McCARTER & ENGLISH, LLP
Two Tower Center Boulevard, 24th Floor
East Brunswick, New Jersey 08816
T: 732-867-9777
F: 732-393-1901
Attorneys for Plaintiff-Petitioner,
Pharmaceutical Manufacturing Research Services, Inc.

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF PENNSYLVANIA

PHARMACEUTICAL MANUFACTURING RESEARCH SERVICES, INC., Plaintiff-Petitioner, v. UNITED STATES FOOD AND DRUG ADMINISTRATION, SCOTT GOTTLIEB, M.D., in his official capacity as the Commissioner of Food and Drugs, and his successors and assigns, and THOMAS E. PRICE, M.D., in his official capacity as the Secretary of the United States Department of Health and Human Services, as well as his successors and assigns, Defendants.	**Civil Action No.**

COMPLAINT FOR WRIT IN THE NATURE OF MANDAMUS RELIEF AND FOR THE ISSUANCE OF A PRELIMINARY INJUNCTION WITH EXPEDITED DISCOVERY AND OTHER EQUITABLE RELIEF

NOW COMES Plaintiff-Petitioner Pharmaceutical Manufacturing Research Services, Inc. ("PMRS"), by and through its attorneys, McCarter & English, LLP, and for its Complaint for Writ in the nature of mandamus relief and for the issuance of a preliminary injunction with expedited discovery and other equitable relief against the United States Food and Drug Administration ("FDA"), Scott Gottlieb, M.D., in his official capacity as the Commissioner of

Food and Drugs and his successors and assigns, and Thomas E. Price, M.D., in his official capacity as the Secretary of the United States Department of Health and Human Services and his successors and assigns, hereby alleges as follows:

INTRODUCTION

1. Plaintiff PMRS brings this action for injunctive and declaratory relief and for a writ in the nature of mandamus due to the failure of the FDA and its Commissioner, Scott Gottlieb, M.D., to respond "promptly" to PMRS's Petition for Stay of Action, as required by the applicable statutory and regulatory authorities.

2. Defendants' failure to provide the required prompt response to PMRS's Petition for Stay of Action violates the Administrative Procedure Act ("APA"), 5 U.S.C. § 702, and the Mandamus Act, 28 U.S.C. § 1361.

3. FDA's unreasonable delay warrants this Court's involvement because it presents serious risks to the health and well-being of the American public in light of the ongoing and devastating opioid epidemic, as well as potentially irreparable economic and competitive harm to PMRS.

4. PMRS seeks an order from this Court compelling FDA to respond to PMRS's urgent Petition for Stay of Action, a Petition that raises pressing public health issues that render further delay by FDA patently unreasonable.

5. That Petition was a timely request that FDA stay the effective date of its approval of Inspirion Delivery Services, LLC's New Drug Application 209777 for a product known as ROXYBOND (oxycodone hydrochloride) tablets, ("ROXYBOND" or "Inspirion NDA"), pending FDA's substantive responses to two pending Citizen Petitions previously submitted by PMRS before FDA's approval of ROXYBOND.

6. PMRS's Citizen Petitions, as well as its public comments at numerous FDA meetings in recent years, highlighted several serious flaws in FDA's process for evaluating and approving opioids and sought to engage FDA in connection with the Agency's role in stemming the opioid epidemic plaguing this nation.

7. PMRS was forced to submit the Petition for Stay to prevent another mislabeled and dangerous opioid from entering the market while FDA considers the life-and-death issues raised in PMRS's various submissions.

8. PMRS submitted the Petition for Stay in accordance with FDA's regulation mandating that such petitions must be submitted within 30 days of an agency's action . 21 C.F.R. § 10.35(b).

9. Those same regulations require a similarly prompt response from FDA. 21 C.F.R. § 10.35(e); Proposed Rule, 40 F.R. 40682 (Sept. 13, 1975)).

10. However, nearly three months after submitting its time-sensitive petition, PMRS still has not received any substantive response and yet another mislabeled and dangerous opioid is poised to enter the market despite the issues and science presented to FDA in PMRS's various submissions.

