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

SUPPLEMENTAL 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 submit this Supplemental Declaration in support of the Government's Motion for a Stay of the Court's order of March 22, 2012. My background qualifications were described in my Declaration dated May 15, 2012 ("First Declaration"), and the statements in this Supplemental Declaration are based on my personal knowledge and belief, and on my background, training, education, and experience as an FDA official.

2. The purpose of this Supplemental Declaration is to provide further information on the resource diversion from important FDA public health programs that would occur if the Agency were to reinitiate withdrawal proceedings ("Withdrawal Proceedings") for the approximately 73 penicillin and tetracycline drug products currently approved for use in animal feed for production uses (*i.e.,* growth promotion and feed efficiency indications) (the "NOOH Products"). As discussed in my First Declaration, CVM estimates that the Withdrawal Proceedings would require the efforts of over a dozen of FDA employees and take a minimum of

five and one half years to complete. (First Declaration ¶ 26.) As I stated then, while this would inevitably drain resources from other FDA and CVM programs, CVM had not then determined yet precisely how it would reallocate resources in order to hold the hearings. (*Id.*)

3. Since my First Declaration, we have conducted further planning to specify which FDA employees would be staffed on the Withdrawal Proceedings. Based on this further planning, we can now be more specific about the consequences of the diversion of CVM resources that would be caused by reinitiating the Withdrawal Proceedings.

4. Reinitiating the Withdrawal Proceedings will compromise FDA's ability to finalize and implement its current plan to end the use of medically important antimicrobial drugs ("Medically Important Antimicrobials") in animals for production uses because of concerns about antimicrobial resistance. FDA's current approach was born out of its experience with the involuntary withdrawal of its approval for Baytril (enrofloxacin), an antibiotic drug in the fluoroquinolone class, for use in poultry because of concerns about antimicrobial resistance. By the time Baytril was ultimately withdrawn for such use in 2005, FDA had expended over five years and $3.3 million on the proceedings.

5. Based on the Baytril experience, CVM became concerned that it would be impracticable to initiate and complete involuntary withdrawal proceedings for the approximately 161 existing individual approved applications for production uses for Medically Important Antimicrobials, to the extent that such withdrawal proceedings might be appropriate. As used by FDA, the term "Medically Important Antimicrobials" generally refers to antimicrobial drugs that are important for therapeutic use in humans, and the classes of such drugs that are currently approved for production uses include penicillins, tetracyclines, macrolides, lincosamides, aminoglycosides, and streptogramins. FDA therefore began to develop an alternate regulatory

strategy that would focus first on eliminating the injudicious use of Medically Important Antimicrobials voluntarily, with the potential for more forceful regulatory action later, if needed.

6. As this Court is aware, FDA's approach was first announced 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") (Attached as Exhibit A). Under Draft GFI 209, FDA set forth its view (a) that it is not in the interest of public health for Medically Important Antimicrobials to be used for production uses, and (b) that therapeutic uses for Medically Important Antimicrobials should occur only under the supervision of a veterinarian. Draft GFI 209 was finalized on April 11, 2012. (Attached as Exhibit B). Also on that date, FDA published Draft Guidance for Industry 213 ("Draft GFI 213"), which describes the Agency's plan to encourage the withdrawal of approvals for production uses of Medically Important Antimicrobials, and transition the remaining therapeutic indications to veterinarian oversight. (Attached as Exhibit C). Under Draft GFI 213, FDA set forth a detailed plan for how drug companies (often times called "sponsors") should update their product labeling to withdraw production uses for their approved drug products containing Medically Important Antimicrobials, and also how to transition remaining therapeutic uses to require veterinarian oversight. (Exhibit C at 5-7.) As discussed in Draft GFI 213, FDA believes that the proposed changes can be implemented within three years of the guidance being finalized. (*Id.* at 7-8.)

