

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NALOX-1 PHARMACEUTICALS, LLC,

Petitioner

v.

ADAPT PHARMA OPERATIONS LIMITED, AND
OPIANT PHARMACEUTICALS, INC.

Patent Owners

IPR2019-00685

U.S. Patent No. 9,211,253

SUPPLEMENTAL DECLARATION OF GÜNTHER HOCHHAUS, Ph.D.

TABLE OF CONTENTS

I.	OVERVIEW	1
II.	MY BACKGROUND AND QUALIFICATIONS	8
III.	LEGAL STANDARDS	11
IV.	THE CLAIMED DOSE OF 4 MG OF NALOXONE WOULD HAVE BEEN OBVIOUS TO A POSA.....	12
	A. Wyse discloses a range of naloxone content that includes 4 mg, and does not “teach away” from such a dose.....	12
	B. A Pharmacologist POSA seeking to develop a community-use intranasal naloxone formulation would have been motivated to choose a naloxone dose of greater than 2 mg.	15
	C. Concerns over inducing acute withdrawal would not have outweighed administering a less than effective dose of naloxone.	21
	D. A Pharmacologist POSA would have tried to achieve a rapid onset of action and high drug exposure with an IN naloxone formulation, and would have known that a naloxone dose higher than 2 mg could achieve these goals.	24
	E. A Pharmacologist POSA would <i>not</i> have expected the differences in drug concentration and excipients between Wyse’s IN formulations and the formulation of the claims to have unpredictable effects on pK.....	28
	F. A Pharmacologist POSA would have reasonably expected that the IN exposure parameters disclosed with Wyse’s 2 mg administration would remain dose proportional at least at 4 mg.	34
	G. The claimed naloxone formulation has fully expected properties.	37
	1. The C _{max} differences between Wyse and the claimed formulation are not statistically significant.	37

*Inter Partes Review of U.S. Patent No. 9,211,253
Supplemental Declaration of Günther Hochhaus, Ph.D. (Nalox1202)*

2.	The relative bioavailability differences between the Wyse formulation and the claimed formulation are not statistically significant.....	40
3.	In an “apples-to-apples” comparison, the terminal half-lives of the Wyse formulation and the claimed formulation are not different.....	41
V.	CONCLUSION.....	44

***Inter Partes Review of U.S. Patent No. 9,211,253
Supplemental Declaration of Günther Hochhaus, Ph.D. (Nalox1202)***

I, Günther Hochhaus, do hereby declare as follows:

I. OVERVIEW

1. I am over the age of 18 and otherwise competent to make this Declaration. This Declaration is based on my personal knowledge and experience in the field of clinical pharmacology, in particular with respect to nasal spray dosage forms. I understand that this Declaration is being submitted in support of Petitioner Nalox-1 Pharmaceuticals, LLC's ("Nalox-1") Reply to Patent Owner's Response to the petition for *Inter Partes* Review ("IPR") of certain claims of U.S. Patent No. 9,211,253 ("the 253 patent") (Nalox1001).

2. This is my second Declaration in this proceeding. Previously, I submitted a Declaration (Nalox1003) in support of Nalox-1's petition for IPR challenging the '253 patent. I refer to that Declaration hereinafter as "my first Declaration."

3. I have now been asked to supplement the opinions I expressed in my first Declaration. I have also been asked to respond to certain opinions contained in the Declarations of Kenneth A. Williams, M.D. (Ex-2001; Ex-2202) and Stuart A. Jones, Ph.D. (Ex-2201).

4. In preparing this Declaration, I have reviewed the '253 patent and its file history. I have also considered each of the documents listed in the table below, in addition to the exhibits disclosed in my first Declaration. *See* Nalox1003, ¶5.

***Inter Partes Review of U.S. Patent No. 9,211,253
Supplemental Declaration of Günther Hochhaus, Ph.D. (Nalox1202)***

Exhibit No.	Description
Nalox1001	U.S. Patent No. 9,211,253 (the '253 patent)
Nalox1002	Expert Declaration of Maureen Donovan
Nalox1003	Expert Declaration of Günther Hochhaus (my first Declaration)
Nalox1007	U.S. Patent No. 9,192,570 (Wyse)
Nalox1008	Chinese Patent No. 1,575,795 (Wang)
Nalox1009	PCT International App. Pub. No. WO00/62757 (Davies)
Nalox1016	Wermeling, D., <i>A Response to the Opioid Overdose Epidemic: Naloxone Nasal Spray</i> , 3 Drug Deliv. & Transl. Res. 63–74 (2013) (Wermeling 2013)
Nalox1017	Alabama Department of Public Health, <i>Alabama EMS Patient Care Protocols</i> (7th ed., Oct. 2013) (Alabama EMS Protocols)
Nalox1020	Barton, E. et al., <i>Intranasal Administration of Naloxone by Paramedics</i> , 6 Prehosp. Em. Care 54–58 (Barton 2002)
Nalox1023	Boyer, E., <i>Management of Opioid Analgesic Overdose</i> , 367(2) N. Engl. J. Med. 146–55 (2012) (Boyer)
Nalox1025	Excerpt of Commonwealth of Kentucky, <i>Kentucky Patient Care Protocols</i> (Mar. 13, 2015) (Kentucky Patient Care Protocols)
Nalox1027	Dowling, J. et al., <i>Population Pharmacokinetics of Intravenous, Intramuscular, and Intranasal Naloxone in Human Volunteers</i> , 30(4) Ther. Drug. Monit. 490–96 (2008) (Dowling)
Nalox1034	Kelly, A-M. et al., <i>Randomised Trial of Intranasal Versus Intramuscular Naloxone in Prehospital Treatment for Suspected Opioid Overdose</i> , 182(1) Med. J. Austl. 24–27 (2005) (Kelly)

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.