

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AGILENT TECHNOLOGIES, INC.,
Petitioner,

v.

THERMO FISHER SCIENTIFIC INC. and
THERMO FISHER SCIENTIFIC (BREMEN) GMBH,
Patent Owner.

Case IPR2018-00298
Patent RE45,386 E

Before MICHAEL R. ZECHER, JOHN F. HORVATH, and
DANIEL J. GALLIGAN, *Administrative Patent Judges*.

HORVATH, *Administrative Patent Judge*.

DECISION
Granting Institution of Inter Partes Review
35 U.S.C. § 314

I. INTRODUCTION

A. Background

Agilent Technologies, Inc. (“Petitioner”) filed a Petition (Paper 1, “Pet.”) requesting an *inter partes* review of claims 1–8, 10, 12–20, 22, 23, and 25–50 (“the challenged claims”) of U.S. Patent No. RE45,386 E (Ex. 1001, “the ’386 patent”). Thermo Fisher Scientific Inc. and Thermo Fisher Scientific (Bremen) GmbH (collectively, “Patent Owner”) filed a Preliminary Response (Paper 14 (“Prelim. Resp.”)).

Upon consideration of the Petition and Preliminary Response, we are persuaded, under 35 U.S.C. § 314(a), that Petitioner has demonstrated a reasonable likelihood that it would prevail in showing the unpatentability of at least one challenged claim of the ’386 patent. Accordingly, we institute an *inter partes* review of all challenged claims on all challenged grounds.

B. Related Matters

Petitioner and Patent Owner identify the following as matters that could affect, or be affected by, a decision in this proceeding: *Thermo Fisher Scientific Inc. v. Agilent Technologies, Inc.*, No. 1:17-cv-00600 (D. Del.), *Thermo Fisher Scientific Inc. v. Agilent Technologies, Inc.*, Case IPR2018-00313 (PTAB), and *Thermo Fisher Scientific Inc. v. Agilent Technologies, Inc.*, Case IPR2018-00299 (PTAB) (challenging U.S. Patent No. 7,230,232, which is related to the ’386 patent). Pet. 1; Paper 7, 2.

C. Evidence Relied Upon

Reference	Publication Date ¹	Exhibit
Yost, R. A., and Fetterolf, D. D., “Tandem mass spectrometry (MS/MS) instrumentation,” <i>Mass Spectrometry Reviews</i> Vol. 2, No. 1, 1-45 (1983) (“Yost”)	Mar. 1983	1015
G.C. Eiden et al., “Beneficial Ion/Molecule Reactions in Elemental Mass Spectrometry,” <i>Rapid Comms. in Mass Spectrometry</i> Vol. 11, No. 1, 37–42 (1997) (“Eiden”)	Jan. 1997	1023
Speakman, U.S. Patent No. 6,222,185 B1	Apr. 24, 2001 ²	1024
Douglas, D.J., “Some Current Perspectives on ICP-MS,” <i>Canadian J. of Spectroscopy</i> , Vol. 34, No. 2, 38–49 (1989) (“Douglas”)	June 1989	1029
King, F.L. and Harrison, W.W., “Collision-Induced Dissociation of Polyatomic Ions in Glow Discharge Mass Spectrometry,” <i>Int’l J. of Mass Spectrometry and Ion Processes</i> , Vol. 89, 171–185 (1989) (“King”)	May 1989	1037

Petitioner also relies upon the Declaration of Richard Yost (Ex. 1004).

D. Asserted Grounds of Unpatentability

Petitioner asserts the following grounds of unpatentability:

Reference(s)	Basis	Claims Challenged
King	§ 102(b)	13, 16, 17, 28, 41, and 46–50

¹ Petitioner relies on the Declaration of Sylvia Hall-Ellis, Ph.D., to establish the publication dates of Exhibits 1015, 1023, 1029, and 1037. *See* Ex. 1008 ¶ 25.

² Claims priority to GB Application No. 9,612,070 filed on June 10, 1996.

Reference(s)	Basis	Claims Challenged
King and Douglas	§ 103(a)	13, 15–17, 28–32, 34, 37, 38, 40, 41, 44, and 47–49
King, Douglas, and Eiden	§ 103(a)	43, 46, and 50
King, Douglas, and Speakman	§ 103(a)	1–3, 6–8, 10, 12, 18–20, 22, 23, 33, 35, 36, 39, 42, 43, 45, and 46
King, Douglas, Speakman, and Yost	§ 103(a)	4, 5, 14, 25–27, 39, 42, and 45

II. ANALYSIS

A. The '386 Patent

The '386 patent is directed toward “inductively coupled plasma mass spectrometry (ICPMS) in which a collision cell is employed to selectively removed unwanted artefact ions from an ion beam by causing them to react with a reagent gas.” Ex. 1001, [57]. According to the '386 patent, “[t]he general principles of ICPMS are well known” and provide “a method of elemental analysis . . . about the elemental composition of a sample.” *Id.* at 1:27–29. In ICPMS, a typically liquid sample is nebulized and passed through a high temperature (e.g., 5000K) plasma that atomizes and ionizes the sample. *Id.* at 1:30–34. The ionized sample is then “introduced, via one or more stages of pressure reduction, into a mass analyzer,” such as a quadrupole, magnetic sector, or time-of-flight analyzer. *Id.* at 1:34–38.

A known problem with ICPMS-based analysis “is the presence . . . of unwanted artefact ions that impair the detection of some elements,” and that depends upon “the chemical composition of both the plasma support gas and . . . the original sample.” *Id.* at 1:39–45. For example, argon (Ar) is a typical ICPMS plasma support gas and results in the production of artefact ions such as argon oxide (ArO⁺) having a mass of 56 atomic mass units

(“a.m.u.”) that interfere with the detection of iron (^{56}Fe) ions having the same atomic mass. *Id.* at 1:45–50.

A known solution for reducing the presence of such artefact ions is the use of a collision cell. *Id.* at 1:53–56. “A collision cell is a substantially gas-tight enclosure through which ions are transmitted” that is “positioned between the ion source and the main spectrometer.” *Id.* at 1:57–59. A target gas, such as a neutral gas with a high ionization potential, is introduced into the collision cell, which promotes multiple collisions between ions transmitted into the cell and the target gas. *Id.* at 1:59–61, 2:12–13. This allows certain analyte ions (e.g., ^{56}Fe)—which are typically stable, singly-charged, and monatomic—to be efficiently transmitted through the collision cell, while unwanted or artefact ions (e.g., ArO^+) are preferentially removed because they are less stable, have a larger collision cross-section, and tend to dissociate into “new ions of lower mass and one or more neutral fragments.” *Id.* at 2:4–22.