7. If FDA's proposed strategy is successful, we anticipate that this will result in the withdrawals of approvals for production uses for Medically Important Antimicrobials much more quickly than through an involuntary withdrawal process (which would involve, among other things, the publication of notices of opportunity for hearing and, possibly, contested withdrawal proceedings). It is impossible to predict with any certainty how long it would take

FDA to involuntarily withdraw approximately 161 individual drug approvals. However, I believe the entire process would take many years to accomplish and it is highly uncertain when we would see the first approval actually withdrawn. Alternatively, if FDA's current proposed strategy is successful, FDA is highly optimistic that a least some sponsors will withdraw voluntarily their approvals for production uses. Even if some approvals for production uses are not withdrawn voluntarily after the expiration of the three-year period as proposed in Draft GFI 213, we anticipate that the number of drug products that might be subject to future regulatory action will have been substantially reduced.

8. If FDA is required to reinitiate the Withdrawal Proceedings with respect to the NOOH Products, however, resources that would otherwise be dedicated to the finalization and implementation of FDA's voluntary strategy would need to be redirected to the Withdrawal Proceedings. Many of the same scientists from CVM's Office of New Animal Drug Evaluation and Office of Research who would be needed to assist with the Withdrawal Proceedings are needed to implement FDA's voluntary strategy. Given the amount of time and effort each project would require, it is unlikely that both projects could be adequately staffed at all times.

9. As noted above, Draft GFI 213 outlines the Agency's plan for withdrawing approvals for production uses for Medically Important Antimicrobials and transitioning the remaining therapeutic indications to veterinarian oversight. Once the public comment period on this draft guidance closes on July 12, 2012, CVM's scientists will be needed to assist in the review and analysis of the public comments received. Although it is difficult to predict the nature and volume of comments that will be submitted on Draft GFI 213, the extent of public comment on Draft GFI 209 issued in June 2010 may provide some indication. In the case of Draft GFI 209, FDA received approximately 1,200 distinct comments from individuals or

organizations and more than 100,000 comments submitted as part of "write-in" campaigns. Once the public comment analysis is completed, CVM's scientists would then be deeply involved in the process of preparing a final version of the guidance.

10. Moreover, as I discussed in my First Declaration, CVM's Office of Research employees who would need to be involved in Withdrawal Proceedings also work on other important efforts to combat antimicrobial resistance, such as the National Antimicrobial Resistance Monitoring System ("NARMS"). As I stated before, NARMS is a national surveillance system that tracks antibiotic resistance in foodborne bacteria. (First Declaration ¶ 26.) 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.

11. Because many of the FDA scientists who are responsible for the NARMS program would need to commit significant amounts of time to the Withdrawal Proceedings, and because (as discussed above) CVM anticipates already that many of the same scientists will have significant responsibilities in implementing GFI 209 and finalizing and implementing Draft GFI 213, I believe that efforts to simultaneously initiate Withdrawal Proceedings and finalize and implement the guidances would likely have significant negative effects on FDA's ability to achieve the goals of the NARMs program. For example, I believe that redirecting resources

would likely 1) delay the preparation of NARMS data reports and hence delay dissemination of important information on antimicrobial resistance, and 2) delay ongoing efforts to implement the NARMS Strategic Plan (http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm305710.htm) which includes instituting important enhancements to the design of the program.

12. As I also discussed in my First Declaration, 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. (First Declaration ¶ 27.) 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. As discussed before, CVM expects that some drug sponsors, in connection with withdrawing their approvals for production uses, will seek approvals for legitimate new therapeutic indications at the same time. (*Id.* ¶ 28.) CVM has determined that many of the same scientists who would be assigned to the Withdrawal Proceedings would also be responsible for reviewing the microbial food safety aspects of these new applications. This resource challenge may slow the review of applications that would result in the removal of approvals for production uses and may pose significant hurdles to reviewing new animal drug applications in accordance with deadlines that are imposed on FDA by statute.

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

Executed on June 1, 2012, in Rockville, Maryland.

WILLIAM T. FLYNN, DVM, MS
Deputy Director for Science Policy
Center for Veterinary Medicine
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