

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CYTEK BIOSCIENCES, INC.,
Petitioner,

v.

BECKMAN COULTER, INC.,
Patent Owner.

U.S. Patent No. 11,703,443
Case No. IPR2025-01319

PATENT OWNER'S PRELIMINARY RESPONSE

TABLE OF CONTENTS

I.	INTRODUCTION	1
II.	TECHNOLOGY BACKGROUND.....	3
A.	Basics of Flow Cytometers	3
1.	Scattered Light Detection	3
2.	Fluorescence Detection	5
B.	Basics of Optical Communications Detection	7
C.	Flow Cytometry Fluorescence Detection and Optical Communications Signal Detection Have Multiple Key Differences	7
1.	Different Optical Fibers	8
2.	Different Detectors.....	9
III.	LEVEL OF ORDINARY SKILL IN THE ART	12
IV.	CLAIM CONSTRUCTION	12
V.	OVERVIEW OF THE ASSERTED REFERENCES	13
A.	Goodman—Optical Communications.....	13
B.	Oostman—Flow Cytometry	15
VI.	OVERVIEW OF U.S. PATENT NO. 11,703,443.....	18
VII.	RELEVANT PROSECUTION HISTORY	20
VIII.	THE PTO HAS ALREADY REJECTED PETITIONER’S REQUEST FOR REEXAMINATION OF PATENT CLAIMS IN THE SAME FAMILY BASED ON OOSTMAN AND GOODMAN	23
IX.	INSTITUTION SHOULD BE DENIED BECAUSE PETITIONER HAS FAILED TO DEMONSTRATE A REASONABLE LIKELIHOOD THAT THE CHALLENGED CLAIMS ARE OBVIOUS OVER OOSTMAN AND GOODMAN	24
A.	Limitations 1[pre] and 18[pre]/[d]: Petitioner Fails to Demonstrate that Oostman and Goodman Disclose “a Wavelength Division Multiplexer (WDM) For a Flow Cytometer”/ “a Flow Cytometer Comprising ... One or More Wavelength Division Multiplexers (WDMs)”	24

1.	A POSA Would Not Have Looked to a Reference from Optical Communications to Solve Problems in Flow Cytometry.....	26
2.	Petitioner Fails to Show that Goodman Is Analogous Art to the Claimed Inventions	34
3.	Oostman’s Purported Shortcomings Are Key Features of Its Patentable Disclosure and Would Not Be Improved By Goodman	35
4.	Petitioner Fails to Explain How Goodman Would Improve Oostman Specifically	47
B.	Limitations 1[d] and 18[d][iii]: Petitioner Fails to Demonstrate that Oostman and Goodman Disclose “a Set of Detectors”	49
C.	Petitioner Fails to Demonstrate a Reasonable Expectation of Success	51
X.	CONCLUSION.....	55

TABLE OF EXHIBITS

Exhibit	Description
EX2001	About Beckman Coulter (https://www.beckmancoulter.com/about-beckman-coulter/history-and-innovation)
EX2002	CytoFLEX Flow Cytometer (https://www.beckman.com/flow-cytometry/research-flow-cytometers/cytoflex)
EX2003	Beckman Coulter Patents (https://www.beckman.com/patents)
EX2004	Cytek Form S-1 Registration Statement (2021)
EX2005	Information Disclosure Statement for Application No. 15/817,237 to U.S. Patent No. 10,436,697 (May 7, 2019)
EX2006	Information Disclosure Statement for Application No. 15/942,430 to U.S. Patent No. 11,333,597 (June 17, 2021)
EX2007	Defendant Cytek Biosciences, Inc.'s Answer to the Complaint and Counterclaims, <i>Beckman Coulter, Inc. v. Cytek Biosciences, Inc.</i> , C.A. No. 24-945, D.I. 16 (D. Del. Oct. 7, 2024)
EX2008	Transcript of Scheduling Conference, <i>Beckman Coulter, Inc. v. Cytek Biosciences, Inc.</i> , C.A. No. 24-945, D.I. 23 (D. Del. Nov. 12, 2024)
EX2009	Defendant Cytek Biosciences, Inc.'s Revised Invalidity Contentions, <i>Beckman Coulter, Inc. v. Cytek Biosciences, Inc.</i> , C.A. No. 24-945 (D. Del. July 11, 2025)
EX2010	Defendant's Opening Brief in Support of Its Motion to Stay Pending <i>Inter Partes</i> Review and Post Grant Review of the Asserted Patent

	Claims, <i>Beckman Coulter, Inc. v. Cytek Biosciences, Inc.</i> , C.A. No. 24-945, D.I. 107 (D. Del. July 22, 2025)
EX2011	Order, <i>Beckman Coulter, Inc. v. Cytek Biosciences, Inc.</i> , C.A. No. 24-945, D.I. 124 (D. Del. July 30, 2025)
EX2012	Transcript of <i>Markman</i> Hearing of August 21, 2025, <i>Beckman Coulter, Inc. v. Cytek Biosciences, Inc.</i> , C.A. No. 24-945, D.I. 151 (D. Del. Aug. 21, 2025)
EX2013	Transcript of <i>Markman</i> Hearing of September 17, 2025, <i>Beckman Coulter, Inc. v. Cytek Biosciences, Inc.</i> , C.A. No. 24-945, D.I. 173 (D. Del. Sept. 17, 2025)
EX2014	U.S. Patent Pub. No. 2004/0165828 (“Capewell”)
EX2015	File History for U.S. Patent No. 9,746,412
EX2016	File History for U.S. Patent No. 10,330,582
EX2017	DocketNavigator, Time-to-Trial Statistics for District of Delaware (Sept. 2025)
EX2018	EP2861956B1
EX2019	EP3206010B1
EX2020	EP2861956 Search Opinion (Mar. 18, 2016)
EX2021	Assignment for U.S. Patent No. 8,922,778
EX2022	Assignment for U.S. Patent No. 8,605,283
EX2023	BD LSRFortessa Cell Analyzer User’s Guide

EX2024	Request for <i>Ex Parte</i> Reexamination of U.S. Patent No. 10,330,582 B2 Under 35 U.S.C. §§ 302-307 and 37 C.F.R. § 1.510 <i>et seq.</i>
EX2025	Petition for Post-Grant Review of US Patent No. 12,174,106, PGR2025-00084
EX2026	Petition for Post-Grant Review of US Patent No. 12,174,107, PGR2025-00088
EX2027	Amended Scheduling Order, <i>Beckman Coulter, Inc. v. Cytek Biosciences, Inc.</i> , C.A. No. 24-945, D.I. 178 (D. Del. Sept. 29, 2025)
EX2028	Declaration of David Schaafsma, Ph.D.
EX2029	Shapiro, Practical Flow Cytometry (2003), Chapter 7
EX2030	U.S. Patent No. 10,330,582
EX2031	Marcus Nebeling, CWDM: Lower Cost for More Capacity in the Short-Haul, Fiber Network Engineering (July 3, 2002)
EX2032	Telecommunication Standardization Sector of ITU, Recommendation G.694.2, Spectral Grids for WDM Applications: CWDM Wavelength Grid (Dec. 2003)
EX2033	Telecommunication Standardization Sector of ITU, Recommendation G.694.1, Spectral Grids for WDM Applications: DWDM Frequency Grid (Dec. 2003)
EX2034	Order Denying Request for <i>Ex Parte</i> Reexamination, Application/Control Number: 90/015,441 (Oct. 6, 2025)
EX2035	M. Arumugam, <i>Optical Fiber Communication—An Overview</i> , 57 Pramana J. Physics 849 (2001)

EX2036	B.E.A. Saleh and M.C. Teich, <i>Fundamentals of Photonics</i> , 2d. Ed. 2007, Chapters 1, 24 (“Saleh”)
EX2037	Warren J. Smith, <i>Modern Optical Engineering</i> (3d ed. 2000, Chapter 9 (“Smith”)
EX2038	W.T. Welford, <i>Optics</i> (3d ed. 1990), Chapter 8 (“Welford”)
EX2039	Mohammad Azadeh, <i>Fiber Optics Engineering</i> (2009), Chapters 1, 2, 6 (“Azadeh”)

I. Introduction

U.S. Patent No. 11,703,443 (the “’443 patent”) claims groundbreaking innovations in flow cytometers. Beckman Coulter, Inc. (“Patent Owner”) utilizes the innovations claimed in the ’443 patent in its CytoFLEX Flow Cytometers and Sorters. EX2003. Before the family that led to the ’443 patent was filed, no one in the field of flow cytometry recognized how a wavelength division multiplexer (WDM), as claimed in the ’443 patent, could be used to improve light detection in a flow cytometer.

Cytek Biosciences, Inc. (“Petitioner” or “Cyttek”), challenges the ’443 patent’s inventions based on a single Ground that proposes taking a component of an optical communications system and inserting it into a flow cytometry system. Specifically, Petitioner proposes removing the detector clusters in Oostman (a flow cytometry system) and replacing them, without modification, with Goodman’s demultiplexer device (an optical communications system). But the only evidence Petitioner submits that suggests adapting optical communications technology into a flow cytometer, apart from its expert’s conclusory assertion, is the *’443 patent itself*. Petitioner’s Goodman reference views comparable technologies as spacecrafts and cable television systems, not flow cytometry. And the only flow cytometry reference Petitioner identifies as even mentioning optical communications technology

(Frazier, not part of Petitioner's only Ground) viewed the technology as suboptimal for flow cytometry.

Petitioner's motivation to combine and reasonable expectation of success analysis is limited to just a handful of pages and does not engage with any limitations of the independent claims. Rather than offering detailed evidence, Petitioner relies solely on its expert's conclusory assertions that a person of ordinary skill in the art (POSA) would spot flaws in Oostman's disclosure and would look to entirely replace its detection modules with a subsystem used in optical communications, supposedly leading to the inventions claimed in the '443 patent. But Petitioner fails to provide any explanation of why, during the decade between the publication of its two primary references and the '443 patent's priority date, no one actually combined the references in this way. That is because the purported deficiencies in Oostman were all in fact *benefits* over prior art flow cytometers, and so a POSA would not have understood that Petitioner's proposed combination would have resulted in an improved system. Petitioner's conclusory statements fall far short of a rational underpinning of why a POSA would have been motivated to combine the references. Because Petitioner's obviousness analysis is deficient at every level, it cannot justify institution of *inter partes* review on any claim.

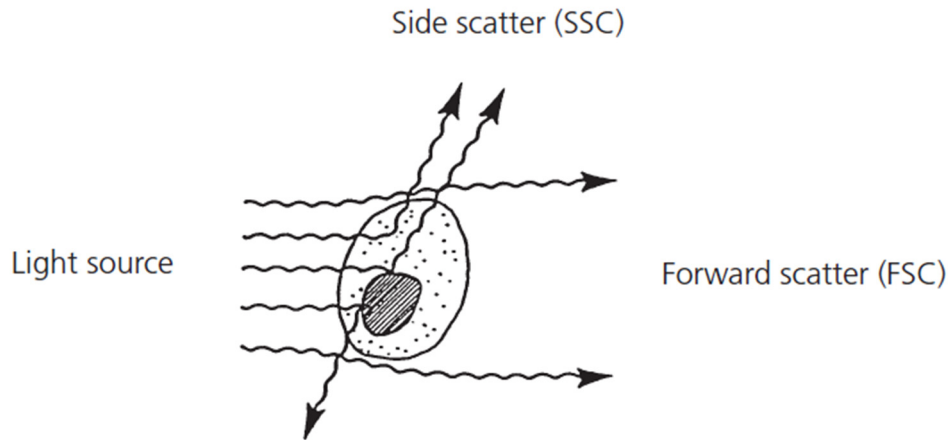
II. Technology Background

A. Basics of Flow Cytometers

In a flow cytometer, cells move in single file through a flow channel where they are illuminated by light, typically from a laser. EX1004 at 10, 17. When the light interacts with the cell, the light will scatter in multiple directions. *Id.* at 19-20; EX2023 at 100-01. Flow cytometers collect and analyze this light to measure multiple parameters of the cells. EX1001, 1:49-55. Flow cytometers perform this analysis on thousands of cells per second. *Id.* Flow cytometry has numerous uses in research and medicine, including cell sorting, rare cell detection, and diagnostics. *Id.*; EX1004 at 10; EX2028, ¶22.