When a collision cell “is operated at a pressure that is sufficiently high to promote removal of . . . artefact ions that originate in the plasma, other artefact ions may form.” *Id.* at 2:29–30. The chemical nature of these other artefact ions “is not always known,” but may result from charge exchange with hydrocarbons in the gas composition, metal oxide or hydroxide ions formed from ion-molecule reactions in the collision cell, and water adduct ions. *Id.* at 2:31–38.

Figure 2 of the '386 patent, which is reproduced below, depicts “a preferred embodiment of the present invention.” *Id.* at 5:66–67.

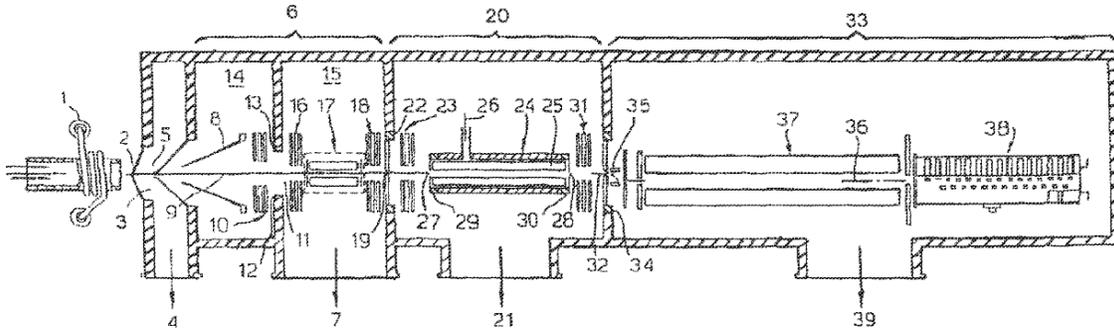


Figure 2 is a schematic illustration of an ICPMS according to the invention described in the '386 patent. An ion source, such as inductively coupled plasma (ICP) ion source 1 generates ions that pass through sampling aperture 2 into expansion chamber 3, which is evacuated by a rotary pump through port 4. *Id.* at 6:26–29. The ions passing through aperture 2 form a supersonic gas jet having a central portion that passes through aperture 5 into high vacuum chamber 6, which is evacuated by a turbo-molecular pump through port 7. *Id.* at 6:29–37. Due to a large negative potential on extractor lens 8, the positively charged ions are accelerated away from aperture 5 and focused by ion lens 10 to travel through aperture 11, where they are subsequently focused by ion lens 16 into ion optical device 17. *Id.* at 6:43–49, 7:6–7.

Ion optical device 17 maybe a quadrupole, higher order multipole, ion guide, or ion lens, and is preferably a mass-selective device such as a quadrupole. *Id.* at 4:64–5:2, 7:14–20. When mass-selective, ion optical device 17 acts as an auxiliary mass filter that can be “set to transmit only ions from the same m/e [mass-to-charge ratio] as the main mass filter.” *Id.* at 4:66–5:7. This “reduce[s] the contribution of artefact ions to the mass

spectrum” because “[a]ny artefact ion that is formed in the collision cell must therefore be a reaction product from an ion of the m/e that is selected in both the auxiliary mass filter and main mass filter.” *Id.* at 5:4–10. Such an “artefact ion must have a different m/e from that selected, and so will not be transmitted by the main mass filter.” *Id.* at 5:10–12.

Ions transmitted through ion optical device 17 are focused by ion lens 18 to pass through aperture 19 into second evacuated chamber 20, which is evacuated by a turbomolecular pump through port 21. *Id.* at 7:21–25. Ion lens 23 focuses these ions into collision cell 24 having entrance aperture 27 and exit aperture 28. *Id.* at 7:40–43. Collision cell 24 contains multiple ion optical assembly 25, which may be a quadrupole, hexapole, or octapole, and is filled with target gas 26, chosen for its capacity to remove—via either an attachment or fragmentation mechanism—unwanted molecular ions from the ion beam. *Id.* at 7:46–52. Target gas 26 can be hydrogen, helium, or any other gas that “may prove beneficial for specific analytical requirements.” *Id.* at 7:52–54. As noted in the background section of the ’386 patent, “[b]y careful control of the conditions in the collision cell,” including selection of the collision gas and pressure, “[it] is possible to transmit the wanted ions efficiently” through the collision cell and to simultaneously “remove unwanted artefact ions.” *Id.* at 2:4–5, 2:14–15.

Ions that pass through collision cell 24 are focused by ion lens 31 through aperture 32 into evacuated chamber 33, which is evacuated by a turbomolecular pump through port 39. *Id.* at 7:63–67, 8:24–27. Deflector lens 35 deflects ions passing through aperture 32 from initial instrument axis 9 to axis 36 of quadrupole mass filter 37. *Id.* at 8:9–13. Quadrupole mass filter 37 selects ions of a given mass/charge (m/e) or range of mass/charge

ratios, which are transmitted to a detector, such as electron multiplier 38. *Id.* at 8:20–21.

Of the challenged claims, claims 1, 13, and 28 of the '386 patent are independent. Other challenged claims depend directly or indirectly from claims 1, 13, and 28. Claim 28 is illustrative and is reproduced below.

28. A mass spectrometer comprising:

an inductively coupled plasma ion source for generating ions from a sample, the generated ions including first atomic ions having a first mass-to-charge ratio and artefact ions having a mass-to-charge ratio that interferes with the first mass-to-charge ratio;

an ion optical device disposed to receive at least a portion of an ion beam generated by the ion source, the ion optical device being configured to mass select at least a portion of the ion beam generated by the ion source at the first mass-to-charge ratio, thereby removing from the ion beam, ions not having the first mass-to-charge ratio;

a collision cell disposed to receive at least a portion of a mass selected ion beam from the ion optical device and configured to remove, from the mass selected ion beam, artefact ions having a mass-to-charge ratio that interferes with the first mass-to-charge ratio, the ion optical device being configured substantially to minimize the formation in the collision cell of interfering artefact ions having the first mass-to-charge ratio; and

a mass analyzer disposed to receive at least a portion of the mass selected ion beam from the collision cell, the mass analyzer being configured to mass analyze the received ion beam at the same mass-to-charge ratio as the ion optical device, wherein the

mass analyzer is configured to detect the first atomic ions when the same mass-to-charge ratio is the first mass-to-charge ratio.

Ex. 1001, 10:43–11:2. Independent claim 13 recites a method of operating a mass spectrometer that incorporates a collision cell pressurized with a target gas, such as the mass spectrometer recited in claim 28. *Id.* at 9:41–57.

Independent claim 1 is a more detailed recitation of a mass spectrometer having a collision cell and further recites additional components of the mass spectrometer, such as its apertures and vacuum pumps. *Id.* at 8:33–9:3.