11. The APA requires federal agencies, like FDA, to conclude all matters presented to them "within a reasonable time" and, more specifically, authorizes reviewing courts to "compel agency action unlawfully withheld or unreasonably delayed." 5 U.S.C. §§ 555(b), 706(1).

12. Under FDA's own regulations, it is required to respond "promptly" to PMRS's Petition for Stay, but it has failed to do so. 21 C.F.R. § 10.35(e).

13. To be clear, PMRS emphasizes that it does *not* request a ruling from this Court dictating what FDA's response should be. PMRS simply requests that this Court exercise the

authority granted to it by the APA and the mandamus statute to compel FDA to provide the response it owes PMRS within 30 days.

14. PMRS also seeks preliminary injunctive relief staying the effective date of the ROXYBOND approval until FDA finally provides a substantive response to PMRS's Petition for Stay.

JURISDICTION AND VENUE

15. This Court has subject matter jurisdiction over this action pursuant to: (a) 28 U.S.C. § 1331 ("[t]he district courts shall have original jurisdiction of all civil actions arising under the Constitution, laws, or treaties of the United States," *i.e.*, federal question jurisdiction); (b) 5 U.S.C. §§ 555(b), 702, 706(1) (judicial review provisions of the APA); and (c) 28 U.S.C. § 1361 ("[t]he district courts shall have original jurisdiction of any action in the nature of mandamus to compel an officer or employee of the United States or any agency thereof to perform a duty owed to the plaintiff.").

16. The declaratory relief requested in this action is authorized by 28 U.S.C. §§ 2201, 2202.

17. Venue is proper in the Eastern District of Pennsylvania pursuant to 28 U.S.C. § 1391(e)(1)(C), because that is the District in which Plaintiff-Petitioner PMRS resides.

PARTIES

18. Plaintiff-Petitioner PMRS is a corporation with headquarters located at 202 Precision Road, Horsham, Pennsylvania 19044.

19. As a world-class supplier of pharmaceutical services, PMRS supports the manufacturing of four FDA-approved drug products, two internationally-approved drug products, and numerous developmental and investigational drugs.

20. Defendant FDA is an agency responsible for, among other duties, protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices.

21. FDA's headquarters are located at 10903 New Hampshire Avenue, Silver Spring, Maryland 20993.

22. FDA is headed by Defendant Scott Gottlieb, M.D., Commissioner of Food and Drugs, and operates under authority delegated by Congress and Defendant Thomas E. Price, M.D., Secretary of the U.S. Department of Health and Human Services ("HHS"), a federal agency headquartered in the District of Columbia.

23. Commissioner Gottlieb and Secretary Price, and their respective successors and assigns, are sued in their official capacities as the government officials with ultimate responsibility for the actions and failures to act complained of herein.

FACTUAL BACKGROUND

A. The Opioid Epidemic and Its Impact on the Public Health

24. The United States of America is mired in a catastrophic opioid epidemic. *See* Robert M. Califf, M.D., et al., *A Proactive Response to Prescription Opioid Abuse*, 374 N. Engl. J. Med. 1480, 1483-85 (2016).

25. Statistics compiled by the Centers for Disease Control and Prevention ("CDC") demonstrate that, in 2014 alone, almost 2,000,000 Americans abused or were dependent on prescription opioids and that opioids killed more than 33,000 people in 2015, more than any previous year on record.

26. CDC also reports that the number of opioid-related overdose deaths has quadrupled since 1999 and that 91 Americans die every day from an opioid overdose.

27. The public health crisis caused by the opioid epidemic has led to substantial economic harm as well. For example, in 2013 alone, the opioid epidemic resulted in approximately $78.5 billion in economic costs in the United States. C.S. Florence, et al., *The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States*, L. Med. Care. 2016 Oct. 54(10):901-06.

28. Analysis of opioid-related economic harms at the state level indicates that Pennsylvania ranks among the top 10 states in terms of total health care spending related to opioid abuse, with conservative estimates suggesting that the state spends $847 million per year on these costs—most likely significantly higher when the costs of opioid-abuse-related criminal justice and lost workplace productivity are taken into account. Matrix Global Advisors, *Health Care Costs from Opioid Abuse: A State-by-State Analysis* 2 (Apr. 2015), https://drugfree.org/wp-content/uploads/2015/04/Matrix_OpioidAbuse_040415.pdf (last visited Aug. 2, 2017).