1. Scattered Light Detection

Flow cytometers typically measure light scattered from the cells in two directions: forward (along the direction of the laser beam) and around 90 degrees to the side (side scatter), shown below.



EX2023 at 100. Light scattered in the forward direction provides information on how large the cell is: larger cells produce wider scattering. EX2028, ¶23. Light scattered in the forward direction is typically stronger in signal than side scattered light and can be detected by a forward scatter detector, or FSC. EX2023 at 100; EX2028, ¶23.

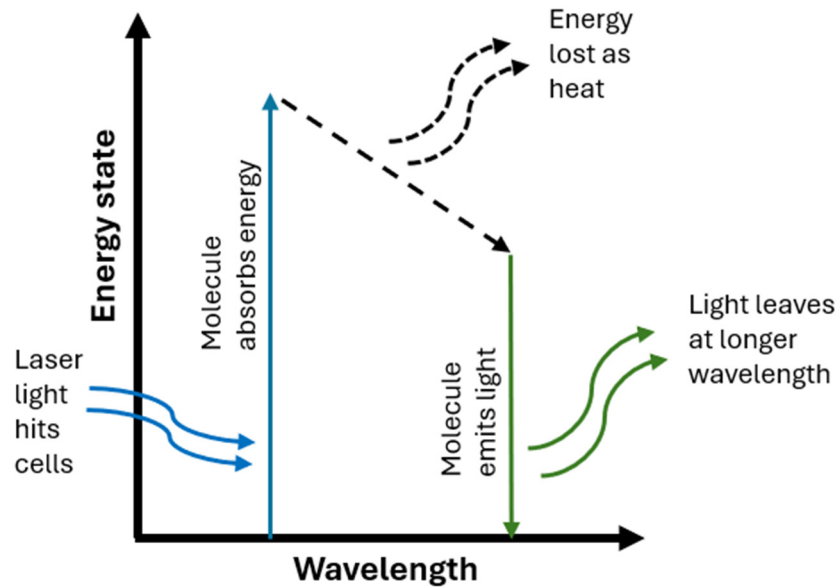
Light scattered in the side direction is used to measure and identify cells by their shape and internal structure and is both weaker and physically more spread out in all directions than forward scattered light. *See* EX2023 at 100; EX2028, ¶24. To capture as much of this scattered light as possible, flow cytometers use optical components having large openings to collect light (termed “apertures”). EX1004 at 19-20. These types of optical components produce a light beam with a wide diameter and high divergence. The combination of the aperture size and divergence angles is often referred to as “étendue,” and flow cytometer optical systems typically require

the étendue to be large to collect scattered light. EX1001, 44:54-67; *see also* EX2028, ¶24. Side scattered light typically significantly has a significantly lower signal than forward scattered light, and fluorescent light has even lower signal. *See* EX1004 at 23-24; EX2028, ¶25.

2. Fluorescence Detection

In addition to forward and side scattering measurements, some flow cytometers also use fluorescent light to detect additional properties of the cells. EX1004 at 10; EX1007 at 33; EX2028, ¶26.

When using fluorescence in flow cytometry, cells are labeled with molecules called fluorophores, which are typically attached to antibodies specific for certain cell surface proteins. EX1004 at 10; EX1007 at 33. Atoms or molecules in these fluorophores absorb light at specific wavelengths, at which point they become “excited” and momentarily move to a higher energy level. EX2028, ¶27. When these atoms or molecules fall back to their original state, they can emit light of a lower energy (i.e., longer wavelength) than the light they initially absorbed. *Id.*



EX2028, ¶27 (adapted from EX1007 at 103). This emitted light, which varies in wavelength¹ depending on the fluorophore, is then analyzed by the flow cytometer using detectors. EX2028, ¶27.

Since fluorescent light is collected from individual cells as part of the side scattered light and is thus similarly weak and diffuse, prior to the '443 patent, PMTs had been the detector typically used for fluorescent light detection in flow cytometers. EX1004 at 23-24; EX1007 at 154; EX2028, ¶¶28-31.

¹ Fluorophores used in flow cytometry emit various wavelengths across the visible spectrum. EX1007, 68; EX1001, 57:28-30; EX2028, ¶27 n.1.

B. Basics of Optical Communications Detection

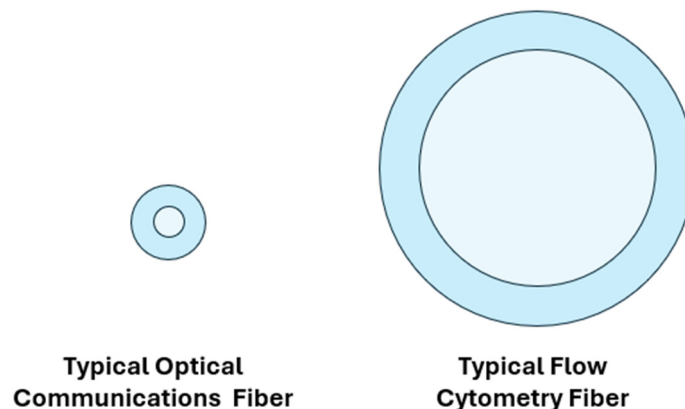
Optical communications refers to the transmission of information—such as with internet traffic and voice or video communication—through optical fibers using light as the carrier signal. EX2036 at 1073. Telecommunications systems increase data transmission capacity by encoding different signals in different wavelengths of light. EX2036 at 1104-05; EX2039 at 50-51. This involves combining (or multiplexing) light from multiple lasers at various wavelengths into one narrow light beam at the signal source and transmitting the combined/multiplexed light signals through an optical fiber. EX2036 at 1104-05. At the destination, a device then separates out (or demultiplexes) the light signals from those lasers according to wavelength. *Id.*; EX2028, ¶32.

C. Flow Cytometry Fluorescence Detection and Optical Communications Signal Detection Have Multiple Key Differences

In optical communications, light in a small range of wavelengths is transmitted directly from a laser into a fiber. *See* EX2035 at 850, 861. But in flow cytometry fluorescence detection, as discussed above in Section II.A, the collected light is scattered from cells, resulting in a wide cone of weak light (i.e., high étendue). Prior to the '443 patent, it was understood that these fundamental differences result in many design differences between flow cytometers and optical communications systems. EX2028, ¶33.

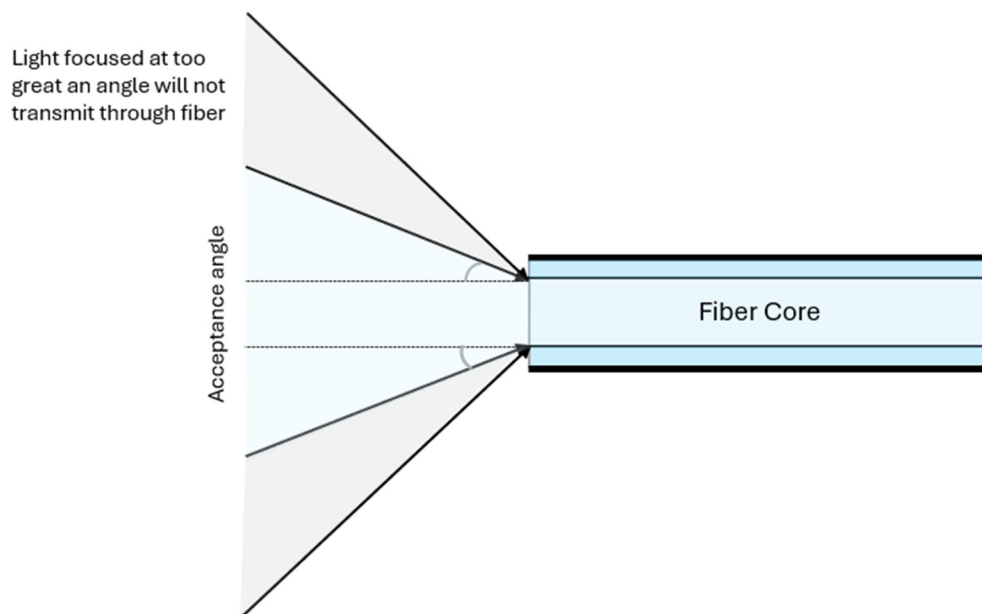
1. Different Optical Fibers

Flow cytometers typically use optical fibers with much greater core diameters than the fibers used in optical communications systems. *See, e.g., See* EX1007 at 148-49; EX2036 at 1076. Optical communications systems use fibers with core diameters ranging from less than 10 microns to around 50 or 62.5 microns. EX2035 at 851-53; EX2036 at 1076. In contrast, in order to collect the wide cone of light scattered from cells, flow cytometers typically use optical fibers with large numerical apertures having core diameters at least ***ten times larger*** than those in optical communications. *See* EX1007 at 148-49 (discussing how “[l]ight collection is limited by the N.A. of the fiber or waveguide” and discussing numerical apertures above 0.4).



EX2028, ¶34.

Fibers from optical communications were not treated as interchangeable with fibers in flow cytometry. EX2028, ¶¶35-36. For example, if light collected in flow cytometry was used with a typical optical communications fiber, the light beam would either (1) be too wide to enter the narrow fiber opening, or (2) have to be focused at such extreme angles that the light would be rejected from the fiber. *Id.* This latter limitation can be understood as an acceptance angle:

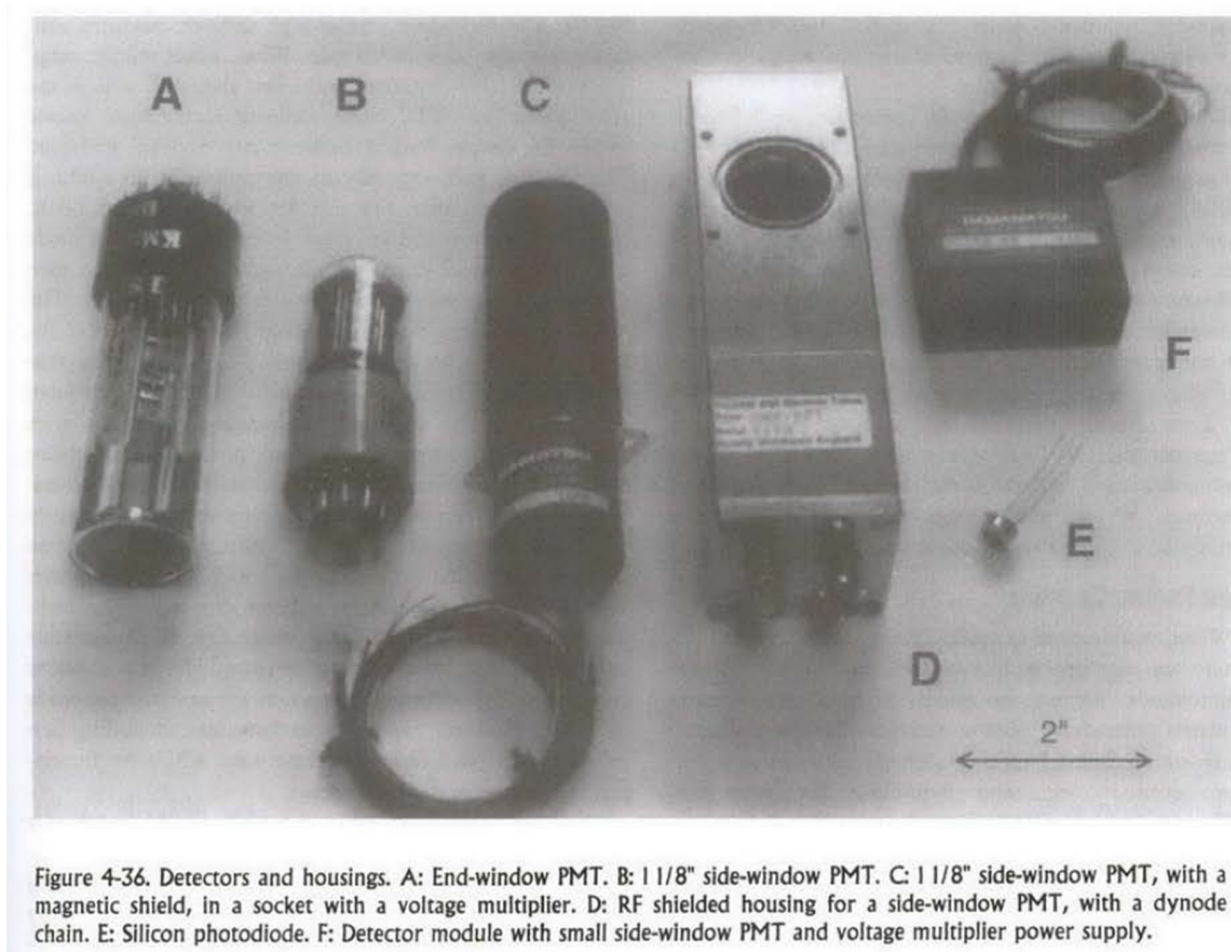


EX2028, ¶¶35-36 (adapted from EX2036 at 16); EX2037 at 282-83; EX2038 at 135-36.