B. Claim Construction

In an *inter partes* review proceeding, claim terms of an unexpired patent are given their broadest reasonable interpretation in light of the specification of the patent in which they appear. 37 C.F.R. § 42.100(b). Under the broadest reasonable interpretation standard, claim terms are generally given their ordinary and customary meaning, as would be understood by one of ordinary skill in the art, in the context of the entire disclosure. *In re Translogic Tech., Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007). Only claim terms which are in controversy need to be construed and only to the extent necessary to resolve the controversy. *See, e.g., Nidec Motor Corp. v. Zhongshan Broad Ocean Motor Co.*, 868 F.3d 1013, 1017 (Fed. Cir. 2017).

Petitioner proposes constructions for the terms “means . . . for generating ions from a sample introduced into a plasma,” “mass-to-charge analyzing means,” “at the same [analyte] mass-to-charge ratio,” and “configured to.” Pet. 27–29. Patent Owner does not challenge Petitioner’s construction of “mass-to-charge analyzing means,” but proposes alternative

constructions for the other terms. Prelim. Resp. 32–38. We construe the terms “means . . . for generating ions,” “mass-to-charge analyzing means,” and “at the same [analyte] mass-to-charge ratio” below, and find the term “configured to” does not need to be construed to resolve any controversy in this proceeding.

1. means . . . for generating ions from a sample introduced into a plasma

Petitioner argues this term, recited in independent claim 1, is a means-plus-function term whose function is “generating ions from a sample introduced into a plasma” and whose corresponding structure is an ICP source and other ion sources. Pet. 27 (citing Ex. 1001, 1:15–23, 6:26–27, claims 13, 41). Patent Owner agrees this term is a means-plus-function term and agrees with Petitioner’s identification of the function to be performed, but argues the corresponding structure is limited to an ICP source. Prelim. Resp. 36–37 (citing Ex. 1001, [57], 6:26–27).

We agree with the parties that the recited “means . . . for generating ions” term is a means-plus-function limitation whose recited function is “generating ions from a sample introduced into a plasma.” The term is, therefore, construed to encompass the structure, materials, and acts disclosed in the specification for performing the recited function, and equivalents thereof. 35 U.S.C. § 112, ¶ 6. A structure disclosed in the specification is corresponding structure only “if the specification or prosecution history clearly links or associates that structure to the function recited in the claim.” *B. Braun Medical, Inc. v. Abbot Labs.*, 124 F.3d 1419, 1424 (Fed. Cir. 1997).

At this stage of the proceeding, we find the only structure disclosed in the specification that is clearly linked to the function of “generating ions from a sample introduced into a plasma” is an ICP ion source. *See* Ex. 1001, 6:26–28. Contrary to Petitioner’s contentions, claim 13 merely recites the function to be performed, without reciting any particular structure to perform that function. Similarly, the specification at column 1, lines 15 through 23 simply states that the concepts disclosed can be applied to any type of mass spectrometer that generates both unwanted artefact ions and analytically significant ions, without disclosing any particular structure for generating such ions.

Accordingly, on the record before us and for purposes of this Decision, we construe the “means . . . for generating ions from a sample introduced into a plasma” to mean an ICP source and equivalents thereof.

2. mass-to-charge ratio analyzing means

Petitioner argues this term, recited in independent claim 1, is a means-plus-function term whose function is “analyzing ions based on their mass-to-charge ratios” and whose corresponding structure is a radio frequency (RF) quadrupole, a magnetic sector, or a time-of-flight (TOF) mass analyzer. Pet. 27 (citing Ex. 1001, 4:60–64, claim 6). Patent Owner does not contest Petitioner’s proposed construction of this term, with which we agree. Prelim. Resp. 32, n.13. The specification discloses “the mass-to-charge ratio analyzing means includes a main mass filter which preferably is an RF quadrupole, although a magnetic sector or a time-of-flight analyser may alternatively be employed.” Ex. 1001, 4:60–64.

Accordingly, on the record before us and for purposes of this Decision, we construe the “mass-to-charge analyzing means” to mean an RF

quadrupole, a magnetic sector, or a time-of-flight analyzer, and equivalents thereof.

3. *at the same [analyte] mass-to-charge ratio*

This term is recited in independent claims 1, 13, and 28. Ex. 1001, 8:63–65 (“the first ion optical device (17) and the mass-to-charge ratio analyzing means (37) operate at the same mass to charge ratio”), 9:56–57 (“mass analyzing the received ion beam at the same analyte mass to charge ratio as in the mass selecting step”), 10:64–67 (“the mass analyzer being configured to mass analyze the received ion beam at the same mass-to-charge ratio as the ion optical device”).

Petitioner argues this term means analyzing the ion beam “at one or more mass-to-charge ratios, one of which is the mass-to-charge ratio of an analyte ion.” Pet. 28. Petitioner argues the open-ended nature of claim 13, due to the use of the “comprising” transitional phrase, and the language of dependent claims 37 and 38 indicating the mass analysis is done at a plurality of analyte mass to charge ratios, support its proposed construction. *Id.* at 28–29.

Patent Owner argues all of the claims require mass analysis of “the ion beam after exiting the collision cell at the same mass-to-charge ratio that was mass selected for . . . the ion beam before entering the collision cell.” Prelim. Resp. 33 (emphasis omitted). Therefore, Patent Owner argues this claim term means analyzing the ion beam “at an identical [analyte] mass-to-charge ratio.” *Id.* Patent Owner argues Petitioner’s proposed construction is improper “because it makes the word ‘ratio’ plural and it reads out the word ‘same.’” *Id.*

On this record, we are persuaded by Patent Owner's argument. The plain and ordinary meaning of the term "at the same [analyte] mass-to-charge ratio" is "at an identical [analyte] mass-to-charge ratio." This term, in the context of independent claims 1, 13, and 28, expresses the limitation that the mass analyzing step performed on the ion beam leaving the collision cell is done at the "same" or at the "identical" mass-to-charge ratio as the mass analyzing step performed on the ion beam prior to its entering the collision cell. The open-ended nature of claim 13 does not change this result but simply allows for other steps to be performed. For example, as expressed in claim 37, the mass analysis performed at the same mass/charge ratio can be performed at a plurality of different mass/charge ratios. That is, the mass analysis can be performed at a first mass/charge ratio and subsequently performed at a second mass/charge ratio, and so forth.

Accordingly, on the record before us and for purposes of this Decision, we construe the term "at the same [analyte] mass-to-charge ratio" to mean "at an identical [analyte] mass-to-charge ratio."

C. Level of Ordinary Skill in the Art

Petitioner, relying on the testimony of Dr. Yost, argues a person of ordinary skill in the art at the time of the invention would have had an M.S. or Ph.D. in chemistry, physics, or a related field, and at least two or three years of experience developing instrumentation for or applications in plasma ionization mass spectrometry or tandem mass spectrometry. Pet. 5 (citing Ex. 1004 ¶¶ 20–22). Patent Owner generally agrees with this definition, but argues a person skilled in the art would have had approximately two to three years of experience rather than at least two to three years of experience. Prelim. Resp. 16, n.6.

