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Paper No. 23
Filed: June 18, 2018

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 IPR2018-00313
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(a)

I. INTRODUCTION

A. Background

Agilent Technologies, Inc. ("Petitioner"), filed a Petition (Paper 1, "Pet.") requesting *inter partes* review of claims 1, 5–11, 13–21, 23, 24, 28–35, and 37–50 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"), disclaimed claims 9, 11, 21, and 24 (Ex. 2001), and filed a Preliminary Response (Paper 13 ("Prelim. Resp.")). Consequently, only claims 1, 5–8, 10, 13–20, 23, 28–35, and 37–50 ("the challenged claims") remain for our consideration.

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 *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 IPR2018-00298 (PTAB) (also challenging the '386 patent); 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 6, 2.

C. Evidence Relied Upon

Reference	**Publication Date**[1]	**Exhibit**
Johnston, Mark, "Energy Filtering in Triple Quadrupole MS/MS," Application Report, Finnigan MAT, No. 203, 1–10 (1984) ("Johnston")	1984	1022
Whitehouse et al., U.S. Patent No. 6,011,259	Jan. 4, 2000	1025
Douglas, D.J., "Some Current Perspectives on ICP-MS," Canadian J. of Spectroscopy, Vol. 34, No. 2, 38–49 (1989) ("Douglas")	June 1989	1029
Louris et. al, "New Scan Modes Accessed with a Hybrid Mass Spectrometer," Analytical Chemistry, Vol. 57, No. 14, 2918–2924 (1985) ("Louris")	Dec. 1985	1030
Rowan, J.T. and Houk, R.S., "Attenuation of Polyatomic Ion Interferences in Inductively Coupled Plasma Mass Spectrometry by Gas-Phase Collisions," Applied Spectroscopy, Vol. 43, No. 6, 976–980 (1989) ("Rowan")	Aug. 1989	1033
Kishi, Yoko, "A Benchtop Inductively Coupled Plasma Mass Spectrometer," Hewlett-Packard Journal, Article 9, 1–10, (1997)	Aug. 1997	1034
Tanner et al., U.S. Patent No. 6,140,638	Oct. 31, 2000	1036

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

[1] Petitioner relies on the Declaration of Sylvia Hall-Ellis, Ph.D., to establish the publication dates of Exhibits 1029, 1030, 1033, and 1034. *See* Ex. 1008 ¶ 26.

D. Asserted Grounds of Unpatentability[2]

Petitioner asserts the following grounds of unpatentability:

References	Basis	Claims Challenged
Douglas and Johnston	§ 103(a)	13, 15–17, 28–32, 34, 37, 38, 40, 41, and 47–50
Douglas, Johnston, and Whitehouse	§ 103(a)	18–20 and 33
Douglas and Louris	§ 103(a)	13, 15–17, 28–32, 34, 37, 38, 40, 41, and 47–50
Douglas, Louris, and Whitehouse	§ 103(a)	18–20 and 33
Turner and Rowan	§ 103(a)	13 and 28
Turner, Rowan, and Kishi	§ 103(a)	1, 5–8, 10, 14, 16, 17, 23, 31–35, and 39–50

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 remove 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

[2] As noted above, Patent Owner has disclaimed claims 9, 11, 21, and 24. *See* Ex. 2001. Accordingly, claims 9, 11, 21, and 24 no longer remain for our consideration.

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 on "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 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 ion[s] 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.