B. Insufficient Data to Support Use of Opioids for Chronic Pain

29. FDA defines chronic pain as "either pain persisting for longer than 1 month beyond resolution of the underlying insult, or pain persisting beyond 3 months." FDA, *Guidance for Industry—Analgesic Indications: Developing Drug and Biological Products*, 2 (Feb. 2014), https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM384691.pdf (last visited Aug. 2, 2017).

30. Critically, however, after conducting a comprehensive review of the scientific evidence supporting the effectiveness of long-term opioid therapy for chronic pain, the CDC found that:

> Most placebo-controlled, randomized trials of opioids have lasted 6 weeks or less, and we are aware of no study that has compared opioid therapy with other treatments in terms of long-term (more than 1 year) outcomes related to pain,

> function, or quality of life. The few randomized trials to evaluate opioid efficacy for longer than 6 weeks had consistently poor results.

Thomas R. Frieden & Debra Houry, *Reducing the Risks of Relief — The CDC Opioid-Prescribing Guideline*, 374 New Eng. J. Med. 1501, 1501 (2016).

31. Indeed, in its March 2016 *Guideline for Prescribing Opioids for Chronic Pain*, the CDC found that "[t]he evidence reviews forming the basis of this guideline clearly illustrate that there is much yet to be learned about the effectiveness, safety, and economic efficiency of long-term opioid therapy." CDC, *Guideline for Prescribing Opioids for Chronic Pain*, at 34 (2016), https://www.cdc.gov/mmwr/volumes/65/rr/pdfs/rr6501e1.pdf (last visited Aug. 2, 2017).

32. Thus, the CDC concluded: "The science of opioids for chronic pain is clear: for the vast majority of patients, the known, serious, and too-often-fatal risks far outweigh the unproven and transient benefits." Frieden & Houry, *Reducing the Risks of Relief — The CDC Opioid-Prescribing Guideline*, 374 New Eng. J. Med. at 1503.

33. In response to the CDC's report, FDA has acknowledged that "[a] key lesson learned during the development of the CDC guideline is that there is very little research on the long-term benefits of opioids for treating chronic pain[,]" in contrast to the "growing evidence of harms associated with such use, and of the benefits of other nonopioid treatment alternatives." Robert M. Califf et al., *A Proactive Response to Prescription Opioid Abuse*, 374 New Eng. J. Med. at 1484.

34. Further, FDA has acknowledged that the Agency "does its best work when high-quality scientific evidence is available to assess the risks and benefits of intended uses of medical products" but that "[u]nfortunately, the field of chronic pain treatment is strikingly deficient in such evidence." *Id.* at 1484.

35. In stark contradiction to both the CDC's findings and its own public statements, FDA continues to approve new opioid products intended for the treatment of chronic pain.

C. PMRS's Identification of Systemic Flaws in FDA's Process for Reviewing and Approving Opioids

36. PMRS's own research and development has revealed systemic flaws with FDA's review and approval of opioids that are undermining FDA's ability to protect the public health and welfare in the face of the opioid-addiction epidemic.

37. Pursuant to 21 C.F.R. §§ 10.20 and 10.30, PMRS raised those critical issues with FDA via Citizen Petitions dated February 19, 2016, and March 6, 2017. Save for a form letter providing an "interim response" to its February 19, 2016, Citizen Petition, however, PMRS has received no substantive response from FDA.[1]

(1) *PMRS's February 2016 Citizen Petition*

38. On February 19, 2016, PMRS submitted a citizen petition to FDA directed at the issue of abuse-deterrent labeling ("February 2016 Citizen Petition"), now pending under Docket No. FDA-2016-P-0645, requesting, in part, that FDA take certain actions, summarized as follows:

a. Apply the existing standards for laboratory-based in vitro manipulation and extraction studies, including both small and large volume extraction, before permitting opioid drug products with potentially abuse-deterrent properties to be approved;

b. Remove Category 3 human abuse-deterrent (liking) studies from the FDA Guidance, "Abuse-Deterrent Opioids Evaluation and Labeling Guidance for Industry" (April 2015), and as a requirement for approval of drug products with

