disease Control and Prevention ("CDC"), and the U.S. Department of Agriculture. The primary objectives of NARMS are to monitor trends in antimicrobial resistance among foodborne bacteria from humans, retail meats, and animals; to disseminate timely information on antimicrobial resistance to promote interventions that reduce resistance among foodborne bacteria; to conduct research to better understand the emergence, persistence, and spread of antimicrobial resistance; and to assist the FDA in making decisions related to the approval of safe and effective antimicrobial drugs for animals.

27. Likewise, the Office of New Animal Drug Evaluation would be required to dedicate substantial 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.

28. In particular, CVM is concerned that the commitment of resources to Withdrawal Proceedings will detract from FDA's ability to work with drug sponsors that choose to withdraw their growth promotion claims in accordance with the principles set out in Guidance for Industry

(GFI) #209. 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. If the review of new NADAs is delayed because CVM personnel are committed to working on Withdrawal Proceedings, CVM is concerned that drug sponsors' willingness to engage in the voluntary process described in GFI #209 and draft GFI #213 will be diminished.

29. Furthermore, it is important that any schedule for the Withdrawal Proceedings, if one is imposed at all, be flexible enough that CVM can respond to public health and animal health crises as they may arise. As an example, FDA is currently monitoring a recall by Diamond Pet Food of several brands of dry pet food formulas due to Salmonella contamination. The recall affects products distributed in multiple states, Puerto Rico, and Canada. As of May 11, 2012, CDC reports 15 human illnesses linked to this pet food, 5 of which required hospitalization. Other emerging issues may also need to be investigated and addressed during the pendency of the Withdrawal Proceedings. For example, 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, and in 2008, 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.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed on May 15, 2012, in Rockville, Maryland.

WILLIAM T. FLYNN, DVM, MS
Deputy Director for Science Policy
Center for Veterinary Medicine
United States Food and Drug Administration