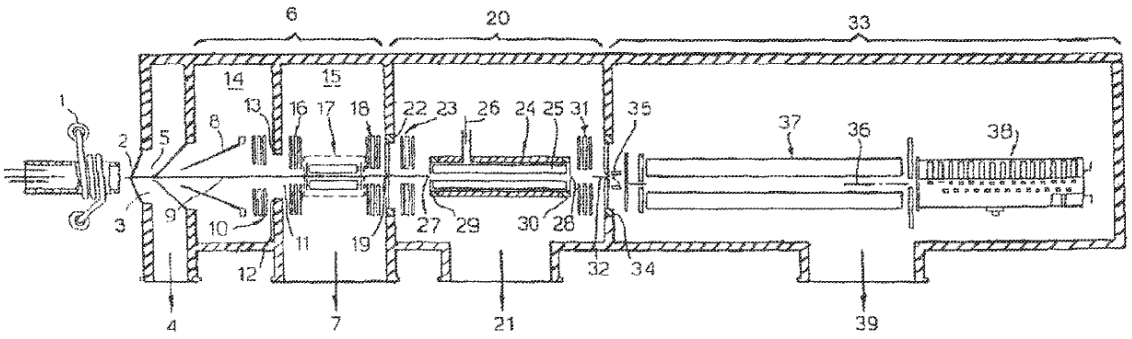


Figure 2 is a schematic illustration of an ICPMS according to the invention described in the '386 patent. An ion source, such as inductively coupled plasma (ICP) ion source 1 generates ions that pass through sampling aperture 2 into expansion chamber 3, which is evacuated by a rotary pump through port 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 aperature 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 that is "chosen for its capacity to remove, via a mechanism such as attachment or fragmentation, unwanted molecular ions from the ion beam." *Id.* at 7:48–52. 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, "[b]y careful control of the conditions in the collision cell," including selection of the collision gas and pressure, "i[t] 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 that is evacuated by a

turbomolecular pump through port 39. *Id.* at 7:63–67, 8:24–27. Deflector lens 35 deflects ions passing through aperature 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 charge/mass (m/e) or range of charge/mass 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, 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. 28–34. 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 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. 32–33 (citing Ex. 1001, Abstract, 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 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 an 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. 28, n.9. 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. *See* 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. 29. 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.*

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. 29 (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. Douglas

Douglas is a research paper reviewing the development of inductively coupled plasma (ICP) mass spectrometry (MS) or ICP-MS. Ex. 1029, 39 (Abstract).[3] Douglas identifies the problem of ionic interferences in obtaining accurate mass spectra and explores using a triple quadrupole mass spectrometer (TQMS) having an ICP source 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 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

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

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 they "react[] to a much lesser extent to produce CeO_2^+ so few ions were detected by the third quadrupole").

2. *Johnston*

Johnston is an application report published by Finnigan MAT entitled, "Energy Filtering in Triple Quadrupole MS/MS." Ex. 1022, Title.[4] Johnston discloses current work (circa 1984) using TQMS's that involves "collision-activated dissociation (CAD) to enhance the formation of new ion species" in the middle MS of a TQMS. *Id.* at 1. Figure 1 of Johnston, reproduced below, depicts the principle of CAD.

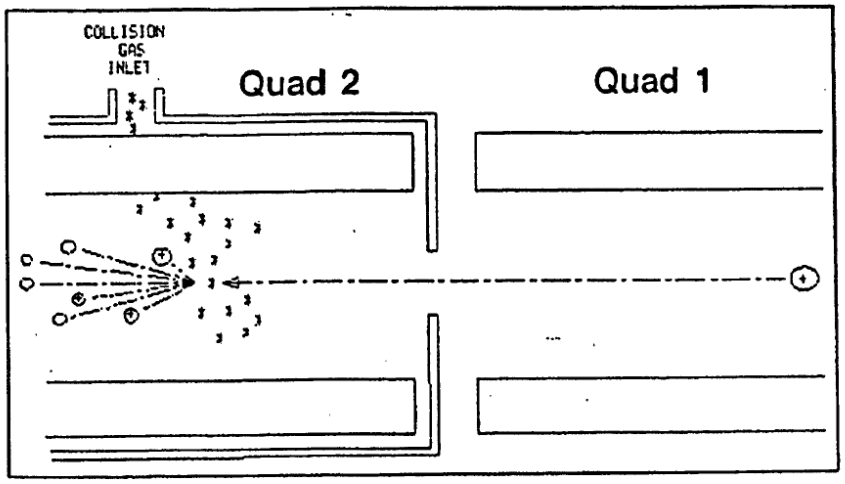


Figure 1 of Johnston depicts the collision-activated decomposition of a parent ion into daughter ions. *Id.* A parent ion selected in a first stage of mass analysis at quadrupole 1 collides with a collision gas filling a collision

