

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

GENEOSCOPY, INC.,
Petitioner,

v.

EXACT SCIENCES CORPORATION,
Patent Owner.

Case No.: IPR2024-00459
U.S. Patent 11,634,781

DECLARATION OF DUNCAN WHITNEY, Ph.D.

TABLE OF CONTENTS

I. Introduction.....1

II. Qualifications and Experience.....2

III. The Person of Ordinary Skill in the Art5

IV. Technical Background.....6

 A. Diagnostic Analysis of Biological Samples..... 7

 1. Diagnostic Tests Based on Detection of Biomarkers, such as Protein and DNA 9

 2. Sensitivity and Specificity as Measures of Diagnostic Performance 12

 3. Diagnostic Tests Commonly Measure Multiple Markers13

 4. Diagnostic Analyses Require Well-Preserved Samples 15

 B. Use of Fecal Diagnostic Tests to Diagnose Colorectal Cancer 23

 1. Fecal Occult Blood Tests 23

 2. Fecal DNA-Based Tests..... 27

 3. RNA Expression was also used to Diagnose Colorectal Cancer 32

 C. Biomarker Panels Empower Broader and Earlier Detection of Colorectal Cancer 33

 1. Panels of Different Fecal DNA biomarkers..... 33

 2. Panels Combining FOBT and DNA Biomarkers..... 34

 D. Home Collection of Fecal Samples 38

 1. Collecting and Partitioning Stool Samples 39

 2. Different Buffers were Used to Preserve Different Biomarkers in Fecal Samples..... 48

DECLARATION OF DUNCAN WHITNEY

3. Partitioning Samples into Multiple Vessels for Stabilization during Shipment..... 53

V. Legal Standards56

VI. The Challenged Patent.....59

 A. The '781 Patent 59

 B. Summary of the Claimed Subject Matter..... 64

VII. SUMMARY OF SELECTED PRIOR ART REFERENCES69

 A. Lenhard (EX1004)..... 69

 B. Vilkin (EX1005)..... 74

 C. Itzkowitz (EX1006)..... 79

 D. Kanaoka (EX1007)..... 84

 E. Derks (EX1008) 86

 F. Shuber (EX1009)..... 88

VIII. OVERVIEW OF GROUNDS OF UNPATENTABILITY91

IX. THE CLAIMS OF THE '781 PATENT ARE OBVIOUS.....92

 A. Lenhard in view of Itzkowitz and Vilkin renders claims 1-9, 11, and 14-20 obvious 92

 1. A POSA would be motivated to use the iFOBT of Vilkin in place of the gFOBT of Lenhard..... 94

 2. A POSA would have been motivated to use the sample collection methodology of Itzkowitz in Lenhard's process 98

 3. A POSA would have been motivated to use the DNA stabilizing buffer of Itzkowitz in Lenhard's process ... 100

 4. Claim 1 104

..

DECLARATION OF DUNCAN WHITNEY

- 5. Claim 2: “The method of claim 1, further comprising delivering the sealable container containing the removed portion of the fecal sample and said buffer and the sealable collection vessel containing the remaining portion of the fecal sample and said stabilizing buffer to a medical diagnostics laboratory” 115
- 6. Claim 3 116
- 7. Claim 4: “The method of claim 3, wherein testing the nucleic acid comprises determining expression from a human gene.” 121
- 8. Claim 5: “The method of claim 4, wherein determining expression from the human gene comprises testing the nucleic acid for the presence of human DNA having an epigenetic modification.” 123
- 9. Claim 6: “The method of claim 5, wherein testing the nucleic acid for the presence of human DNA having an epigenetic modification comprises measuring an amount of a methylated human DNA.” 124
- 10. Claim 7: “The method of claim 5, wherein the epigenetic modification comprises aberrant methylation.” 125
- 11. Claim 8: “The method of claim 7, wherein the aberrant methylation comprises hypermethylation” 126
- 12. Claim 9: “The method of claim 7, wherein the human DNA having an epigenetic modification comprises a gene and/or a promoter region of a gene.” 126
- 13. Claim 11: “The method of claim 5, wherein testing the nucleic acid for presence of human DNA having an epigenetic modification comprises modifying the nucleic acid with bisulfate ions under conditions wherein unmethylated cytosine is converted to uracil..... 127
- 14. Claim 14: “The method of claim 3, wherein testing for an amount of blood protein in the removed portion comprises testing for a concentration of hemoglobin in the removed portion.” 128

...

DECLARATION OF DUNCAN WHITNEY

15. Claim 15: “The method of claim 14, wherein the testing for the concentration of hemoglobin comprises immunochemical detection of hemoglobin.” 129

16. Claims 16-20: “The method of claim 14, wherein the removed portion of the fecal sample is considered positive for the presence of blood when the concentration of hemoglobin detected in the removed portion is at least [5, 10, 20, 50, or 200] ng/ml.” 129

B. Lenhard in view of Itzkowitz and Vilkin, in further view of Kanaoka renders obvious claims 12 and 13 132

1. Claim 12: “The method of claim 4, wherein determining expression from the human gene comprises measuring an amount of RNA expressed from the gene.” 132

2. Claim 13: “The method of claim 12, wherein measuring an amount of RNA expressed from the gene comprises reverse transcriptase polymerase chain reaction (RT-PCR) 135

C. Lenhard in view of Itzkowitz and Vilkin, in further view of Derks renders obvious claim 10..... 136

D. Shuber and Vilkin render obvious claims 1-9, 11, and 14-20 137

1. Claim 1 143

2. Claim 2: “The method of claim 1, further comprising delivering the sealable container containing the removed portion of the fecal sample and said buffer and the sealable collection vessel containing the remaining portion of the fecal sample and said stabilizing buffer to a medical diagnostics laboratory” 150

3. Claim 3 152

4. Claim 4: “The method of claim 3, wherein testing the nucleic acid comprises determining expression from a human gene.” 155

5. Claim 5: “The method of claim 4, wherein determining expression from the human gene comprises testing the

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.