2. Different Detectors

Optical communication devices “almost exclusively” use diodes, either photodiodes or avalanche photodiodes (APDs) depending on the application.

EX2039 at 173. Both photodiodes and APDs “provide very good responsivity in the wavelengths used in fiber optics.” EX2039 at 173; EX2028, ¶37. Before the inventions described in the '443 patent, flow cytometers historically used PMTs for fluorescence detection. If used in flow cytometers, photodiodes were primarily used for measuring the comparatively stronger forward scattered light. EX2028, ¶38.



EX1007 at 154 (showing relative sizes of PMTs (Figure 4-36 A-C) and photodiodes (Figure 4-36 E)); EX2028, ¶38.

Compared to signals in optical communications, the fluorescence intensity in flow cytometry can be over 1,000,000 times weaker.² PMTs are bulky, fragile, and expensive, but they can amplify signals from low light conditions with excellent noise characteristics while also being tolerant of wide, diffuse light beams with their large active areas. *See* EX1004 at 24 (“Photomultipliers are photosensitive electron tubes with a more restricted spectral response [than diodes], but with high gain and good signal-to-noise characteristics suitable for the detection of weak

² Optical communications networks measure signal in decibel-milliwatts, a logarithmic scale proportional to milliwatts. EX2039 at 23-24. Optical communications signals typically range in milliwatts or microwatts. *Id.* Dr. Schaafsma explains how this correlates to *trillions* of photons per second or more. EX2028, ¶39. In contrast, in flow cytometry fluorescent light detection, only “*hundreds* of photons are likely to be emitted from each fluorescent molecule in or on a cell during the cell’s traverse of an illuminating beam at a wavelength at or near the molecule’s excitation maximum.” EX2029 at 283 (all emphasis added unless otherwise stated). Indeed, “even the most efficient fluorescence collection optics collect no more than about 20% of the total emission from cells,” meaning many such photons will not even reach the detector. *Id.*; EX2028, ¶39.

fluorescence.”); EX1007 at 152-153. In contrast to PMTs, an APD with equivalent size active area would produce a high amount of background noise. *See* EX1001, 43:57-62. Thus, before the inventions of the ’443 patent, the large diverging beam (i.e., high étendue) prevented the use of APDs and other small area detectors in flow cytometry. *See* EX1001, 44:24-30, 44:54-57. Prior art flow cytometers did not have mechanisms that enabled maintaining the beam diameter and focusing it down to sufficiently small spot sizes. *Id.*, 44:10-67. Thus, PMTs had been the detector of choice for fluorescence detection in flow cytometry for decades. *See id.*, 43:49-44:9; EX2028, ¶¶40-45.

III. Level of Ordinary Skill in the Art

For purposes of this POPR, Patent Owner does not currently dispute Petitioner’s proposed definition of a POSA. Pet. at 17-18; EX1002, ¶13. If a trial is instituted, Patent Owner reserves the right to submit a different definition than proposed by Petitioner. EX2028, ¶¶19-21.

IV. Claim Construction

In the time since the Petition was filed, the district court has held two claim construction hearings. EX2012; EX2013. The Court construed “first filter” and “second filter” in claim 9 of the ’443 patent “to require that the first filter occur sequentially before or temporally before the second filter.” EX2012 at 73:18-25.

The Court also construed “portion of the...” in claims 1 and 18 of the ’443 patent as “subset of the spectrum of the wavelength of the....” EX2013 at 92:21-24. The Court also construed “optical element configured to detect scattered light” in claims 13 as being means plus function and having the structure of either the forward or side scatter detectors 408 or 413 described in the ’443 patent. *Id.* at 180:16-18. The Court also held that “collimated beam” in claims 8 and 10 of the ’443 patent should be given its plain and ordinary meaning. EX2012 at 134:14-16, 193:5-7. The Court did not construe any other claim limitations, and no further claim limitations in the ’443 patent are before the Court at this time.

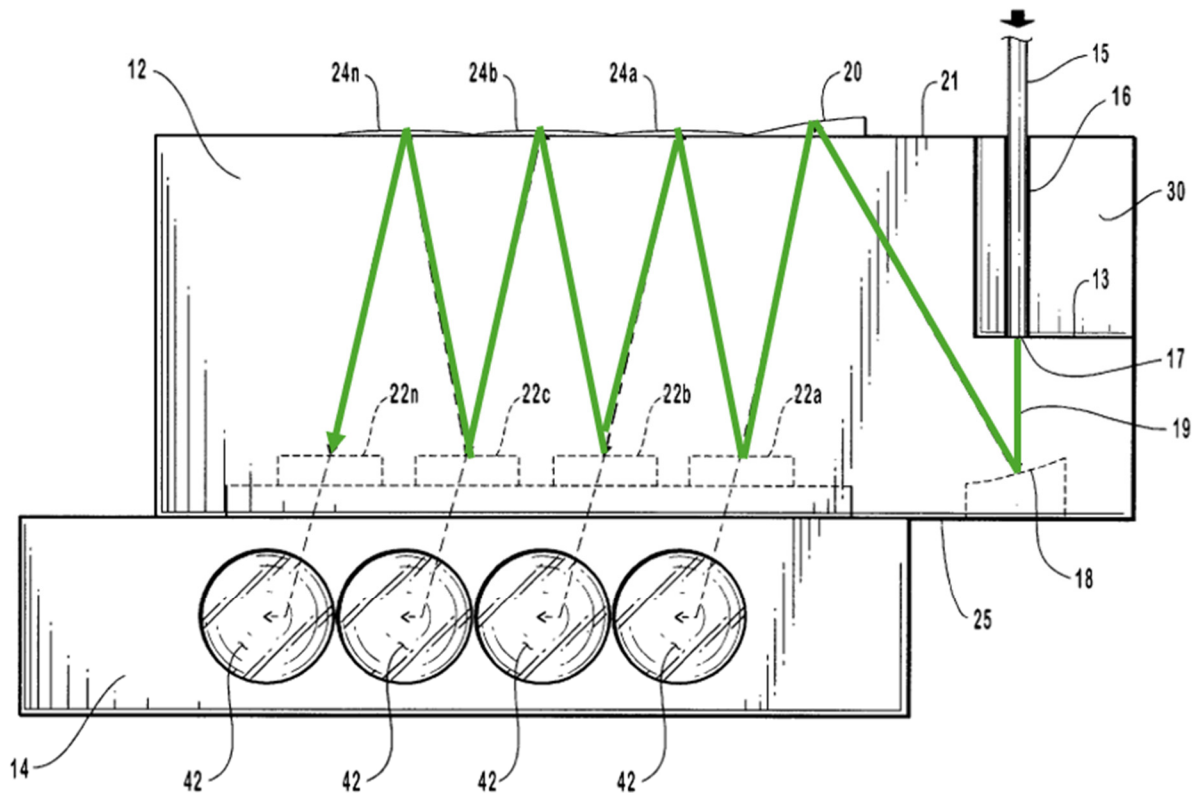
V. Overview of the Asserted References

A. Goodman—Optical Communications

U.S. Patent No. 6,542,306 (“Goodman”—EX1016) is a patent arising from an application filed on March 16, 2001. Goodman solely describes components for optical communications systems. EX1016 at 2:7-14, 3:47-50. It describes an alternative light detection system for optical communications, primarily for use in “wide wavelength division multiplexing (WWDM) systems.” EX1016 at 5:41-47. “WWDM” was not an industry-defined term by the time Goodman issued in 2004, but from the description in Goodman (wavelengths centered at 1310 nm and spaced

25 nm apart), its primary use case was for coarse wavelength division multiplexing (CWDM). EX1016 at 2:21-29, EX2032 at 3; EX2028, ¶48.

Goodman describes demultiplexing devices that are “low cost,” “easy to mold and fabricate accurately,” and that could be produced at scale and easily inserted into optical systems ranging from “spacecraft and aircraft applications to closed circuit and cable television systems.” EX1016 at 3:47-67, 6:62-64, 2:10-13. Goodman discloses a zig-zag configuration for the path of the light beam travelling through its device:



EX1016 at FIG. 1 (annotated); EX2028, ¶50. Light coming into Goodman’s demultiplexing device from optical fiber 15 contacts two mirrors 18 and 20 before being directed into a series of filters and reflectors. EX1016 at 7:17-8:27. Light passing through the filters goes through a beam-directing member, reflected at a 90-degree angle in a first-disclosed embodiment, and is then focused to detectors outside the demultiplexing device. EX1016 at 11:8-16; EX2028, ¶¶49-50.

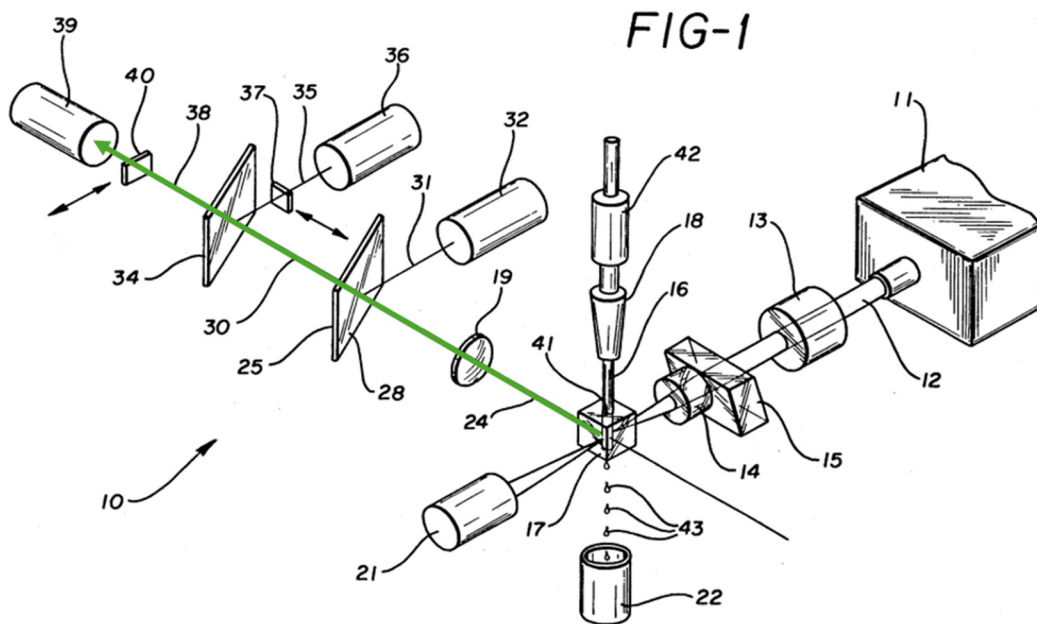
Goodman’s optical block and beam-directing member are both preferably “formed of a moldable thermoplastic material” so as to “facilitat[e] high volume production at low cost.” EX1016 at 6:60-64. As Goodman’s device is not designed to be customized or adjusted after its manufacture, its filters are “affixed therein such as by an optical adhesive.” EX1016 at 8:44-47; EX2028, ¶51.

