

UNITED STATES PATENT AND TRADEMARK OFFICE

---

BEFORE THE PATENT TRIAL AND APPEAL BOARD

---

ACTAVIS LLC,  
Petitioner

v.

ABRAXIS BIOSCIENCE, LLC,  
Patent Owner

---

Case IPR2017-01101  
Patent 7,820,788 B2

---

**DECLARATION OF CORY J. BERKLAND, Ph.D.  
IN SUPPORT OF PETITION FOR *INTER PARTES* REVIEW**

## TABLE OF CONTENTS

	<b>Page</b>
I. INTRODUCTION .....	1
II. BACKGROUND AND QUALIFICATIONS.....	2
III. LEGAL STANDARDS USED IN MY ANALYSIS .....	5
A. Prior art.....	5
B. Person of ordinary skill in the art.....	6
C. Anticipation .....	7
D. Obviousness.....	8
IV. THE '788 PATENT .....	11
A. The alleged invention .....	11
B. Challenged claims .....	16
C. Claim construction .....	17
V. THE PRIOR ART.....	19
A. Desai (EX1006).....	19
B. Kadima (EX1004) .....	27
C. Liversidge (EX1005).....	29
VI. ANTICIPATION .....	31
A. Claims 1–9 and 11–12 of the '788 patent are anticipated.....	31
1. Claim 1 is anticipated by Desai. ....	31
a. Albumin-paclitaxel combination .....	31
b. Particle size of less than about 200 nm .....	32
c. Albumin-paclitaxel ratio of about 1:1 to 9:1 .....	33

2.	Claims 2–9 and 11–12 are anticipated by Desai.....	34
B.	The “starting” ratio of albumin to paclitaxel does not change.....	37
VII.	OBVIOUSNESS.....	40
A.	Claim 1 of the ’788 patent would have been obvious.....	41
1.	Obviousness over Desai alone .....	41
a.	The albumin-paclitaxel ratio of about 9:1 falls within a range disclosed by Desai. ....	44
b.	A skilled artisan would have been motivated to lower Capxol’s 13.3:1 albumin-paclitaxel ratio. ....	46
c.	A skilled artisan would have reasonably expected an albumin-paclitaxel ratio of 9:1 to retain stability. ....	48
2.	Obviousness over Desai, Kadima, and Liversidge .....	51
a.	Kadima and Liversidge also disclose ranges of albumin-paclitaxel ratios, including about 9:1.....	51
b.	Kadima teaches additional reasons to lower a 13.3:1 ratio of albumin to paclitaxel to about 9:1.....	53
B.	The other challenged claims would have been obvious.....	56
C.	There are no relevant secondary considerations indicating that the challenged claims would not have been obvious. ....	59
1.	The allegedly “unexpected” cell-binding results lack a nexus to the ’788 patent and would have been expected.....	61
2.	The allegedly “unexpected” clinical data did not compare the closest prior art and would have been expected. ....	64
VIII.	CONCLUSION.....	68

## EXHIBITS CITED

EX	Description
<b>1001</b>	Desai et al., U.S. Patent No. 7,820,788 B2, "Compositions and Methods of Delivery of Pharmacological Agents" (issued Oct. 26, 2010) (the "'788 patent")
<b>1004</b>	Kadima et al., WO 00/06152, "Pharmaceutically Acceptable Composition Comprising an Aqueous Solution of Paclitaxel and Albumin" (published Feb. 10, 2000) ("Kadima")
<b>1005</b>	Liversidge et al., U.S. Patent No. 5,399,363, "Surface Modified Anticancer Nanoparticles" (issued Mar. 21, 1995) ("Liversidge")
<b>1006</b>	Desai et al., WO 1999/000113, "Novel Formulations of Pharmacological Agents, Methods for the Preparation thereof and Methods for the Use thereof" (published Jan. 7, 1999) ("Desai")
<b>1007</b>	Li et al., "Fluorescein Binding to Normal Human Serum Proteins Demonstrated by Equilibrium Dialysis," Arch Ophthalmol. vol. 100, 484–87 (March 1982)
<b>1009</b>	FDA Guideline on Sterile Drug Products Produced by Aseptic Processing (June 1987, reprinted June 1991 and Feb. 1997)
<b>1010</b>	EMEA Guidance on Manufacture of the Finished Dosage Form (April 1996)
<b>1011</b>	<i>Elan Pharma Int'l Ltd. v. Abraxis BioScience, Inc.</i> , Judgment and Verdict Form, No. 06-438-GMS, Dkt. 614 (D. Del. June 16, 2008)
<b>1017</b>	Damascelli, B et al. "Intraarterial chemotherapy with polyoxyethylated castor oil free paclitaxel, incorporated in albumin nanoparticles (ABI-007)," Cancer 2001 Nov; 92(10):2592–2602 ("Damascelli")
<b>1018</b>	Ibrahim et al., "Phase I and pharmacokinetic study of ABI-007, a Cremophor-free, protein-stabilized, nanoparticle formulation of paclitaxel," Clin Cancer Res. 2002 May; 8:1038–44 ("Ibrahim")
<b>1023</b>	U.S. Application No. 11/553,339, Declaration of Neil P. Desai Pursuant to 37 C.F.R. § 1.132 (dated Apr. 14, 2010)

I, Cory J. Berkland, Ph.D., hereby declare as follows:

## **I. INTRODUCTION**

1. I am currently appointed as the Solon E. Summerfield Distinguished Professor in the Department of Pharmaceutical Chemistry and the Department of Chemical and Petroleum Engineering at the University of Kansas. I have been retained by Petitioner Actavis LLC in connection with its request for *inter partes* review of U.S. Patent No. 7,820,788 (“the ’788 patent”). A copy of the ’788 patent has been marked EX1001. I have reviewed and am familiar with the ’788 patent. Generally, it describes and claims pharmaceutical compositions comprising the anticancer drug paclitaxel bound to the protein albumin and formulated as nanoparticles, and methods of using such compositions to treat diseases including cancer.

2. I have been asked to provide my opinions regarding the patentability of claims 1–12 of the ’788 patent (the “challenged claims”). This declaration includes a discussion of my background and qualifications, the legal standards used in my analysis, an overview of the ’788 patent from the perspective of a person of ordinary skill in the art at the time that the patent was filed (a “skilled artisan”), and my opinions regarding the patentability of the challenged claims.

3. I am being compensated for my work in this proceeding at my standard hourly consulting rate of \$500.00 per hour. My compensation is in no way contingent on the substance of my opinions or the outcome of this proceeding.

# 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.