[4] All references to the page numbers in Johnston refer to the original page numbers in the top right- or left-hand corner of each page in Exhibit 1022.

cell that surrounds quadrupole 2, resulting in the fragmentation of the parent ion into daughter ions and neutrals. *Id.*

Johnston discloses various studies that can be performed using a TQMS whose middle MS is used as a collision cell, including a neutral loss study. *Id.* at 1–2. In a neutral loss study, the first and third quadrupoles or "mass analyzers are scanned in parallel," that is, "[b]oth are scanned at the same rate over mass ranges of the same width." *Id.* at 1. In general, the first mass analyzer "is offset from the second mass analyzer by a selected mass" that "corresponds to the mass of the neutral moiety that must be ejected from an ion upon collision in order for it to be passed by the second analyzer and detected." *Id.* However, for certain stable analyte ions, Johnston discloses using the CAD mechanism "to remove interferences and achieve a better signal-to-noise ratio" in so-called "neutral loss of zero" studies. *Id.* at 2.

A TQMS configuration for performing neutral loss of zero studies is depicted in Figure 4 of Johnston, which is reproduced below.

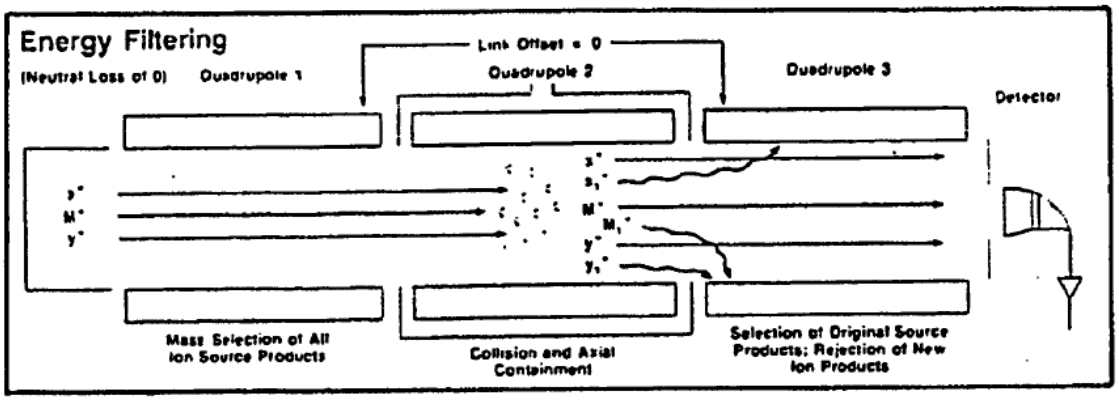


Figure 4. Energy filtering (Neutral loss of Zero). Both mass analyzers are scanned over the same mass range at the same time. Only ions which survive collisions intact are transmitted through the analyzer.

Figure 4 of Johnston is a schematic illustration of a TQMS used in a neutral loss of zero study showing a "Link Offset" of zero between Quadrupole 1 and Quadrupole 3. In neutral loss of zero studies, "both mass analyzers [i.e.,