B. Oostman—Flow Cytometry

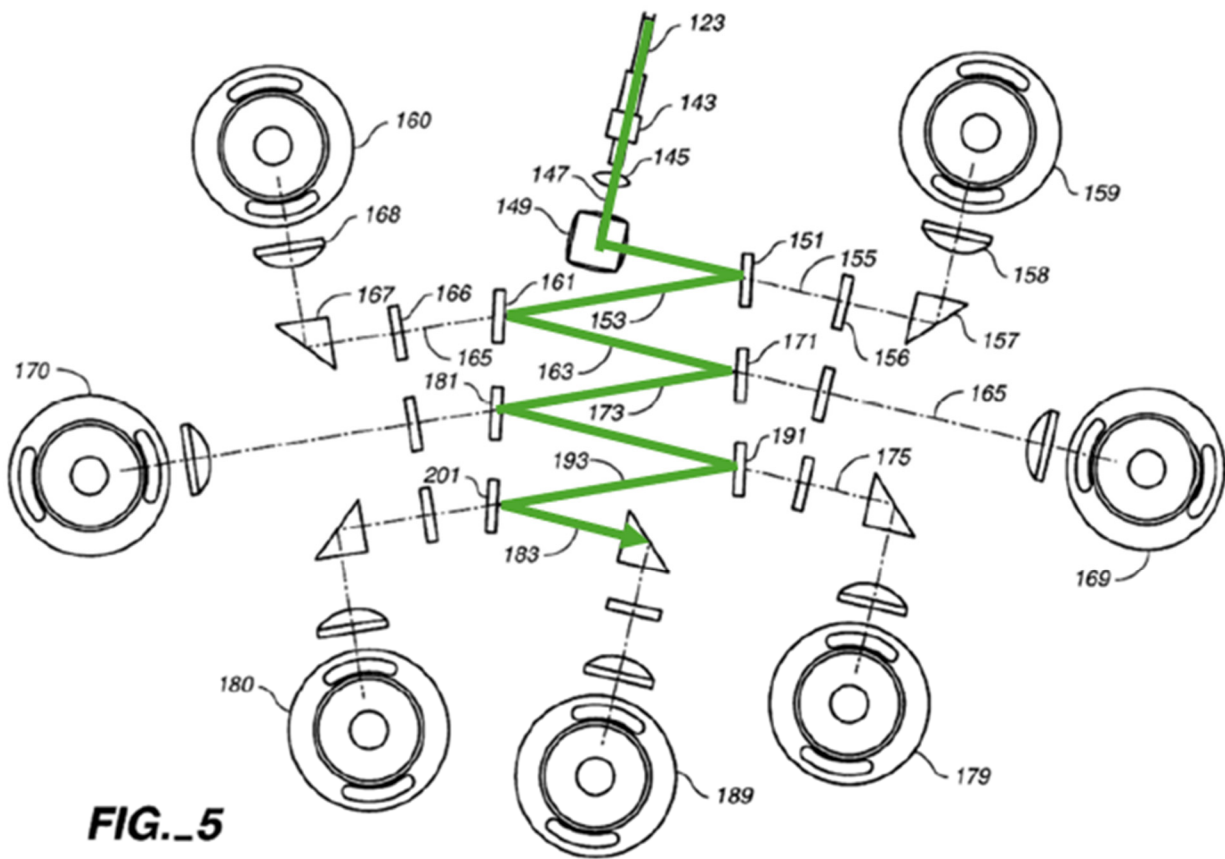
U.S. Patent No. 6,683,314 (“Oostman”—EX1005) is a patent arising from an application filed on August 28, 2001, and is directed to fluorescence detection instruments (e.g., in a flow cytometer) capable of separating more fluorescent colors over smaller areas than prior art flow cytometers. EX1005 at 4:10-13, 4:65-5:2; EX2028, ¶52.

Oostman discloses two primary improvements over prior art flow cytometers. EX1005 at 3:44-57, 4:14-16, 6:40-7:36, 8:18-9:3. The first improvement is

changing the path of the fluorescent light: in the prior art, light from a flow cytometer would go along one straight optical path, and planar beam splitters would reflect certain wavelengths of light to detectors. EX1005 at 1:54-2:16. The optical path of light in the prior art is annotated in green below:



EX1005 at FIG. 1 (annotated); EX2028, ¶53. Light passing through beam splitters has loss from absorption compared to light reflected, so the signal attenuates as it passes through each beam splitter. See EX1005 at 3:29-34, 4:16-24. Oostman flips this strategy, so that light transmitted through each beam splitter would go straight to a detector, and light would repeatedly be reflected across planar beam splitters in a zig-zag pattern:



EX1005 at FIG. 5 (annotated); *id.* at 3:44-57, 6:40-7:34; EX2028, ¶53.

Oostman's second improvement is developing an alternative optical path and PMT detector arrangement. FIG. 5 of Oostman depicts a zig-zag optical path, but use of PMTs means the overall detector cluster size is still large. *See* EX1005 at 7:34-36; EX2028, ¶54. Therefore, Oostman proposes an alternative "star-shaped pattern yielding a more compact polygonal arrangement of detectors." EX1005 at 7:34-36.

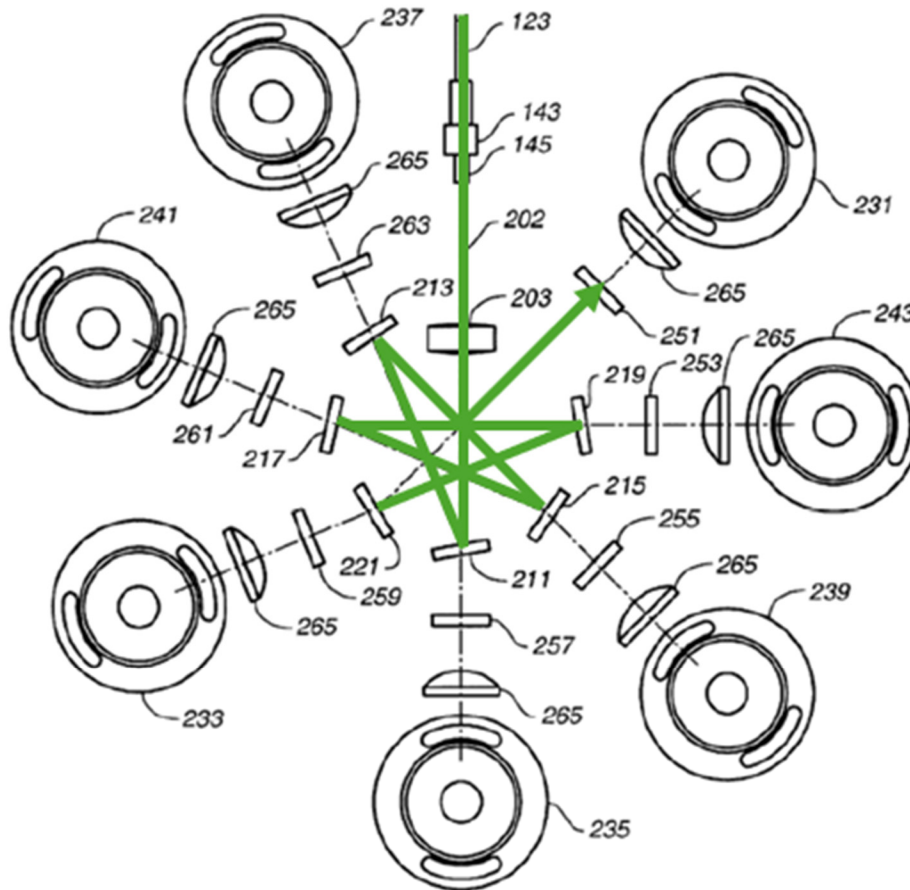


FIG. 6

EX1005 at FIG. 6 (annotated); EX2028, ¶54. Oostman emphasizes the ability to add more detector clusters in a modular fashion, remove and replace beam splitters depending on the application, and adjust the clusters to improve light detection for specific applications. EX1005 at 4:14-16, 8:18-9:3; EX2028, ¶54.

VI. Overview of U.S. Patent No. 11,703,443

The '443 patent is titled "Flow Cytometer" and was filed on November 4, 2022. EX1001, Cover. The '443 patent claims the benefit of applications filed on

or after May 2012. *Id.* The '443 patent names Yong Qin Chen as the sole inventor. *Id.*; EX2028, ¶55.

The '443 patent sought to enhance the performance of flow cytometers while making them more compact and easier to use. EX1001, 2:22-24. The '443 patent describes innovative, compact wavelength division multiplexers ("WDMs") that permit the use of low noise, millimeter-sized detectors not previously used in flow cytometry, resulting in improved sample analysis and a smaller instrument footprint. *Id.* at 2:39-44, 45:26-64; EX2028, ¶56.

Flow cytometer detection systems present different challenges from light detection in other fields. For example, unlike in optical communications, flow cytometers must detect light with a wide range of wavelengths of unknown and uncontrolled signal strength. *See* EX1016 at 2:20-64; EX1007 at 67, 151. Furthermore, in flow cytometry, light typically enters a detection system from a large optical fiber which produces a much larger light beam than the laser beam detected in optical communications. EX1001, 44:47-67. This presents challenges in controlling the light beam over an extended distance and focusing the beam onto the detectors, as needed for effective detection. *Id.* at 44:24-44. The '443 patent recognized and overcame these challenges with its innovative WDM designs. EX2028, ¶57.

VII. Relevant Prosecution History

The '443 patent issued on July 18, 2023 as a continuation in a family of patents that has undergone extensive and thorough prosecution including multiple prior-art based rejections by multiple examiners, including a Supervisory Patent Examiner. EX2028, ¶58.

During prosecution of a grandparent to the '443 patent—U.S. Patent Application No. 14/555,102, which was filed November 26, 2014 and issued as U.S. Patent No. 9,746,412—the Examiner rejected the claims as obvious over the published application for Oostman, and U.S. Patent Pub. No. 2004/0165828 (“Capewell”) (EX2014), a reference from the optical communications field. EX2015 at 1070-1071. Initially, the Examiner combined Oostman’s flow cytometer with “the WDM of Capewell,” an optical communications device, alleging that the references were “[i]n a similar field of endeavor.” *Id.* Applicant made no amendments in response, explaining that “the fluorescence detection instrument, as taught by *Oostman*, and the optical communication system, as taught by *Capewell*, are actually different kinds of optical systems with different sizes of light sources,” and therefore obviousness had not been established. *Id.* at 1107-1109. The Examiner “fully considered” Applicant’s arguments and found them “persuasive.” *Id.* at 1132. During prosecution of U.S. Patent No. 10,330,582 (the “’582 patent”), another patent

in the '443 patent family, in an Office Action dated July 30, 2017, the Examiner also rejected the claims based on Oostman. EX2016 at 537-542. Applicant again overcame this rejection. *Id.* at 599. EX2028, ¶¶59-60.

Following the extensive prosecution in the earlier family members of the '443 patent, the '443 patent was filed on November 4, 2022. EX1003 at 2. On March 7, 2023, the Examiner signed an Information Disclosure Statement verifying that they considered both Oostman and Goodman:

No.	Pub. No.	Pub. Date	Disclosure
A72	6,542,306	4/1/2003	Goodman
A73	6,572,255	6/3/2003	Husher
A74	6,808,682	8/19/2003	Ortyn et al.
A75	6,618,143	9/9/2003	Roche et al.
A76	6,638,481	10/28/2003	Sklar et al.
A77	6,647,175	11/11/2003	LoRegio et al.
A78	6,683,314	1/27/2004	Oostman Jr. et al.
A79	6,713,019	3/30/2004	Ozasa et al.
A80	6,748,133	6/8/2004	Liu et al.
A81	6,767,188	7/27/2004	Vrane et al.
A82	6,768,593	7/27/2004	Jutamulla
A83	6,788,409	9/7/2004	Goodwin
A84	6,794,671	9/21/2004	Nicoli et al.

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EXAMINER: /MEENAKSHI S SAHU/	DATE CONSIDERED: 03/07/2023
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EXAMINER: INITIAL IF REFERENCE CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP 609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED. INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.

INFORMATION DISCLOSURE STATEMENT — PTO-1449 (MODIFIED)

EX1003 at 225 (annotated); EX2028, ¶61.

On March 14, 2023, the Examiner had an interview with the Applicant's attorney, who authorized an Examiner amendment to limit the claims to be "for a flow cytometer." EX1003 at 242. On March 27, 2023, the Examiner and

Supervisory Patent Examiner entered the Examiner's amendment and allowed the '443 patent claims. EX1003 at 241-43. EX2028, ¶62.

The Notice of Allowability explained:

[The] prior art fail to disclose or suggest:

Claim 1: A wavelength division multiplexer (WDM) *for a flow cytometer* comprising:

receive one or more portions of the light from the set of filters; and reflect the one or more portions of the light to the set of filters; and a set of detectors, each detector of the set of detectors corresponding to a filter of the set of filters and configured to receive a portion of the light at the detector that passed through the filter corresponding to the detector.