On the record before us, we find a person skilled in the art would have had an M.S. or Ph.D. in chemistry, physics, or a related field, and approximately two or three years of experience developing instrumentation for or applications in plasma ionization mass spectrometry or tandem mass spectrometry.

D. Overview of the Prior Art

1. King

King is a research paper entitled “Collision-Induced Dissociation of Polyatomic Ions in Glow Discharge Mass Spectrometry.” Ex. 1037, 171.³ King discloses:

The problem of isobaric interferences resulting from polyatomic ions that overlap analytically significant isotopes is a major hindrance encountered in elemental mass spectrometry. The use of collision-induced dissociation (CID) as a means of removing these polyatomic species from the ion beam prior to mass analysis is reported here. Low energy CID in the second stage of a triple stage quadrupole mass spectrometer is seen to reduce isobaric interferences due to polyatomic ions in glow discharge mass spectra.

Id., Abstract. King identifies isobaric interferences from polyatomic ions as “a problem common to *all elemental mass spectrometry techniques.*” *Id.* at 172 (emphasis added). King reports on experiments that “show the removal of molecular interferences by CID [collision-induced dissociation], the

³ All references to the page numbers in King refer to the original page numbers in the top, right-hand corner or top, left-hand corner of each page in Exhibit 1037.

identification of ion composition from daughter spectra, and the prediction of interfered m/z [mass-to-charge ratio] from parent spectra.” *Id.* at 173.

King’s experiments are conducted on a modified Finnigan MAT series 4500 triple quadrupole mass spectrometer (TQMS) having a custom built glow discharge ion source. *Id.* Ions generated by the source are focused onto a first quadrupole (Q1) that can be operated in a mass filtering mode that selects ions within a particular mass window (i.e., having a particular m/z ratio). *Id.* at 174. The ion beam exiting Q1 is focused by ion optics into a second quadrupole (Q2) that serves as a collision cell and is operated in r.f. only mode (i.e., passing all ions). *Id.* The ion beam exiting Q2 is focused into a third quadrupole (Q3) that is operated in the same manner as Q1. *Id.*

King reports on several experiments conducted using different samples and methods of analysis. One experiment reported on efficiently removing metal argide ions (e.g., $^{56}\text{Fe}^{40}\text{Ar}^+$) that interfered with the detection of molybdenum ($^{96}\text{Mo}^+$) ions from a steel sample. *Id.* at 177–78. King discloses that by choosing a suitable pressure (i.e., 2.4 mtorr) for the target gas in the collision cell, “a correct molybdenum isotope ratio is obtained . . . indicating that at this level of sensitivity the isobaric interference due to the iron argide is effectively eliminated.” *Id.* at 178. Another experiment reported on identifying various isobaric interferences that occur at a charge/mass ratio of 81. King reports:

A well known molecular ion observed in GDMS [glow discharge mass spectrometry] is the Ar_2H^+ species at $m/z = 81$. Utilizing a brass sample the daughter spectrum of $m/z = 81$ shown in Fig. 6 was acquired. If the signal at $m/z = 81$

corresponded to an atomic ion the daughter spectrum would consist only of a signal at $m/z = 81$. The daughter spectrum in Fig. 6 shows a signal at $m/z = 41$ due to fragmentation of Ar_2H^+ yielding ArH^+ . An unexpected contribution attributed to CuH_2O^+ at $m/z = 81$ is identified from the fragment appearing at $m/z = 63$. This demonstrates the ability to evaluate any peak in the mass spectrum for the presence of isobaric interferences and to identify the interfering species.

Id. at 183.

2. Douglas

Douglas is a research paper reviewing the development of inductively coupled plasma (ICP) mass spectrometry (MS) or ICP-MS. Ex. 1029, 38, Abstract.⁴ Douglas also identifies the problem of ionic interferences in obtaining accurate mass spectra and explores the use of TQMS having ICP sources as a means to reduce such interferences. *Id.* at 47. For example, Douglas describes using the middle mass spectrometer (MS) as a collision cell filled with a non-reactive gas (Ar) to dissociate unwanted molecular ions. *Id.* Douglas also describes using the middle MS as a collision cell filled with a reactive gas (air) that differentially reacts with ions entering the cell. *Id.* at 48. For example, Douglas describes obtaining the mass spectra of cerium (Ce) and terbium (Tb). *Id.* When these elements are introduced into the ICP source, Ce^+ , CeO^+ , and Tb^+ ions are produced. *Id.* When the Ce^+ and Tb^+ ions produced by the ICP source are selected by the first MS

⁴ All references to the page numbers in Douglas refer to the original page numbers in the top, right-hand corner or top, left-hand corner of each page in Exhibit 1029.

and transported to the collision cell, they readily react with oxygen to form CeO^+ and TbO^+ ions. *Id.* These ions are readily detected by the third MS by scanning the third MS synchronously with the first MS, but with a 16 a.m.u. (atomic mass unit) offset to account for the oxygen mass these ions pick up by reaction in the collision cell. *Id.* Conversely, when the CeO^+ ions produced by the ICP source are selected by the first MS and transported to the collision cell, they do not readily react with oxygen to form CeO_2^+ . *Id.* Thus, when the third MS is synchronously scanned with the first MS with a 16 a.m.u. offset, the CeO^+ ions produced by the ICP source are rejected by the third MS. *See id.* (explaining that the CeO^+ ions generated at the ICP source are rejected because in the collision cell they “react[] to a much lesser extent to produce CeO_2^+ so few ions were detected by the third quadrupole”).

3. *Eiden*

Eiden is a research paper entitled “Beneficial Ion/Molecule Reactions in Elemental Mass Spectrometry.” Ex. 1023, 37.⁵ Eiden discloses that:

A plasma source ion trap (PSIT) mass spectrometer has been modified to incorporate a radiofrequency octopole ion guide/collision cell between the ion source and the mass spectrometer. This modification allows ions sampled from the plasma to undergo reactions prior to mass spectrometric analysis. This capability can obviate the need for chemical or chromatographic separation of the sample, remove mass spectral interferences [sic]

⁵ All references to the page numbers in Eiden refer to the original page numbers in the top, right-hand corner or top, left-hand corner of each page in Exhibit 1023.

and enable formation of analytically useful molecular ions.

Id., Abstract. Eiden's ion trap mass spectrometer utilizes an "inductively coupled plasma (ICP) ion source[]" for elemental/isotopic analysis" and an "RF octopole ion guide/collision cell" and achieves "selective reduction in the intensity of certain problematic ion currents, including Ar^+ , ArO^+ , and Ar_2^+ ." *Id.* at 37–38. Eiden discloses that "[b]y judicious choice of the reagent gas added to the collision cell, undesirable ions in the ion beam sampled from the ICP can be *selectively removed or shifted in mass-to-charge ratio* prior to mass analysis." *Id.* at 38 (emphasis added).