[1] PMRS's Citizen Petitions are pending under docket numbers FDA-2016-P-0645 and FDA-2017-P-1359. PMRS does not seek court intervention at this time in respect of those pending Citizen Petitions, but both petitions provide necessary context regarding the critical issues addressed in PMRS's Petition to Stay Action, which is the subject of this suit, and therefore are discussed in this Section of the Complaint.

potentially abuse deterrent properties as inherently flawed, subjective, and highly prone to manipulation; and

c. Require post-marketing empirical proof through epidemiological or other scientifically rigorous studies that shows that opioid drug products with potential abuse deterrent properties do in fact result in a *meaningful* reduction in misuse, abuse, addiction, overdose and/or death before approving abuse deterrent labeling for opioid drug products and before permitting opioid drug products to be marketed as abuse deterrent.

39. PMRS's February 2016 Citizen Petition also requested that all opioid drug products currently labeled with abuse-deterrent claims be required to meet all three of the requirements specified above or have their abuse-deterrent labeling removed within a reasonable period of time not to exceed six months.[2]

(2) *PMRS's March 2017 Citizen Petition*

40. On March 6, 2017, PMRS submitted a citizen petition to FDA directed at the issue of chronic-use labeling, now pending under Docket No. FDA-2017-P-1359 ("March 2017 Citizen Petition"), requesting, in part, the revocation of all immediate-release ("IR") opioid drug product labeling that "support[s] use for the treatment of chronic pain." PMRS further requested that all IR opioid drug product labeling state that the indication is for "acute pain for a limited duration."

(3) *FDA's Failure to Respond Substantively to PMRS's Citizen Petitions*

41. PMRS has raised the above-discussed issues directly with FDA on multiple occasions, publicly advocating for the agency to reassess its approach to approving opioid products.

[2] In addition, the February 2016 Petition included a request for actions pertaining to OXYCONTIN specifically. (February 2016 Petition, No. FDA-2016-P-0645 at 4.) The OXYCONTIN-specific requests are not addressed in this action.

42. In addition to its two Citizen Petitions, PMRS also has participated in numerous FDA Advisory Committee meetings and public workshops. *See generally* PMRS's comments at the advisory committee meetings pertaining to VANTRELA ER (Jun. 7, 2016), TROXYCA ER (Jun. 8, 2016), ARYMO ER (Aug. 4, 2016), the use of opioids in pediatric patients (Sep. 16, 2016), OPANA ER (Mar. 14, 2017), ROXYBOND (Apr. 5, 2017), and REXISTA (Jul. 26, 2017), as well as the public meeting on premarket evaluation of abuse-deterrent properties (Nov. 1, 2016).

43. To date, however, PMRS has received no substantive response to its Citizen Petitions, no substantive information, and no substantive rationale for FDA's continuation of a seemingly status quo approach that permits flooding the market with opioids labeled as abuse-deterrent and appropriate for chronic use, despite the absence of sufficient data to support those claims.

D. PMRS's May 11, 2017 Petition for Stay of Action

44. Notwithstanding the significant public-health issues discussed in PMRS's various submissions, and notwithstanding FDA's acknowledgment of CDC findings confirming the lack of sufficient data to support use of opioids to treat chronic pain, on April 20, 2017, FDA approved the Inspirion NDA.

45. FDA's treatment of the Inspirion NDA creates a rigid and harmful dichotomy, wherein FDA delays responding substantively to PMRS's Citizen Petitions that raise fundamental questions about FDA's role in facilitating the opioid epidemic, but then rushes to approve yet another opioid product with chronic use labeling and purported abuse-deterrent properties, despite the scientific community's recognition that the evidence needed to support such claims is lacking.

46. On May 11, 2017, and within the 30-day window mandated by FDA, PMRS filed a Petition for Stay of Action ("PSA") pursuant to 21 C.F.R. § 10.35, requesting that FDA stay the effective approval date of ROXYBOND until such time as FDA provides substantive responses to PMRS's Citizen Petitions raising serious safety issues concerning opioids, like ROXYBOND, that are approved for chronic use and/or as abuse-deterrent.