Claim 18: A flow cytometer comprising:

at least one mirror including at least one curved mirror, the at least one mirror configured to: receive one or more portions of the light from the set of filters; and reflect the one or more portions of the light to the set of filters; and a set of detectors, each detector of the set of detectors corresponding to a filter of the set of filters and configured to receive a portion of the light at the detector that passed through the filter corresponding to the detector and one or more optical fibers, each optical fiber configured to receive light from the optical element provide the light to a WDM of the one or more WDMs.

EX1003 at 242-243 (emphasis in original); EX2028, ¶63.

The Notice of Allowability stated that the '443 patent provides for “the ability to multiplex, or detect and identify multiple biomarkers simultaneously” which “allows for high sensitivity and specificity.” EX1003 at 243. And, “[s]ince in

WDM[s,] all spectral channels are routed through the same physical space, this allows for increasing the compactness of the device.” *Id.* EX2028, ¶64.

The Notice of Allowability further noted that U.S. Patent No. 11,333,597 to Yan et al. “discloses a compact multi-color flow cytometer with a compact detection module but claims priority of provisional application 62/366580 filed 7/25/16” but was later than the ’443 patent’s PCT filing date of May 30, 2013. EX1003 at 243. Accordingly, the ’443 patent issued on July 18, 2023. *Id.* at 255; EX2028, ¶65.

VIII. The PTO Has Already Rejected Petitioner’s Request for Reexamination of Patent Claims in the Same Family Based on Oostman and Goodman

On October 6, 2025, the PTO issued an order denying Petitioner’s request for *ex parte* reexamination of claims of the ’582 patent. EX2034. The ’582 patent is in the same family as the ’443 patent, claims priority to the same applications and shares the same specification, and is also being asserted against Petitioner in the parallel district court litigation. *See* Paper 7 at 3-4. Like all of the challenged claims of the ’443 patent, the ’582 patent claims require a “curved mirror.” EX2030, cls. 1, 14. The PTO rejected multiple proposed substantial new questions of patentability (SNQs) based on Oostman and/or Goodman. EX2034 at 11-15. Specifically, four of Petitioner’s five proposed SNQs were obviousness combinations utilizing Goodman, and two of those utilized both Goodman and Oostman (as well as Frazier (EX1009) and one additional reference). *Id.* at 6. The PTO found that Goodman’s

failure to disclose a “curved mirror” was fatal to all of Petitioner’s claims of obviousness. *Id.* at 11-15. The PTO has thus already denied Petitioner’s validity challenges involving the same claim limitations and the same references at issue here.

IX. Institution Should Be Denied Because Petitioner Has Failed to Demonstrate a Reasonable Likelihood that the Challenged Claims Are Obvious Over Oostman and Goodman

The Petition fails to establish a reasonable likelihood that the Petitioner will prevail on at least one of the challenged claims. *First*, Petitioner has failed to show that the references cited in the Petition disclose or render obvious a WDM for a flow cytometer as required by all claims. *Second*, Petitioner has failed to show that the references cited in the Petition disclose or render obvious a set of detectors for a flow cytometry WDM as required by all claims. *Third*, Petitioner fails to demonstrate a reasonable expectation of success in combining these disparate references. EX2028, ¶66.

A. Limitations 1[pre] and 18[pre]/[d]: Petitioner Fails to Demonstrate that Oostman and Goodman Disclose “a Wavelength Division Multiplexer (WDM) For a Flow Cytometer”/ “a Flow Cytometer Comprising ... One or More Wavelength Division Multiplexers (WDMs)”

All of the challenged claims require a “wavelength division multiplexer” for use in “a flow cytometer.” To argue this is disclosed in the cited prior art, Petitioner’s

combination proposes incorporating Goodman's demultiplexing device, without modification, into Oostman's flow cytometer. Pet. at 29. This combination ignores that a POSA would not have been motivated to replace the detection module of Oostman with Goodman's demultiplexing device because of the fundamental differences between detecting light for optical communications and detecting scattered fluorescent light in flow cytometry. *See infra* Section IX.A.1, IX.A.3, IX.A.4; EX2028, ¶¶70-89, 95-124. Petitioner also fails to recognize that a POSA would neither view Goodman as analogous art to the claimed inventions nor combine Goodman and Oostman. *See infra* Section IX.A.2; EX2028, ¶¶90-94. Petitioner's motivations for combining the prior art references are based on hindsight and ignore the disclosures of the references themselves. EX2028, ¶¶67-69.

Petitioner's combination thus fails to render obvious a WDM for a flow cytometer. EX2028, ¶¶67-124. Institution should therefore be denied. *See, e.g., Liberty Energy Inc. v. U.S. Well Services, LLC*, IPR2025-00066, Paper 10 at 19 (PTAB Apr. 29, 2025) (denying institution because Petitioner failed to establish why a POSA would have combined prior art references that use their components for "different types of devices" and "are designed for different purposes"); *R.J. Reynolds Vapor Co. v. Philip Morris Prods. S.A.*, IPR2021-00826, Paper 11 at 15 (PTAB Nov. 9, 2021) ("Petitioner's rationale for combining Alarcon and Rabin does

not account adequately for these fundamental differences between Alarcon's electronic cigarette and Rabin's capillary force vaporizer.”).

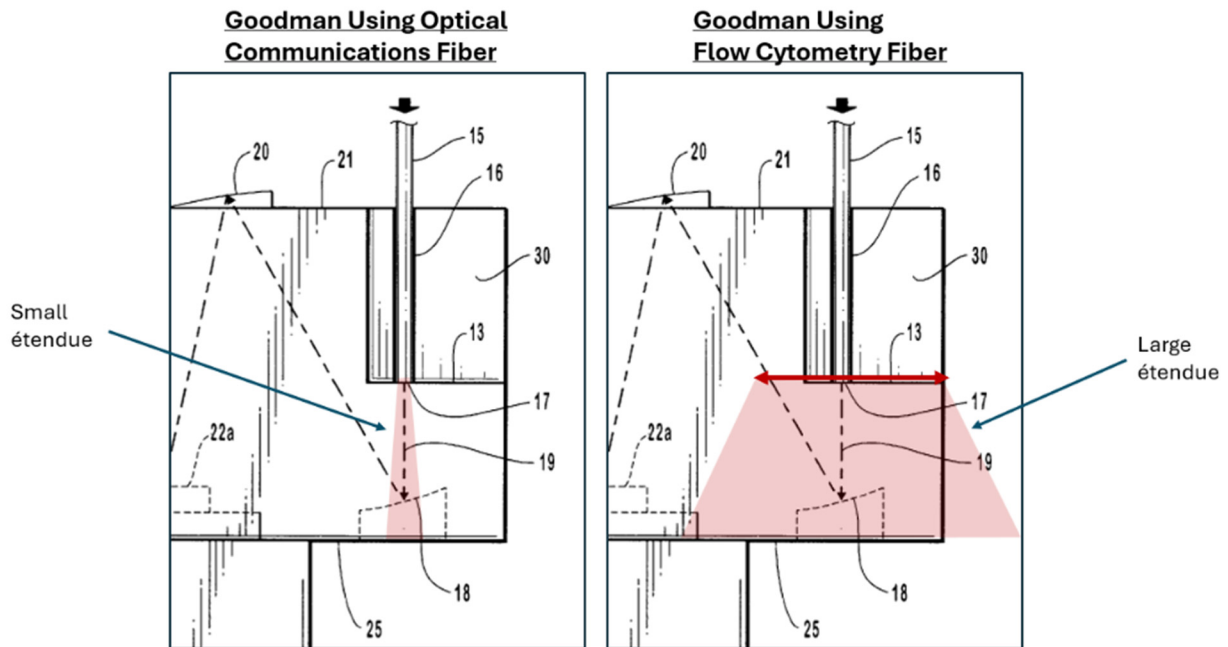
1. A POSA Would Not Have Looked to a Reference from Optical Communications to Solve Problems in Flow Cytometry

The fields of optical communications and flow cytometry faced entirely different problems. EX2028, ¶70. The light detection system built for Goodman was in a different type of device, it was designed for a different purpose, and it addressed different problems than the light detection system in Oostman. *Id.* Petitioner fails to account for these differences and explain why a POSA would have been motivated to combine these references to arrive at the claimed wavelength division multiplexer (WDM) for a flow cytometer. *Id.*

One fundamental difference between an optical communications system and a flow cytometer is how light propagates in the system. Optical communications systems, like Goodman, detect intense light at narrow infrared wavelength ranges with light beams having a small diameter. *See* EX1016 at 5:42-47, 2:20-29; EX2036 at 1080 (discussing how “narrow spectral widths” are “critical for the efficient operation of 1.3 and 1.55 μm wavelength-division-multiplexed (WDM) optical communications systems”). In contrast, flow cytometers as disclosed in Oostman needed to detect a wide range of wavelengths of unknown and uncontrolled signal

strength in the visible light spectrum. *See* EX1016 at 2:20-64; EX1007 at 67, 151. Thus, even if a POSA were motivated to improve or modify Oostman, they would not have considered doing so by integrating Goodman's light detection device because of the significant differences in the light propagation between the two systems. EX2028, ¶¶70-76.

The significant differences in the light that travels through, and is ultimately detected by, the two different systems in Oostman and Goodman demonstrates the incompatibility and inoperability of Petitioner's combination. For example, the imaging optical element 18 (e.g., imaging mirror) in Goodman's demultiplexing device is not configured to receive light from a large core flow cytometer optical fiber, but instead from an optical communications optical fiber that is at least ten times smaller in diameter than optical fibers used in flow cytometers. EX1016 at 7:17-30. Goodman's imaging optical element 18, as designed for optical communications, would thus fail to reflect the majority of the light coming from a flow cytometer optical fiber because of the significantly larger etendue or spread of the light emerging from such as fiber optic. *See supra* Section II.C.1; EX2028, ¶78. The differences in the light path are illustrated below:



EX1016 at FIG. 1 (annotated); EX2028, ¶78. The only way to make Goodman partially workable would be to reduce the distance from the fiber 15 to the imaging optical element 18. EX2028, ¶78. However, the necessary distance would be so small that the light reflected by the mirror would not clear the fiber coupling 30 to reach mirror 20 and would render Oostman inoperable for separating and detecting fluorescent light.³ *Id.*; see *Deere & Co. v. David's Sozer V-Lov System, Inc.*,

³ Conversely, Goodman's optical communications optical fiber, being significantly smaller than that typically used in flow cytometry, would fail to transmit much of the fluorescent light. See *supra* Section II.C.1; EX2028, ¶78.

IPR2024-01442, Paper 10 at 40 (PTAB Mar. 18, 2025) (“[W]here a prior art reference’s modification—in order to satisfy the claim language—would render ‘inoperable for its intended purpose,’ the reference ‘teaches away from the ... proposed modification.’”) (quoting *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984)); *see also* EX2028, ¶¶77-78.

Petitioner does not address these fundamental incompatibilities. Instead, Petitioner asserts without evidence that a POSA would have identified numerous deficiencies of Oostman and “would naturally have consulted alternate WDM arrangements, including Goodman’s WDM.” Pet. at 26. Yet in the nearly ten years since Goodman’s and Oostman’s applications published, there is no art identified by Petitioner combining these disclosures or suggesting to do so until the inventions of the ’443 patent.⁴ EX2028, ¶¶79-80.

⁴ The only flow cytometry reference Petitioner identifies as even acknowledging an optical communication device is Frazier, which rejected the teachings in those disclosures because it viewed “prefabricated blocks” as not optimal compared to more “customizable” options. EX1009 at 2:9-46; EX2028, ¶80.

Petitioner, seeking to minimize the differences between these fields, alleges that Goodman is in the same field as the alleged inventions by being broadly “related to optical fibers” and “modular optical instruments for color separation and detection.” Pet. at 26. But Petitioner’s high-level characterization of the ’443 patent’s field being related to “optical instruments” overgeneralizes the field. *See R.J. Reynolds*, IPR2021-00826, Paper 11 at 15 (finding no motivation to combine and noting that Petitioner’s characterization of the field was “overly broad”); *see also* EX2028, ¶81.