4. Speakman

Speakman is directed to an inductively coupled plasma mass spectrometer (ICP-MS) for use in determining isotopic ratios. Ex. 1024, 1:3–6. Figure 1 of Speakman is reproduced below.

FIG. 1

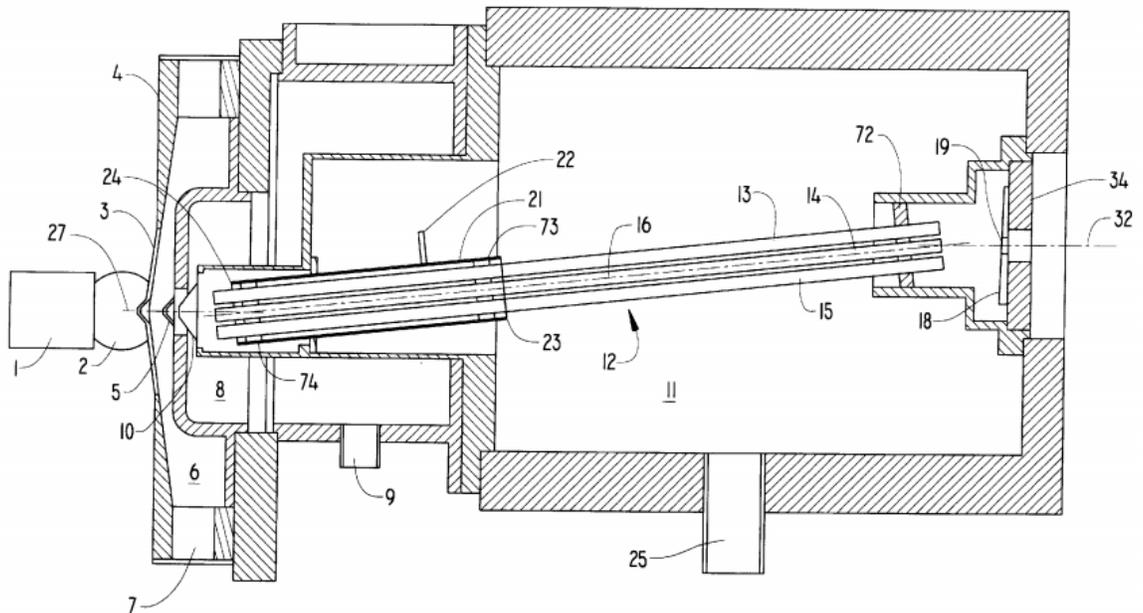


Figure 1 illustrates the interface and ion guiding regions of Speakman's mass spectrometer, including plasma torch 1 for generating plasma 2. Ex. 1024, 8:25–26, 8:42–44. Also depicted are sampling cone 3, skimmer 5, electrostatic lens 10, evacuated chambers 6, 8, and 11, and hexapole ion guide 12, which is partially enclosed in tube 21. *Id.* at 8:45–9:3. Ions traversing ion guide 12 are directed by electrode 18 to pass through aperture 19 into evacuated chamber 20 (not shown), which contains a mass analyzer such as quadrupole mass filter 29. *Id.* at 9:14–25, Fig. 3. Speakman further discloses that other mass analyzers, such as magnetic sector analyzer 38, time-of-flight analyzer 63, and ion-trap mass analyzer 71 can be used instead of quadrupole mass analyzer 29. *Id.* at 8:27–41, 9:56–58, 10:52–53, 11:25–27, Figs. 4–6.

Regardless of the mass analyzer used, Speakman discloses ICP-MSs suffer from

the presence of interfering ion signals, sometimes very intense, due to species generated in the plasma other than the atomic ions characteristic of the elements present in a sample. These interfering ion species comprise atomic or molecular ions such as Ar^+ , Ar^{++} , ArH^+ , ArN^+ etc. which are generated by the plasma in the absence of any introduced sample, and also molecular ions such as oxides, argides and hydride ions formed by reaction of the elements present in a sample with other species present in the sample. Not only do some of these interfering ions mask the signals from atomic ions for which a measurement is required because they have the same mass-to-charge ratio as that of an atomic ion to be measured, but they also result in a very high total ion current, much greater than that typically available from a sample.

Id. at 1:7–26.

5. *Yost*

Yost is a research paper entitled “Tandem Mass Spectrometry (MS/MS) Instrumentation.” Ex. 1015, 1.⁶ Figure 5 of Yost, reproduced below, depicts a Finnigan MAT series 4500 TQMS, of the type that is used in King.

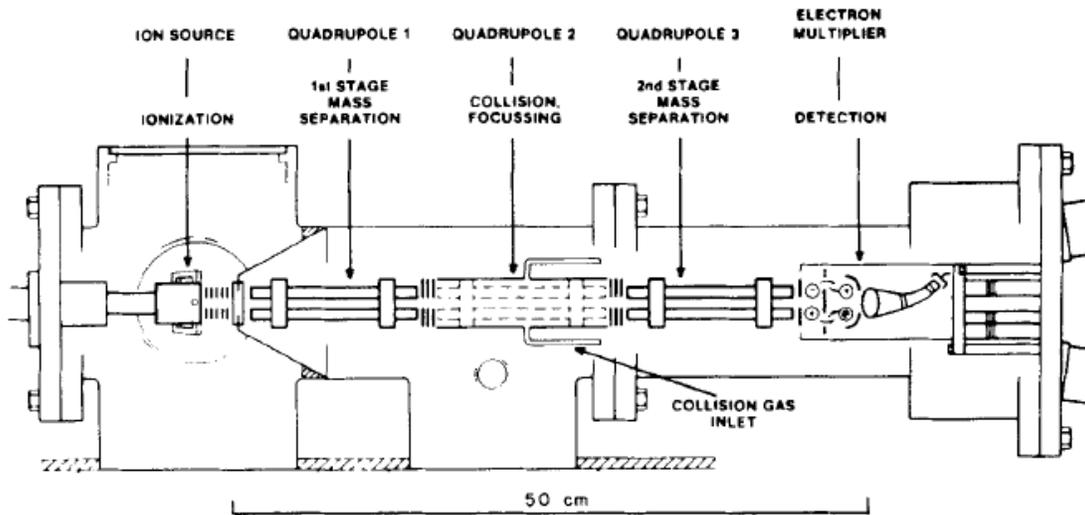


Figure 5 of Yost is a schematic illustration of a Finnigan MAT series 4500 TQMS. *Id.* at 21.

