

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME CORP.
Petitioner

v.

GENENTECH, INC. AND CITY OF HOPE
Patent Owners

U.S. Patent No. 6,331,415

“Methods of Producing Immunoglobulins, Vectors and
Transformed Host Cells for Use Therein”

Inter Partes Review No. 2017-00047

**DECLARATION OF MARGARET H. BARON IN SUPPORT OF PETITION
FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 6,331,415**

TABLE OF CONTENTS

I.	BACKGROUND AND QUALIFICATIONS, PRIOR TESTIMONY, AND COMPENSATION	1
A.	Background and Qualifications	1
B.	Prior Testimony and Compensation	5
II.	MATERIALS CONSIDERED	5
A.	Anticipation	6
B.	Obviousness	7
C.	Person of Ordinary Skill in the Art	9
D.	Claim Construction	9
III.	SUMMARY OF OPINIONS	10
IV.	OVERVIEW OF THE '415 PATENT AND THE CHALLENGED CLAIMS	11
A.	Description of the Technology of the '415 Patent and the Challenged Claims	11
B.	The Prosecution and Reexamination History of the '415 Patent	19
V.	PRIOR ART RELEVANT TO MY OPINIONS	22
A.	Technology Background	22
1.	The Sophistication of Recombinant DNA Technology Was Advanced by April 8, 1983, and Mammalian Proteins Were Being Made in Host Cells Transformed with Foreign Genes	22
2.	Prior Art Production of Single Immunoglobulin Chains	25
3.	The Prevailing Mindset by April 1983 Was That One or More Proteins of Interest Could be Made in a Single Host Cell	28
B.	References Underlying Merck's Challenge to the Patentability of Claims of the '415 Patent	33

1.	The Bujard Patent Discloses Expressing a “Plurality of Genes” in Bacterial or Mammalian Host Cells and Identifies “Immunoglobulins” as a Protein of Interest.....	33
2.	The Cohen & Boyer Patent Discloses Expressing “One or More Genes” in Bacteria and Identifies “Antibodies” as a Protein of Interest	40
3.	Riggs & Itakura Discloses Hybridomas as a Source of Antibody Genes and the <i>In Vitro</i> Assemble of Heavy and Light Chains	46
4.	Southern Discloses One Host Cell Transformed with Two Vectors	47
VI.	ANTICIPATION AND OBVIOUSNESS OF THE CHALLENGED CLAIMS	49
A.	Opinions in Support of Merck’s Anticipation and Obviousness Arguments Concerning the Challenged Claims Based on the Bujard Patent	49
1.	Bujard Discloses Each and Every Limitation of Claims 1, 15, 17 and 33	49
2.	Bujard Discloses Each and Every Limitation of Claims 3, 4, 9, 11, 12, 16 and 19	53
3.	Claims 1, 3, 4, 11, 12, 14, 19 and 33 in View of Bujard in Combination with Riggs & Itakura	55
4.	Claims 1, 2, 18, 20 and 33 in View of Bujard in Combination with Southern	58
B.	Opinions in Support of Merck’s Obviousness Arguments Concerning Claims 1, 3, 4, 11, 12, 14 and 33 Based on the Cohen & Boyer Patent and the Riggs & Itakura Publication	60
1.	The Disclosures of Cohen & Boyer	60
2.	Claims 1, 3, 4, 11, 12, 14, and 33 in View of Cohen & Boyer in Combination with Riggs & Itakura.....	63
VII.	CONCLUSION.....	66

I, Margaret H. Baron, hereby declare and state as follows:

1. I have been retained as an expert by counsel for Merck Sharp & Dohme Corp. (“Merck”). I have prepared this declaration in connection with Merck’s related petition for *Inter Partes* Review of U.S. Patent No. 6,331,415 (“the ’415 patent,” Ex. 1001), which I am informed is being filed concurrently with this declaration. I have been asked to provide certain opinions relating to the patentability of the ’415 patent. Specifically, I have been asked to provide my opinion regarding whether claims 1, 2, 3, 4, 9, 11, 12, 14, 15, 16, 17, 18, 19, 20, and 33 of the ’415 patent would have been obvious in view of the prior art.

I. BACKGROUND AND QUALIFICATIONS, PRIOR TESTIMONY, AND COMPENSATION

A. Background and Qualifications

2. As further detailed in my CV, attached as Exhibit A, I received a bachelor’s degree from Harvard University (Cambridge, MA) in 1976 *summa cum laude* in Biochemical Sciences. My senior thesis involved a structural analysis of the aqueous central cavity (containing the active site) of the enzyme Aspartate Transcarbamylase (ATCase) of *Escherichia coli*. The research for this thesis was performed in the Department of Chemistry under the direction of the late William N. Lipscomb, Ph.D. (Nobel Laureate, 1976).

3. In September 1976, I started medical and Ph.D. graduate studies in the Harvard-M.I.T. Program in Health Sciences and Technology (HST Program) at

Harvard Medical School (Boston, MA) and Massachusetts Institute of Technology (M.I.T., Cambridge MA). I took medical school courses at Harvard Medical School and at M.I.T. and graduate courses in Biology at M.I.T. From July 1978 through December 1981, I performed Ph.D. dissertation research in the laboratory of Nobel Laureate (1975) David Baltimore, Ph.D., in the Department of Biology at M.I.T. This research focused on the mechanism of replication of poliovirus, using protein and RNA nucleic acid biochemistry techniques. I received my Ph.D. from M.I.T. in March, 1982.

4. From January 1982 through December 1982, I returned to Harvard Medical School to complete the clinical clerkship requirements for my M.D. degree, which was awarded in June 1983.

5. From January 1983 through June 1983, I returned to David Baltimore's laboratory at M.I.T. and carried out recombinant DNA studies of Abelson murine leukemia virus.

6. From July 1983 through June 1984, I completed an internship in Internal Medicine at Massachusetts General Hospital. I subsequently became licensed in medicine and surgery (Diplomate, National Board of Medical Examiners) in the Commonwealth of Massachusetts.

7. From August 1984 through March 1989, I was a postdoctoral fellow in the laboratory of Tom Maniatis, Ph.D., in the Department of Biochemistry and

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.