In fact, Goodman and Petitioner’s other cited references only further support the conclusion that Goodman and other optical communication references are directed to completely different fields with completely different problems than flow cytometry and the ’443 patent. Nothing in Goodman implies that its inventions can or should be used in flow cytometry or any life sciences application. Goodman states its devices “are particularly suited for use in wide wavelength division multiplexing (WWDW) systems,” i.e., wavelengths centered at 1310 nm with channel spacing 25 nm apart, far above flow cytometry’s typical visible light wavelength ranges. EX1016 at 5:42-47, 2:20-29, EX1001 at 57:28-30. Petitioner points to Goodman’s statements that its invention “is easy to incorporate into other optical systems,” EX1016 at 3:65-67; however, Goodman already makes clear what optical systems it

is referring to: “The scope of applications for WDM devices ranges from spacecraft and aircraft applications to closed circuit and cable television systems.” EX1016 at 2:10-13; EX2028, ¶82.

As for flow cytometry references, Petitioner does not contend that Oostman contains any suggestion that POSAs would have considered optical communications art as being within the same field or reasonably pertinent to problems in flow cytometry. Indeed, the *only life sciences reference* Petitioner identifies as even mentioning art from optical communications is Frazier. Pet. at 11-12. However, Frazier merely identifies a single detector array configuration from a patent claiming priority to the 1970s, and then explicitly rejects that reference’s disclosures as *not beneficial* for Frazier’s goals. EX1009 at 2:9-46 (discussing and rejecting a reference from optical communications because its “prefabricated blocks” were not optimal compared to more “customizable” options). EX2028, ¶¶83-85.

Rather than provide support from prior art, Petitioner relies on two statements from the ’443 patent itself discussing its inventions. See Pet. at 26-27, 29. This is improper, and nevertheless, Petitioner misconstrues the statements in the patent. EX2028, ¶86.

First, Petitioner’s excerpted quote leaves out the specification’s explanation that it is “[a]s a result” of the claimed inventions, which allow, e.g., for “extend[ing]

the collimated optical path length without large beam expansion,” that “WDM techniques well-established in the optical communication industry can be readily adapted for fluorescence light detection,” EX1001, 4:60-5:3. The fact that techniques from a different field can be adapted “[a]s a result” of the claimed invention simply demonstrates how to now adapt WDMs from a different field using the benefit of the claimed inventions. *See Sci. Plastic Prods., Inc. v. Biotage AB*, 766 F.3d 1355, 1359 (Fed. Cir. 2014) (whether prior art is analogous is analyzed with “the foresight of a person of ordinary skill, not with the hindsight of the inventor’s successful achievement”); *see also* EX2028, ¶87.

Second, Petitioner’s cherry-picked quote from the specification, that color separation devices in flow cytometry “are almost identical in function and architecture to the wavelength division multiplexers (WDM) widely used in optical communication” (Pet. at 27 (citing EX1001, 44:18-24)), omits the very next sentence, which emphasizes fundamental differences between optical communications and flow cytometry, and the challenges therein. Specifically, the specification explains that light in flow cytometry enters a detection system from a large optical fiber which produces a much larger light beam than produced in optical communications. EX1001, 44:47-67; *see supra* Section II.C.1. The ’443 patent explains that this presents challenges in controlling the light beam over an extended

distance and focusing the beam onto the detectors, as needed for effective detection. *Id.* at 44:24-44. Indeed, the '443 patent states that these fundamental differences “prevent[ed] the use of small area APD in fluorescence detection instrumentation,” despite APDs having “wide acceptance [] in optical communication.” EX1001, 44:10-44; *see also* EX2028, ¶88.

Petitioner’s unsupported assertions that a POSA would have combined a demultiplexing device from optical communications to improve a flow cytometer is pure hindsight. *See Liberty Energy*, IPR2025-00066, Paper 10 at 12 (citing *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007) and warning to “be aware ‘of the distortion caused by hindsight bias and [] be cautious of arguments reliant upon *ex post* reasoning’”); *R.J. Reynolds*, IPR2021-00826, Paper 11 at 18 (“That lack of explanation [as to how disclosed advantages of one reference were applicable to another] appears on this record as a classic exercise of impermissible hindsight reconstruction.”). Petitioner makes no attempt to explain how Goodman’s demultiplexing device would work with light emitted from a flow cytometry fiber optic (or how Goodman’s fiber optic would work in a flow cytometer). Petitioner proposes no modifications to Goodman that would allow it to function as a flow cytometry WDM as recited in independent claim 1 or 18. Nor does Petitioner rely on any disclosure from Oostman in the alternative. Petitioner’s combination thus

fails to render obvious a “wavelength division multiplexer (WDM)” for use in “a flow cytometer.” EX2028, ¶89.

2. Petitioner Fails to Show that Goodman Is Analogous Art to the Claimed Inventions

Prior art references must qualify as “analogous art” to be considered in an obviousness analysis. *K-TEC, Inc. v. Vita-Mix Corp.*, 696 F.3d 1364, 1375 (Fed. Cir. 2012). To be “analogous art,” the reference must (1) be from “the same field of endeavor;” or (2) be “reasonably pertinent to the particular problem with which the inventor is involved.” *Id.* Notwithstanding Petitioner’s two-sentence explanation, Pet. at 26-27, and for similar reasons as discussed above in Section IX.A.1, Goodman (EX1016) is **not** analogous art that can be afforded any weight in the obviousness analysis. EX2028, ¶¶90-91.

First, Petitioner’s overly broad characterization of the field of endeavor ignores the “explanations of the invention’s subject matter in the patent application, including the embodiments, function, and structure of the claimed invention.” *Airbus S.A.S. v. Firepass Corp.*, 941 F.3d 1374, 1380 (Fed. Cir. 2019). As Petitioner concedes, Goodman is related to a **different** field of endeavor—the field of “optical communications,” not flow cytometry. Pet. at 1; EX2028, ¶92.

Second, Petitioner improperly argues that Goodman and the ’443 patent were directed to the overly general problem of “efficiently demultiplexing and detecting

light.” Pet. at 26-27. This ignores that the ’443 patent specifically describes the problems that its inventor was able to solve: to create “an improved flow cytometer” that is “reliable, compact and easy to manufacture,” and “provides a Wavelength Division Multiplexing (WDM) system to separate a light beam into multiple colored bands” that “may be compatible with low noise semiconductor detectors” and “may be reconfigurable.” EX1001, 2:5-44. A POSA faced with these same problems, e.g., how to control and focus a large, diffuse beam diameter over an extended distance would not have found optical communications references dealing with intense light with narrow beam diameters “reasonably pertinent to the particular problem with which the inventor is involved.” *See K-TEC*, 696 F.3d at 1375; *see also* EX2028, ¶¶93-94.

3. Oostman’s Purported Shortcomings Are Key Features of Its Patentable Disclosure and Would Not Be Improved By Goodman

Even if a POSA would have considered teachings from optical communications, Petitioner has not demonstrated that a POSA would have looked to Goodman to modify Oostman. Petitioner argues that a POSA reviewing Oostman would have immediately become aware of various purported shortcomings in its fluorescence detection design, and that Goodman would solve these shortcomings. Pet. at 24-26. However, Petitioner provides no explanation or rationale beyond its

expert’s verbatim say-so, and these “conclusory statements” do not provide “some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *See Wasica Finance GmbH v. Continental Automotice Systems, Inc.*, 853 F.3d 1272, 1286 (citing *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)). Indeed, Oostman’s disclosure expressly contradicts Petitioner’s conclusory assertions, as discussed below. EX2028, ¶95.

i. Oostman’s number of detectors was a feature to improve the prior art

Petitioner puts forth various arguments, largely supported only by expert say-so, to suggest that Oostman’s number of detectors was a “constraint” which would have led a POSA to seek “to improve Oostman’s design” with Goodman. Pet. at 24-26. But as discussed below, this argument fails because each of Oostman’s purported constraints were *features to improve* the prior art, including Goodman. EX2028, ¶96.

First, Petitioner asserts that “Oostman’s polygonal WDM clusters only permit ‘between five and ten light detectors in a common plane,’ a potential design constraint that limits how finely grained light fed into a detector cluster from an optical fiber can be separated. (Goodman [*sic*], 3:53-55.)” Pet. at 24. But Oostman expressly describes its number of detectors and its modular nature as a *feature* of the invention and an *improvement* over the prior art, not a “potential design constraint”

of its device. EX1005 at 3:42-55 (noting differences over the prior art and concluding that “[b]y using reflective transfer legs for most detectors, the detectors may be clustered in a polygonal arrangement of between five and ten light detectors in a common plane”); *id.* at 4:14-16 (“Moreover, the apparatus is modular because a greater number of fibers can feed a greater number of clusters.”); EX2028, ¶¶97-99.

Oostman states that, due to its detector clusters, “the instrument of the present invention has a wide spectral response.” EX1005 at 6:36-39. Petitioner cites *no evidence* to support its assertion that “between five and ten detectors in a common plane” is a potential design constraint in flow cytometry. Pet. at 24. Indeed, Petitioner concedes, Oostman’s device was expressly designed to “provide an improved system for detecting fluorescent light having multiple colors emitted from a target using a greater number of detectors than has been achieved in the prior art.” Pet. at 24 (quoting EX1005 at 2:60-64); *see also id.* (quoting EX1005 at 4:14-16; EX2028, ¶99).

Second, Petitioner does not provide any evidence or even argue that Goodman would provide an improvement other than bare citations to Goodman stating its design “is easily scalable” (Pet. at 27 (citing EX1016 at 3:48-68)). Indeed, Goodman discloses its preferred embodiment has four “wavelength selective elements [e.g., filters] 22a-22n,” which corresponds to four channels for wavelength separation and

four detectors. EX1016 at 8:28-29. And while Goodman contemplates that more wavelength selective elements may be added to separate additional wavelengths, it specifically notes that the number of channels is limited by “the attenuation of the beam of light that will occur and the number of wavelength channels that can be multiplexed.” EX1016 at 8:27-35. In other words, Goodman teaches that there are practical limits for how many channels its device can maintain a strong beam of light for demultiplexing. A POSA would have understood that this practical challenge of maintaining signal strength is similarly present in flow cytometry, and a POSA would thus not assume that Goodman provides for an increased number of detectors over Oostman. *See, e.g.*, EX1005 at 3:42-57, 4:16-24; EX2031 at 4, 8-9; EX2028, ¶¶100-102.

Third, Petitioner argues that a POSA would have relied on Goodman and added more detectors per cluster to Oostman instead of adding additional detector clusters. Pet. at 25. According to Petitioner, additional clusters would “increase complexity in geometry of the optical fibers” feeding to each separate detector cluster and “does not reduce but merely redistributes the flow cytometer’s overall footprint.” Pet. at 25. This argument fails for multiple reasons. First, as discussed in the preceding paragraph, there is no evidence that Goodman’s demultiplexing device would allow an increased number of detectors than one of Oostman’s detector

clusters. Thus, each of Petitioner’s arguments—which Petitioner relies solely on expert say-so for support—is irrelevant because one would still need to use multiple of Goodman’s demultiplexing devices. Second, even if Goodman did allow for more filters and detectors in one device, Goodman would similarly just “redistribute[]” the footprint in only a vertical or horizontal direction (i.e., one long row of filters and detectors).⁵ Petitioner does not attempt to explain how the orientation in Goodman would reduce a flow cytometer’s footprint compared to Oostman or what effect doing so would have on Oostman’s functionality. EX2028, ¶¶103-105.

Thus, Petitioner’s rationale for combining Goodman and Oostman ignores Oostman’s express improvements over the prior art and instead suggests that improvement be replaced. Petitioner fails to explain why a POSA would be motivated to take such action. Instead, Petitioner’s argument is merely a hindsight driven approach that attempts to arrive at the claimed invention. EX2028, ¶106.

ii. Oostman’s detector clusters are intentional design choices that would be negated by Goodman’s optical block

⁵ As discussed in Section IX.A.3.iii, Petitioner cites no evidence that Oostman’s configuration is actually more compact than Goodman’s when accounting for the size of PMTs. EX2028, ¶105 n.2.

Petitioner also points to Goodman’s “optical block with integrated filters and reflectors” as a key feature supporting motivation to combine, arguing that it “reduces optical alignment challenges with thermoplastic molded components, reducing the time, labor, and costs associated with optical component calibration that would have been more prevalent in the Oostman detector arrays.” Pet. at 28; *see also id.* at 26. This argument is flawed for multiple reasons. EX2028, ¶107.