E. Patentability of Claims 13, 15–17, 28–32, 34, 37, 38, 40, 41, 44, and 47–49 over King and Douglas

Petitioner argues these claims are unpatentable as obvious over the combination of King and Douglas. Pet. 41–50. For purposes of determining whether to institute, we focus on Petitioner’s contentions with respect to claim 28.

⁶ All references to the page numbers in Yost refer to the original page numbers in the top, right-hand corner or top, left-hand corner of each page in Exhibit 1015.

1. Reasons to Combine King and Douglas

Petitioner's analysis for this ground relies on a combination of King and Douglas and is based on modifying King's TQMS to use Douglas's ICP ion source rather than King's glow discharge ion source. *See* Pet. 43; Ex. 1004 ¶ 86. Petitioner argues a person skilled in the art would have combined the teachings of King and Douglas in this way because both references teach using TQMSs to perform elemental analysis and because both references address the problem of reducing interferences in elemental analysis. Pet. 42 (citing Ex. 1029, 47–49; Ex. 1037, 172; Ex. 1004 ¶ 80). Petitioner further argues that King teaches the problem of interferences exists in TQMSs having both glow discharge and ICP ion sources and teaches a method (i.e., CID) for removing interferences in TQMSs having glow discharge ion sources. *Id.* at 43 (citing Ex. 1037, 173; Ex. 1004 ¶¶ 72, 73, 86). Relying on the testimony of Dr. Yost, Petitioner argues a person skilled in the art interested in solving this interference problem would have consulted mass spectrometry references having a variety of ion sources and would have modified King's TQMS to include Douglas's ICP source to explore using King's CID method of removing interferences in TQMSs having ICP sources. *Id.* at 42 (citing Ex. 1004 ¶ 80).

Patent Owner argues Petitioner's proposed combination is deficient because Petitioner has failed to provide sufficient reasoning to combine the teachings of King and Douglas, especially as to *why* a person skilled in the art would have combined these teachings, and has failed to argue the proposed combination would have had a reasonable expectation of success. Prelim. Resp. 50–53.

At this stage of the proceeding, we are persuaded that Petitioner has

provided sufficient reasoning to combine the teachings of King and Douglas. As discussed above, King discloses a CID method of solving the elemental analysis interference problem using a TQMS having a glow discharge ion source, and Douglas discloses a different method of solving the same elemental analysis interference problem using a TQMS having an ICP ion source. Petitioner argues a person skilled in the art would have modified King's TQMS to use an ICP ion source to explore the efficacy of King's CID interference reduction method on TQMSs having ICP ion sources. *See* Pet. 42; Ex. 1004 ¶ 80. Petitioner's proposed combination, therefore, falls under any of a number of rubrics that indicate the claimed invention would have been obvious to a person skilled in the art, including using a technique (i.e., CID) that has been used to improve one device (King's TQMS with a glow discharge source) to improve similar devices (King's TQMS modified to have an ICP source) in the same way. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416–17 (2007).

At this stage of the proceeding, we do not find that this proposed combination fails simply because Petitioner has not alleged that a person skilled in the art would have found it had a reasonable expectation of success. The U.S. Supreme Court has rejected overly rigid, formalistic approaches to determining obviousness, finding “[r]igid preventative rules that deny factfinders recourse to common sense . . . are neither necessary under our case law nor consistent with it.” *KSR*, 550 U.S. at 421. Thus, to demonstrate obviousness, a petitioner need not slavishly repeat, like some talismanic mantra, that any and every proposed combination has a reasonable expectation of success. Such a “rigid preventative rule[]” would deny recourse to common sense and, in this case, to the common sense

notion that TQMSs can be modified to receive ions from different ion sources. Indeed, King teaches doing exactly that—replacing the ion source for the Finnigan MAT series 4500 TQMS with “[a] glow discharge ion source, designed and built in our laboratory.” Ex. 1037, 173; *see also In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009) (“This court cannot, in the face of *KSR*, cling to formalistic rules for obviousness . . . or discount the significant abilities of artisans of ordinary skill in an advanced area of art.”).

2. Claim 28

Claim 28 is an independent claim for a mass spectrometer having an inductively coupled plasma ion source for generating ions from a sample, including first atomic ions having a first mass-to-charge ratio and artefact ions having a mass-to-charge ratio that interferes with the first mass-to-charge ratio. Ex. 1001, 10:43–48.

Petitioner argues the combination of King and Douglas teaches all of the limitations recited in claim 28 because both references disclose using a TQMS and because Douglas discloses TQMSs can receive ions from an ICP ion source. Pet. 43. According to Dr. Yost, a person skilled in the art would have known an ICP source could have been used to generate ions for King’s TQMS, that an ICP ion source would have generated both analyte and artefact ions having the same mass-to-charge ratio, and that a TQMS having an ICP source could have been used to remove artefact ions using King’s CID method. Ex. 1004 ¶¶ 72, 73 (cited by Pet. 43).

Patent Owner argues that Petitioner has failed to demonstrate the combination of King and Douglas discloses a mass spectrometer having an ICP ion source that generates first atomic ions and artefact ions having an interfering (i.e., the same) mass-to-charge ratio. Prelim. Resp. 48.

Specifically, Patent Owner argues that Douglas does not remedy King's purported deficiencies because Douglas fails to disclose an ICP source generates both atomic ions and artefact ions having the same (interfering) mass-to-charge ratio. *Id.*

At this stage of the proceeding, we are persuaded by Petitioner's analysis that the combination of King and Douglas discloses a mass spectrometer having an ICP ion source. Petitioner's analysis relies on Dr. Yost's testimony that a person skilled in the art would have known that Douglas's ICP source could be used in the experiments of King to remove artefact ions. *See* Pet. 43 (citing Ex. 1004 ¶¶ 72–73). Dr. Yost testifies that such a person "would have understood that ions generated from an ICP source include analyte ions and artefact ions having the same mass-to-charge ratio." Ex. 1004 ¶ 73. At this stage of the proceeding, we find this testimony credible because the prior art provides numerous examples of ICP sources producing both analyte ions and interfering artefact ions. *See Randall Mfg. v. Rea*, 733 F.3d 1355, 1362 (Fed. Cir. 2013) (recognizing that prior art may be considered as "part of the store of public knowledge that must be consulted when considering whether a claimed invention would have been obvious"). For example, Douglas teaches ICP sources can produce artefact ions such as ArO^+ , ArCl^+ , and CeO^+ in addition to analyte ions. Ex. 1029, 47. Similarly, Speakman teaches that ICP sources can produce "molecular ions such as oxides, argides, and hydride ions formed by reaction of the elements present in the sample with other species present in the sample" and that these "interfering ions [can] mask the signals from atomic ions for which a measurement is required because they have the same mass-to-charge ratio as that of an atomic ion to be measured." Ex. 1024,

1:14–24.