47. After 30 days passed with no response from FDA, PMRS sent Commissioner Gottlieb a letter to ensure his awareness of the PSA and to reiterate the urgency of PMRS's PSA.

48. To date, however, FDA has not provided any response to PMRS's Petition for Stay of Action, except for a two-paragraph letter acknowledging receipt of the PSA but providing no information concerning the time period in which PMRS could expect a response. Months have now passed, opioid addiction rates are climbing, and people continue to die.

49. FDA's continued delay is unreasonable and warrants this Court's intervention to compel a substantive response to the PSA by a date certain.

CLAIM FOR RELIEF

50. The foregoing allegations are incorporated by reference and repeated as though set forth in full herein.

51. PMRS submitted a timely PSA to FDA on May 11, 2017, requesting a stay of the effective approval date of ROXYBOND until FDA provides a substantive response to PMRS's two pending Citizen Petitions.

52. The Administrative Procedure Act requires FDA to respond to PMRS's Petition for Stay of Action "[w]ith due regard for the convenience and necessity of the parties . . . and within a reasonable time." 5 U.S.C. § 555(b).

53. Moreover, the submission of PMRS's PSA imposed a mandatory, non-discretionary duty on Defendant Scott Gottlieb, M.D., Commissioner of Food and Drugs, to review and respond to the Petition "promptly" and with the same type of diligence with which PMRS acted when submitting the Petition for Stay within 30 days of the FDA action at issue. 21 C.F.R. § 10.35(e); Proposed Rule, 40 F.R. 40682 (Sept. 13, 1975).

54. Despite the passage of nearly three months and the urgency presented by the opioid epidemic plaguing the nation, Defendants have failed to provide any substantive response to PMRS's PSA.

55. Requiring PMRS to wait any longer for a response to its Petition before seeking judicial intervention to compel the unreasonably delayed response would be unjust, wasteful, and significantly harmful to the public health, because absent the stay sought by PMRS, Inspirion is free to market another mislabeled and dangerous opioid.

56. Defendants' failure to respond to PMRS's PSA represents "agency action" that has been "unreasonably delayed," and therefore PMRS is entitled to an order from this Court pursuant to the APA and in the nature of mandamus compelling Defendants to provide a substantive response to the pending PSA within 30 days. 5 U.S.C. § 706(1); 28 U.S.C. § 1361.

57. Moreover, PMRS has experienced harm and will experience irreparable harm if ROXYBOND is permitted to launch before FDA decides PMRS's PSA.

58. The critical importance of being first to market is well-established in the pharmaceutical industry.

59. Companies spend considerable research seeking to increase the odds of beating their competitors to market because of the significant commercial disadvantage to missing first approval.

60. In the industry, every month of lead time ahead of a competitor is significant.

61. First-approved and first-moved products are able to establish themselves with physicians and patients in a way that cannot be changed after the fact.

62. FDA's failure to act promptly on PMRS's PSA, therefore, is causing substantial and irreparable harm to PMRS.

WHEREFORE, Plaintiff-Petitioner PMRS prays that this Court enter an Order:

a. Declaring that Defendants have unreasonably delayed in responding to PMRS's PSA submitted on May 11, 2017, and that such unreasonable delay is a violation of the Administrative Procedure Act and applicable FDA regulations;

b. Compelling Defendants, by injunction and/or writ in the nature of mandamus, to provide a substantive response to PMRS's PSA within 30 days of the entry of this Court's Order;

c. Preliminarily staying the effective date of Inspirion Delivery Services, LLC's New Drug Application 209777 for ROXYBOND (oxycodone hydrochloride) tablets until Defendants issue a substantive response to PMRS's PSA; and

d. Awarding PMRS attorneys' fees, reasonable expenses incurred in connection with this action, and such other relief as this Court deems equitable, just, and proper under the circumstances.

McCARTER & ENGLISH, LLP
Attorneys for Plaintiff-Petitioner,
Pharmaceutical Manufacturing Research Services, Inc.

Dated: August 4, 2017

By: _____
Natalie S. Watson
A Member of the Firm
Pennsylvania Attorney ID # 322345