First, Oostman rejects a fixed, prefabricated configuration for wavelength detection. Goodman’s prefabricated optical block configuration with integrated filters, *see* EX1016 at 8:37-50, 10:45-59, cl. 9, goes against Oostman’s express teachings of providing an adjustable flow cytometer. EX1005 at 8:35-40 (“The dichroic mirror holders and the filter holders are mounted in vertically removable housings so that dichroic mirrors and associated filters may be interchanged or replaced.”); *see also, e.g.*, EX1009 at 2:27-38. Optical communications demultiplexing devices have industry-standard channels that rarely, if ever, need to be changed, and predictable inputs of light size and intensity entering the demultiplexing device. *See, e.g.*, EX2032; EX2033; EX2028, ¶109. Meanwhile, Oostman recites interchangeability of its detector clusters as a feature of its invention, not a limitation. *See, e.g.*, EX1005 at 8:19-20 (“Each lens 265 is movable

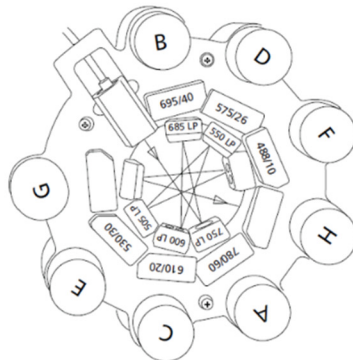
for adjusting the focal spot during calibration of the instrument.”) 8:35-40; *see also id.* at 5:62-6:5; 8:48-9:3. EX2028, ¶¶108-109.

In contrast to Oostman, Goodman, consistent with standards for optical communications demultiplexing devices, discloses using adhesives for permanently affixing its filters 22a-22n to its optical block, meaning that the filters cannot be easily switched. EX1016 at 8:44-47; EX2028, ¶110. Frazier cites similar considerations as key reasons to reject application of an optical communications device for its life sciences fluorescence detection instruments. *See* EX1009 at 2:27-38. For example, the BD LSR Fortessa (which is marked with Oostman’s patent, EX2023 at 2) shares multiple variations of mirror/filter combinations depending on the fluorochromes:

Five-color blue laser configuration

The following map shows the five-color configuration for the 488-nm blue laser.

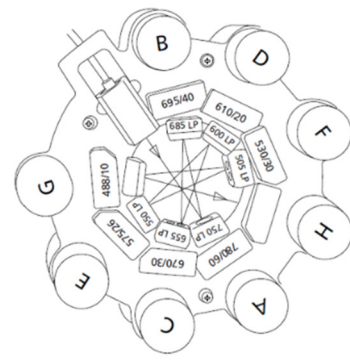
PMT	LP mirror	BP filter	Fluorochromes
A	750	780/60	PE-Cy7
B	685	695/40	PerCP-Cy5.5
C	600	610/20	PE-Texas Red®
D	550	575/26	PE
E	505	530/30	FTTC, Alexa Fluor® 488
F	Blank	488/10	SSC



Six-color blue laser configuration

The following map shows the six-color configuration for the 488-nm blue laser.

PMT	LP mirror	BP filter	Fluorochromes
A	750	780/60	PE-Cy7
B	685	695/40	PerCP-Cy5.5
C	655	670/30	PE-Cy5
D	600	610/20	PE-Texas Red®
E	550	575/26	PE
F	505	530/30	FTTC, Alexa Fluor® 488
G	Blank	488/10	SSC



EX2023 at 140-141 (annotated). EX2028, ¶110.

Second, Oostman provides its own features for adjusting alignment. Petitioner contends alignment challenges would motivate a POSA to use Goodman's "block with integrated filters and reflectors." Pet. at 28. But Petitioner ignores that Oostman teaches that the option of adjusting alignment is an important feature for its flow cytometers and its detector clusters. *E.g.*, EX1005 at 8:49-50 ("The beam splitter mirror 321 is held in a mirror holder frame *at a desired angle.*"), 8:61-65 (emphasizing ability to adjust focusing lenses to focus light at more sensitive spots on PMTs). And Oostman discloses its detector clusters made with mechanically-stabilized mounts (*see, e.g.*, Oostman FIG. 7) that allow correction of alignment issues such that using adhesives such as in Goodman were not the only (or even best) way of achieving alignment and mechanical stability. *See* EX2023 at 140-141; *see also* EX1005 at 5:63-6:23, cl. 32. EX2028, ¶¶111-112.

iii. Petitioner does not explain why a POSA would select Goodman's zig-zag pattern over Oostman's own star-shaped configuration

Petitioner also argues it would have been obvious to try Goodman's demultiplexing device in Oostman's flow cytometer because Goodman's zig-zag pattern is an alternative arrangement involving routine application of known techniques. Pet. at 29. Petitioner states that "[t]he Goodman demultiplexers are also

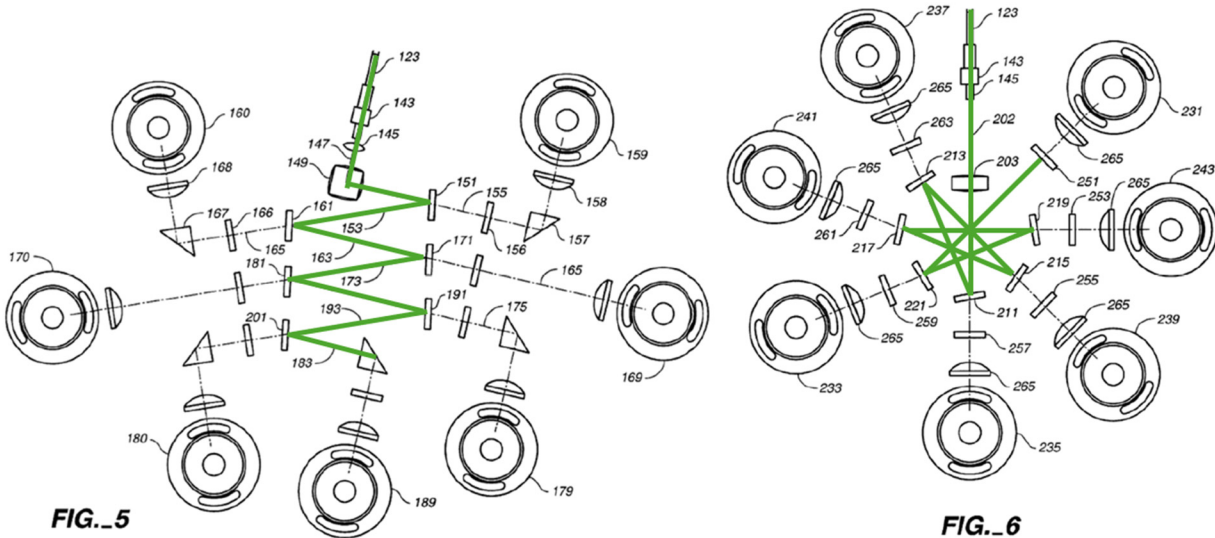
smaller, more scalable, and more portable than Oostman's configuration." Pet. at 28. This argument fails because Petitioner does not actually establish that Goodman's demultiplexer would result in a smaller detector module in Oostman, and Oostman specifically notes that a zig-zag pattern results in a less compact detector module. EX2028, ¶113.

Petitioner's sole evidence to support this argument is a single figure from Oostman with no comparator as to scale or relative size compared to Goodman's demultiplexing device. Pet. at 25. Petitioner does not explain how a POSA would adapt Goodman for Oostman's flow cytometer, or whether, if adapted, Goodman's demultiplexing device would actually be smaller than Oostman's detector module. "It is not enough merely to quote the comparative advantages disclosed in [one prior art reference] without explaining why a POSA would have expected to achieve similar improvements when modifying a different device...disclosed in" another reference. *R.J. Reynolds*, IPR2021-00826, Paper 11 at 21-22. EX2028, ¶114.

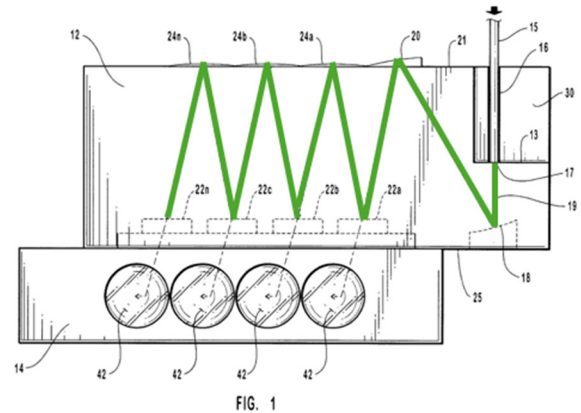
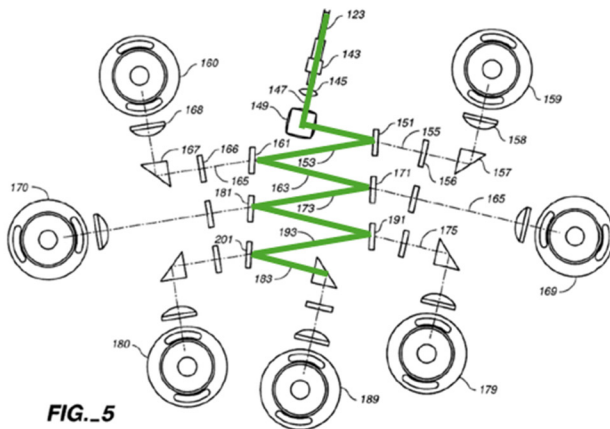
Indeed, Petitioner ignores that Oostman discloses that its star-shaped configuration is ***more compact*** than a zig-zag configuration:

In FIG. 5, the transfer leg forwarded upstream from one beam Splitter to the next follows a zigzag pattern. In FIG. 6, the transfer legs intersect in a star-shaped pattern yielding a ***more compact*** polygonal arrangement of detectors.

EX1005 at 7:32-36.



EX1005 at FIGS. 5 and 6 (annotated). EX2028, ¶115. As Oostman itself makes clear, Oostman’s star-shaped cluster design was an intentional departure from other detector array patterns and was designed to provide a narrow and compact optical path while accounting for its PMT detectors. *See* EX1005 at 7:34-36, 8:21:40; *see also* EX1001 at 43:52-44:9. Petitioner misleadingly describes Oostman FIG. 5 as a “polygonal WDM arrangement[],” Pet. at 23, but the light path annotated below demonstrates a zig-zag configuration. Petitioner provides no explanation as to why a POSA would jettison Oostman’s star-shaped configuration for Goodman’s zig-zag configuration when Oostman already discloses that a zig-zag configuration is less compact than its star-shaped configuration in FIG. 6:



EX1005 at FIGS. 5 (annotated); EX1016 at FIG. 1 (annotated); Pet. at 29 (“Goodman provides a zig-zag pattern in an optical block that was widely accepted in optical communications and had long found adoption within flow cytometry applications.”). EX2028, ¶115.

The petition fails to provide any reason why a skilled artisan would add features from one prior art system to another that were already contemplated by the second reference but were not preferred. *See MacDermid, Inc. v. Rohm and Haas Electronics Materials LLC*, PGR2016-00017, Paper 11 at 15-16 (PTAB Oct. 19, 2016) (denying institution where combination relied on substituting a component that from one reference that the other reference taught was “not preferred”); *see also Virtek Vision Int’l ULC v. Assembly Guidance Sys., Inc.*, 97 F.4th 882, 887 (Fed. Cir. 2024) (“The mere fact that these possible arrangements existed in the prior art does not provide a reason that a skilled artisan would ... make this substitution...”);

R.J. Reynolds, IPR2021-00826, Paper 10 at Denial of Institution (“Petitioner does not explain how or why eliminating this intentional gap would minimize heating of unnecessary thermal mass, improve response times, or reduce the maximum heater temperature in a device, such as Alarcon’s, that produces vapor by an entirely different mechanism....”). EX2028, ¶115-116.