Claim 28 further requires the mass spectrometer to have an ion optical device disposed to receive at least a portion of an ion beam generated by the ion source, and configured to mass select at least a portion of the ion beam generated by the ion source at the first mass-to-charge ratio, thereby removing from the ion beam ions not having the first mass-to-charge ratio. Ex. 1001, 10:49–54.

Petitioner argues King discloses this limitation by disclosing the first quadrupole Q1 can be run in mass selection mode to select a portion of the source ion beam at a first mass-to-charge ratio (e.g., at $m/z = 81$). *See* Pet. 38, 44 (citing Ex. 1037, 182–83; Ex. 1004 ¶¶ 74, 87–88). We are persuaded, at this stage of the proceeding, that the combination of King and Douglas teaches this limitation.

Claim 28 further requires the mass spectrometer to have a collision cell disposed to receive at least a portion of a mass selected ion beam from the ion optical device and configured to remove artefact ions having a mass-to-charge ratio that interferes with the first mass-to-charge ratio. Ex. 1001, 10:55–59.

Petitioner argues King discloses this limitation by disclosing a collision cell, pressurized with argon, that receives a mass selected ion beam from Q1 (e.g., at $m/z = 81$) and dissociates polyatomic ions having the selected mass-to-charge ratio. *See* Pet. 38–39, 44 (citing Ex. 1037, 174, 182–83; Ex. 1004 ¶¶ 75, 87–88). We are persuaded, at this stage of the proceeding, that the combination of King and Douglas teaches this limitation.

Claim 28 further requires the mass spectrometer's ion optical device to be configured substantially to minimize the formation in the collision cell of interfering artefact ions having the first mass-to-charge ratio. Ex. 1001, 10:59–62.

Petitioner, relying on the testimony of Dr. Yost, argues King teaches or suggests this limitation because a person skilled in the art would have understood that because Q1 (ion optical device) selects and transports to the collision cell only ions having a particular mass-to-charge ratio (e.g., at $m/z = 81$), any new ions formed in the collision cell would not have this selected mass-to-charge ratio. *See* Pet. 39, 44 (citing Ex. 1037, 174, 182–83; Ex. 1004 ¶¶ 75, 87–88). Therefore, according to Petitioner, Q1 substantially minimizes the formation of interfering artefact ions in the collision cell. *See id.* We are persuaded, at this stage of the proceeding, that the combination of King and Douglas teaches this limitation.

Finally, claim 28 requires the mass spectrometer to have a mass analyzer disposed to receive at least a portion of the mass selected ion beam from the collision cell, and configured to mass analyze the received ion beam at the same mass-to-charge ratio as the ion optical device, wherein the mass analyzer is configured to detect the first atomic ions when the same mass-to-charge ratio is the first mass-to-charge ratio. Ex. 1001, 10:63–11:2.

Petitioner presents two alternative arguments with respect to this limitation. First, Petitioner argues King alone discloses this limitation. *See* Pet. 39–40, 44–45. In particular, relying on the testimony of Dr. Yost, Petitioner argues that King's quadrupole Q1 (ion optical device) mass selects and delivers to the collision cell a portion of the ion beam at a first mass-to-charge ratio (e.g., at $m/z = 81$), and that King's quadrupole Q3

(mass analyzer) mass analyzes ions received from the collision cell over a range of mass-to-charge ratios that includes the first mass-to-charge ratio. *Id.* at 40 (citing Ex. 1037, 182–83; Ex. 1004 ¶ 76). Petitioner argues that, when Q3 mass analyzes ions received from the collision cell at the first mass-to-charge ratio, it is doing so at the same mass-to-charge ratio selected by ion optical device Q1. *Id.* (citing Ex. 1004 ¶ 76).

Although Patent Owner does not dispute Petitioner’s contentions in the context of Petitioner’s claim 28 analysis, Patent Owner does argue that King does not disclose that Q3 (mass analyzer) performs mass analysis at the same mass-to-charge ratio selected by Q1 (ion optical device) in the context of Petitioner’s claim 13 analysis. Prelim. Resp. 44, 48–54. In particular, Patent Owner argues that King does not teach or suggest this limitation because Q3 performs mass analysis over a range of mass-to-charge ratios rather than at the same mass-to-charge ratio selected by Q1. *Id.*

At this stage of the proceeding, we are persuaded by Petitioner’s analysis that King teaches Q3 performs mass analysis at the same mass-to-charge ratio as Q1 because the range over which Q3 performs mass analysis includes the mass-to-charge ratio selected by Q1. *See* Ex. 1037, 182–83, Fig. 6. As Dr. Yost testifies, “when the third quadrupole is mass analyzing at the first mass-to-charge ratio of 81, it is mass analyzing at the same mass-to-charge ratio as that of the first quadrupole.” Ex. 1004 ¶ 76 (citing Ex. 1037, 182–83). This is shown, for example, in Figure 6 of King, where the daughter spectrum of ions selected by Q1 to have a mass-to-charge ratio of 81 is obtained, in part, by Q3 selecting ions having the same mass-to-charge ratio of 81 for detection and counting. Ex. 1037, 182.

Second, Petitioner argues the combination of King and Douglas discloses this limitation. *See* Pet. 44–45. In particular, Petitioner argues that Douglas discloses a first quadrupole that mass selects and delivers to a collision cell ions having a first mass-to-charge ratio and a third quadrupole that is synchronously scanned with the first quadrupole to mass select ions received from the collision cell having a 16 a.m.u. offset from the selected mass-to-charge ratio. *Id.* at 45 (citing Ex. 1029, 47–48; Ex. 1004 ¶ 89). Relying on the testimony of Dr. Yost, Petitioner argues a person skilled in the art would have found it obvious to synchronously scan King’s Q1 and Q3 quadrupoles as taught by Douglas, but at a 0 a.m.u. offset rather than a 16 a.m.u. offset, in order to detect atomic ions in the sample. *Id.* (citing Ex. 1004 ¶ 89). According to Dr. Yost, Douglas teaches both “a collision-induced dissociation experiment in which the third quadrupole is the ‘mass analyzer’ at the first mass-to-charge ratio of atomic ions of interest” and “an ion-molecule reaction experiment where the third quadrupole is scanned synchronously with the first quadrupole” but at a 16 a.m.u. offset. Ex. 1004 ¶ 89.

Patent Owner argues the combination of King and Douglas does not teach this limitation because Douglas teaches the third quadrupole scans at a mass-to-charge ratio offset from the ratio selected by the first quadrupole and, therefore, fails to remedy the purported deficiencies in King. Prelim. Resp. 48–49. As explained above, at this stage of the proceeding, we do not find King’s disclosure to be deficient in this regard.