Furthermore, even if a POSA were to consider replacing the star-shaped configuration of FIG. 6 of Oostman with Goodman’s zig-zag demultiplexing device, Petitioner fails to establish that the combination would have a more “simple geometric design.” Pet. at 28. Although Petitioner does not provide further context for this statement, the only component of Oostman’s FIG. 5 that could arguably be described as introducing complex geometry is its beam turning elements (e.g., 157, 167) reflecting light at 90-degree angles into the PMT detectors. But these types of components **would also** be present upon combining Goodman and Oostman. For example, although Goodman Fig. 1 does not show the full optical path like in Oostman Figs. 5 and 6, Goodman’s disclosure specifies that its configuration also includes a “beam folding mirror” that “bends the wavelength beams and redirects them toward the series of focusing lenses,” including bending light at angles of 90 degrees. EX1016 at 12:26-32. Thus, Petitioner even fails to establish that the

proposed combination of Goodman's zig-zag design with Oostman would be less complex. EX2028, ¶¶117-118.

4. Petitioner Fails to Explain How Goodman Would Improve Oostman Specifically

Petitioner reproduces a series of six quotes from Goodman's summary section to contend that "Goodman's teachings address and provide an improvement on Oostman's design constraints." Pet. at 27. These quotes do not explain how Oostman would specifically be improved. EX2028, ¶119.

The first four quotes Petitioner relies on are all directed towards ease of fabrication; however, Petitioner provides no explanation how or why Goodman's manufacturing method would be simpler to manufacture than Oostman, or even if it was, why such benefits would outweigh Oostman's benefits of customizability and reduced size.⁶ Petitioner's fifth quote, that Goodman's WDM is "easy to incorporate into other optical systems," Pet. at 27, ignores that Goodman's description of

⁶ Petitioner later suggests that Goodman's design is smaller and "reduc[es] the bill of material (BOM) costs by using less materials." Pet. at 28. But as discussed above, Goodman's design is *not* necessarily smaller, and Petitioner provides no evidence or benchmarks to assess costs of manufacturing between Oostman and Goodman. EX2028, ¶120 n.4.

relevant applications for its technology was “spacecraft and aircraft applications” and “closed circuit and cable television systems,” not flow cytometry. EX1016 at 2:10-13. And Petitioner’s final quote, that Goodman “is easily scalable or modified,” ignores that Oostman’s system is similarly, or more, easily scalable as discussed above. *See* Section IX.A.3.iii; *see also* EX2028, ¶¶120-121.

Furthermore, Petitioner does not ***attempt*** to explain why, rather than modify Oostman’s configuration, a POSA would have changed every other aspect of Oostman’s design (e.g., its lenses, mirrors, filters, etc.), in favor of Goodman, or even more drastically, jettison Oostman’s detector clusters completely and just try to plug in Goodman’s demultiplexing device. *See Axonics, Inc. v. Medtronic, Inc.*, 73 F.4th 950, 957 (Fed. Cir. 2023) (“The proper inquiry is whether the relevant artisan would be motivated to make the combination to arrive at the claims’ actual limitations[.]”); *Free-Flow Packaging Int’l, Inc. v. Automated Packaging Sys., Inc.*, IPR2016-00444, Paper 8 at 13 (PTAB Jun. 22, 2016) (requiring “‘some articulated reasoning with some rational underpinning’ to combine the known elements in the manner required in the claim at issue”) (quoting *KSR*, 550 U.S. at 418). It is not enough to provide some motivation to change certain features of a reference and assume, without analysis, that a POSA would have made multiple additional changes to achieve the claimed invention. Petitioner’s motivation to combine analysis is

completely absent in this respect, and should be rejected for this additional reason.

EX2028, ¶¶122-124.

B. Limitations 1[d] and 18[d][iii]: Petitioner Fails to Demonstrate that Oostman and Goodman Disclose “a Set of Detectors”

All challenged claims require “a set of detectors” as part of a wavelength division multiplexer for a flow cytometer. Petitioner states that the combination of Oostman and Goodman disclose this claim limitation, but Petitioner only points to disclosure of Goodman as teaching the claimed elements. Pet. at 39 (citing Goodman’s disclosure of “optical receptors” for the “set of detectors” limitation); *id.* at 69 (referring back to claim 1[d]). Petitioner fails to explain how these “optical receptors” of Goodman’s optical communications device would be integrated *into a flow cytometer*. Petitioner’s combination fails as a result. EX2028, ¶125.

Goodman discloses that its selected wavelength beam is focused onto an “optical receiver such as an optical detector[.]” EX1016 at 11:40-41. Goodman does not disclose what type of optical detectors are contemplated and Petitioner does not include any further explanation. *See* EX1016 at 11:40-44. However, a POSA reading Goodman would have understood that it is directed to for a demultiplexing device for optical communications that uses laser light in the infrared spectrum (centered at the 1310 nm wavelength). EX1016 at 2:20-29, 5:42-47; Pet. at 26-27 (acknowledging Goodman describes a demultiplexing device “in the optical

communication industry”). A POSA would have understood that such a device would use detectors designed for use in high-intensity light systems such as in optical communications. *See* EX1016 at 2:20-29, 5:42-47; Pet. at 26-27; EX2028, ¶126.

Before the inventions of the ’443 patent, flow cytometers typically used PMTs for detection of the low intensity light produced in flow cytometry. EX1004 at 24; EX1001, 43:49-44:9; *see also, e.g.*, EX1007 at 156. Indeed, the intensity of the light detected in flow cytometers is orders of magnitude lower than that in optical communications. *See supra* Section II.C.2. Petitioner provides no explanation of how Goodman’s detectors can be used as part of a detection system for a flow cytometer once incorporated into Oostman’s flow cytometer where only a fraction of the light beam would be transmitted through the optical components in Goodman’s detector. As a result, Petitioner’s combination fails to disclose “a set of detectors” for use within a WDM of a flow cytometer, as required by all claims. *See Deere & Co.*, IPR2024-01442, Paper 10 at 40 (“[W]here a prior art reference’s modification—in order to satisfy the claim language—would render ‘inoperable for its intended purpose,’ the reference ‘teaches away from the ... proposed modification.’”) (quoting *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984)); *see also* EX2028, ¶127.

Additionally, Petitioner does not explain how Goodman's demultiplexing device comprises detectors. Goodman states that its beam directing member could direct light onto focusing lenses, which then focus light onto optical receivers separate from its device. *See, e.g.*, EX1016, cls. 37-38 (stating that the demultiplexer device comprises a beam-directing member comprising focusing lenses that "focus each of the beams of optical energy on *an optical receiver*"). Petitioner does not explain how the detectors described in Goodman could be incorporated into a WDM within a flow cytometer, or even that such detectors would be incorporated into the WDM, and Petitioner's combination fails to meet this limitation as a result. EX2028, ¶¶128-129.

C. Petitioner Fails to Demonstrate a Reasonable Expectation of Success

Petitioner devotes a single paragraph of its Petition to argue that a POSA would have had a reasonable expectation of success in implementing Goodman's WDM into Oostman. Pet. at 29-30. But Petitioner's sole evidence on this front are (1) two statements from Goodman stating its WDM could be incorporated into other generic optical systems; (2) statements from the '443 patent itself; and (3) cursory statements from a preliminary search opinion applying European inventive step law. Each of these pieces of evidence are flawed, and Petitioner fails to meaningfully engage with actual facts in assessing reasonable expectation of success. *See*

Broadcom Corp. v. Emulex Corp., 732 F.3d 1325, 1335 (noting that reasonable expectation of success “requires a ‘plausible rational [sic] as to why the prior art references would have worked together’”) (quoting *Power-One, Inc. v. Artsyn Techs., Inc.*, 599 F.3d 1343, 1351 (Fed. Cir. 2010)); *see also* EX2028, ¶130.

First, as discussed above, Goodman’s generalized statements do not explain how its optical communications demultiplexing device could be incorporated into a flow cytometer fluorescent detection system, and Goodman itself states that relevant applications for its technology range from “spacecraft and aircraft applications to closed circuit and cable television systems.” EX1016 at 2:10-14; *see supra* Section IX.A.1. None of these applications have any connection to life science fluorescence detection systems, and Petitioner has not explained how a POSA would have had a reasonable expectation of success based on this general statement. EX2028, ¶131.

Second, as discussed above, the statements cited from the ’443 specification, actually highlight the **challenges** in translating WDMs from optical communications to flow cytometry prior to the inventions disclosed in the ’443 patent. EX1001, 44:54-45:3. And regardless, the obviousness inquiry is not whether a POSA, reading a patent specification, would have had a reasonable expectation of success in achieving the inventions disclosed therein—it is whether a POSA would have had a reasonable expectation of success ***in view of the prior art***. *PAR Pharmaceutical,*

Inc. v. TWI Pharms., Inc., 773 F.3d 1186, 1196 (Fed. Cir. 2014) (“Proper analysis under § 103 requires, *inter alia*, consideration of ... (2) ***whether the prior art*** would also have revealed that in so making or carrying out [a claimed invention], those of ordinary skill would have a reasonable expectation of success.”) (internal citations omitted); *see also Standard Oil Co. v. Am. Cyanamid Co.*, 774 F.2d 448, 454 (Fed. Cir. 1985) (“[O]ne should not go about determining obviousness under § 103 by inquiring into what *patentees* (i.e., inventors) would have known or would likely have done, faced with the revelations of references.”); *Amgen Inc. v. F. Hoffman-La Roche Ltd*, 580 F.3d 1340, 1363 (Fed. Cir. 2009) (quoting *Standard Oil*, 774 F.2d at 454, to support that an inventor’s “personal expectations are not conclusive of an ordinarily skilled artisan’s reasonable expectations”). EX2028, ¶132.

Third, Federal Circuit precedent is clear that European patent prosecution is not relevant to USPTO examination. *AIA Eng’g Ltd. v. Magotteaux Int’l*, 657 F.3d 1264, 1279 (Fed. Cir. 2011) (declining to consider foreign applications because “theories and laws of patentability vary from country to country, as do examination practices”). Regardless, the EPO’s preliminary search report provided a single sentence objecting to dependent claims that a “skilled person would implement the WDM device” in flow cytometry art. EX1028 at 41. Since then, Applicant amended claim 1 to recite a “flow cytometer,” and explained in detail why a skilled artisan

would not have implemented WDMs in flow cytometry. EX1028 at 16-30. The European Patent Office has not yet addressed this response. *See* EPO Guidelines for Examination, C-II, 3.1 (“The applicant’s response to the search opinion ... will be taken into account by the examining division.”). Indeed, two other European patent applications in the same family that recited “flow cytometer” limitations were allowed. EX2018 at 20 (requiring a “flow cytometer”); EX2019 at 20 (same). In one of those granted patents, the European Patent Office also considered Oostman. EX2020 at 2. EX2028, ¶133.

Finally, though Petitioner proposes incorporating Goodman’s entire detection system into Oostman’s flow cytometer, Petitioner does nothing to explain how a POSA would have reasonably expected Goodman’s entire system to work. For example, Petitioner does not explain whether Goodman’s imaging elements 18 and 20 would function when receiving light from a large diameter flow cytometry fiber optic which produces light at an etendue hundreds of times greater than what they were designed for, nor whether Goodman’s optical communications fiber optic would receive sufficient fluorescent light, nor whether Goodman’s detectors designed for optical communications would be operable in a flow cytometer. Petitioner’s conclusory statements on reasonable expectation of success fall short of “some articulated reasoning with some rational underpinning to support the legal

conclusion of obviousness.” *KSR*, 550 U.S. at 418 (internal citations omitted).

EX2028, ¶¶134-135.

X. CONCLUSION

For the above reasons, Patent Owner respectfully requests that the Board deny Petitioner’s Petition for *inter partes* review of the ’443 patent in its entirety.

Respectfully submitted,

Dated: October 31, 2025

/Alexis R. Cohen/

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CERTIFICATE UNDER 37 CFR § 42.24(d)

Under the provisions of 37 CFR § 42.24(d), the undersigned hereby certifies that the word count for the foregoing Patent Owner Preliminary Response totals 10,059, which is less than the 14,000 words allowed under 37 CFR § 42.24(a)(1)(i).

Respectfully submitted,

Dated: October 31, 2025

/Patrick E. Nyman/
Patrick Nyman
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CERTIFICATE OF SERVICE

I hereby certify that on October 31, 2025, I caused a true and correct copy of the following materials:

- Patent Owner's Preliminary Response
- Exhibit List
- Word Count Certification Under 37 CFR § 42.24(d)
- Exhibits for Patent Owner's Preliminary Response (EX2028-2039)

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