Patent Owner also argues that Petitioner fails to provide adequate reasoning to combine the teachings of King and Douglas because King discloses a daughter scan, Douglas discloses a neutral gain scan with a

positive offset, and neither of the references discloses a neutral loss of zero scan. Prelim. Resp. 53–54. Patent Owner argues that Petitioner fails not only to explain why a person skilled in the art would have combined the teachings of King and Douglas, but where a person skilled in the art would come up with the idea of doing a neutral loss of zero scan as Petitioner contends. *Id.* at 54.

At this stage of the proceeding, we are persuaded that Petitioner has provided sufficient reasoning not only to combine the teachings of King and Douglas, as explained in section II.E.1, *supra*, but also why such a person would have tried a neutral loss of zero scan. In particular, Dr. Yost testifies that King teaches a daughter scan in which a first quadrupole “mass select[s] at the first mass-to-charge ratio . . . atomic ions of interest in a collision-induced dissociation experiment,” and in which a third quadrupole mass selects “at the same mass-to-charge ratio as that of the first quadrupole” during at least a portion of the daughter scan. Ex. 1004 ¶ 89 (citing Ex. 1037, 182–83). Dr. Yost further testifies that Douglas teaches both “a collision-induced dissociation experiment” and an “ion-molecule reaction experiment where the third quadrupole is scanned synchronously with the first quadrupole. . . . at 16 amu offset (neutral gain scan).” *Id.* (citing Ex. 1029, 47–48). As discussed in section II.D.2, *supra*, Douglas scans the first/third quadrupoles at a 16 a.m.u. offset because Douglas detects the reaction product of the atomic ion of interest (e.g., CeO^+) in the ion-molecule reaction experiment, rather than the atomic ion of interest itself (e.g., Ce^+). *See* Ex. 1029, 48. We are persuaded, at this stage of the proceeding, that a person skilled in the art would have known that using Douglas’s first/third quadrupole scanning technique in a collision-induced

dissociation experiment (as taught by both King and Douglas) would have required scanning the first/third quadrupoles at the same mass-to-charge ratio to detect the atomic ions of interest selected by the first quadrupole, rather than at the mass offset that would be needed to detect the atomic ion reaction product in an ion-molecule reaction experiment.

For the reasons discussed above, after considering the arguments and evidence presented by both Petitioner and Patent Owner, we find Petitioner has demonstrated a reasonable likelihood that it will prevail on its challenge that claim 28 is unpatentable over the combined teachings of King and Douglas.

F. Denial Under 35 U.S.C. § 325(d)

Petitioner acknowledges that King was cited in an Information Disclosure Statement in the reissue prosecution of the '386 patent, Douglas is cited as admitted prior art in the specification, and Eiden was cited by the Examiner, but Petitioner contends that none of these references was substantively discussed during the original or reissue prosecution. Pet. 32, 41, 50–51; *see also* Ex. 1001, [56]. Petitioner further acknowledges that a European counterpart to Speakman was substantively discussed in the original prosecution, but contends that the discussion focused on the combined teachings of Speakman with two other references, rather than the combined teachings of Speakman with King and Douglas. *Id.* at 52–53.

Patent Owner does not dispute Petitioner's contention that the Examiner did not discuss the disclosures of King, Douglas, Eiden, or the combined disclosures of King, Douglas, and Speakman in the original or reissue prosecutions. Nonetheless, Patent Owner argues we should exercise our discretion to deny the Petition under 35 U.S.C. § 325(d) because the

references cited in the challenges based on anticipation by King, obviousness over King and Douglas, obviousness over King, Douglas, and Eiden, obviousness over King, Douglas, and Speakman, or obvious over King, Douglas, Speakman, and Yost “were before the Examiner during original and/or reissue prosecution.” Prelim. Resp. 38.

The Director has the discretion, delegated to the Board, to “reject [a] petition or request because [] the same or substantially the same prior art or arguments previously were presented to the Office.” 35 U.S.C. § 325(d); 37 C.F.R. §42.4(a). The Board has determined that it has discretion to institute or deny any petition for *inter partes* review under 35 U.S.C. § 314(a) and, in doing so, may consider whether the petition is based on the same or substantially the same prior art or arguments previously presented to the Office as set forth in 35 U.S.C. § 325(d). *See General Plastic Industrial Co. v. Canon Kabushiki Kaisha*, Case IPR2016-01357, slip. op. (PTAB Sept. 6, 2017) Paper 19, 18–19.

Although we have the discretion to deny the instant petition, as Patent Owner requests, we decline to do so because we find the Office has not previously considered the specific challenges of anticipation by King, obviousness over King and Douglas, obviousness over King, Douglas, and Eiden, obviousness over King, Douglas, and Speakman, or obviousness over King, Douglas, Speakman, and Yost. *See* Pet. 4.

G. Denial as Unconstitutional

Patent Owner “reserves its right to move for these proceedings to be terminated, to the extent the Supreme Court decides that *inter partes* review is unconstitutional in *Oil States Energy Servs., LLC v. Greene’s Energy Grp., LLC*, 137 S. Ct. 2239 (2017).” Prelim. Resp. 64. On April 24, 2018,

the Supreme Court held that “*inter partes* review does not violate Article III or the Seventh Amendment” of the Constitution, rendering Patent Owner’s reservation moot. *Oil States Energy Servs., LLC v. Greene’s Energy Grp., LLC*, 138 S. Ct 1365, 1379 (2018) (emphasis added).

III. CONCLUSION

We have reviewed the Petition and Patent Owner’s Preliminary Response to the same. We have considered all of the evidence and arguments presented by Petitioner and Patent Owner and have weighed and assessed the entirety of this evidence as a whole. We find, on this record, Petitioner has demonstrated a reasonable likelihood of showing at least one claim of the ’386 patent is unpatentable over the prior art.

Accordingly, we institute *inter partes* review of the ’386 patent on all claims and all grounds presented in the Petition. *See SAS Institute Inc. v. Iancu*, 138 S. Ct. 1348, 1359–60 (2018) (holding that a decision to institute under 35 U.S.C. § 314 may not institute on fewer than all claims challenged in the petition); *see also* “Guidance on the impact of SAS on AIA trial proceedings” (stating that, “if the PTAB institutes a trial, the PTAB will institute on all challenges raised in the petition”).⁷

We have not yet made a final determination with respect to the patentability of any claim or the construction of any claim term.

⁷ <https://www.uspto.gov/patents-application-process/patent-trial-and-appeal-board/trials/guidance-impact-sas-aia-trial>.

IV. ORDER

It is ORDERED that, pursuant to 35 U.S.C. § 314, an *inter partes* review is hereby instituted on all claims and all grounds raised in the Petition; and

FURTHER ORDERED that, pursuant to 35 U.S.C. § 314(c) and 37 C.F.R. § 42.4, notice is hereby given of the institution of a trial commencing on the entry date of this Decision.

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