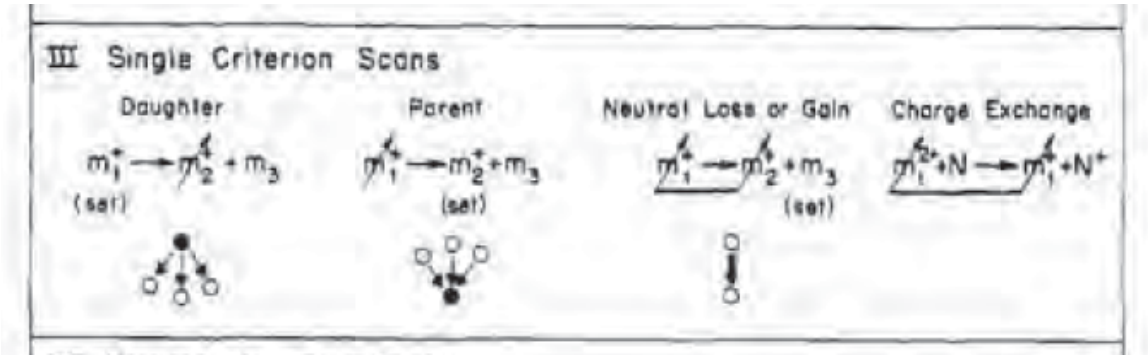
Quadrupole 1 and Quadrupole 3] must be scanned over the same mass range at same time so that only unfragmented ions may pass completely through the system." *Id.* In such studies, the collision cell (i.e., Quadrupole 2) filters out "interferences . . . by fragmentation, while the more stable [analyte] species pass through the collision cell intact and are detected." *Id.* This is because interfering ions or "[i]ons that lose any neutral fragment will be rejected by the final mass analyzer." *Id.*

3. Louris

Louris is a research paper disclosing "several new types of tandem mass spectrometry (MS/MS) experiments" performed on a hybrid mass spectrometer. Ex. 1030, 2918 (Abstract).[5] The hybrid mass spectrometer consists of a Finnigan MAT 212 double focusing mass spectrometer (BE), a quadrupole collision cell (Q1) and a quadrupole mass analyzer (Q2). *Id.* at 2918. Ions mass selected by BE are focused onto the entrance aperature of Q1. *Id.* There, "the ions undergo collision-induced dissociation," and the fragment ions are passed into "Q2 where they are mass analyzed prior to detection." *Id.*

Table I of Louris depicts different scan types that can be performed with a mass spectrometer, including a "Neutral Loss or Gain" scan. *Id.* at 2919. Although Louris describes performing these scans with the hybrid mass spectrometer described above, Louris describes the information presented in Table 1 as being "independent of the type of spectrometer used." *Id.* Louris schematically illustrates the reaction mechanism studied by a Neutral Loss or Gain scan in section III of Table I, reproduced below.

[5] All references to the page numbers in Louris refer to the original page numbers in the top right- or left-hand corner of each page in Exhibit 1030.



Section III of Table I is a schematic illustration of the reaction mechanism studied by a Neutral Loss or Gain scan. *Id.* at 2919. Ions m_1^+, m_2^+, and neutral m_3 refer to the mass/charge ratios of "the parent, the daughter species, and the neutral fragment, respectively." *Id.* Although the depicted reaction mechanism is dissociative (i.e., ion m_1^+ dissociates in the collision cell into ion m_2^+ and neutral m_3), Louris cautions that no mass relationship is to be implied between ions m_1^+ and m_2^+ because "associative ion/molecule reactions are not excluded." *Id.*

In addition to the Neutral Loss or Gain scan described above, Louris discloses experiments that "monitor unconverted reactant (together with products that have the same mass-to-charge ratio as the reactant)." *Id.* at 2924. Such experiments yield "a spectrum of ions [that] survive the experimental probe." *Id.* (citing, *inter alia*, Johnston). Louris discloses such experiments are advantageous because they represent "all loss (reaction) mechanisms cumulatively. The condition $m_3 = 0$ allows one to combine these processes with those already given in Table I and so allows a still more general classification of MS/MS processes." *Id.*

4. Whitehouse

Whitehouse "relates to the field of mass analysis and the apparatus and methods used in analyzing chemical species." Ex. 1025, 1:27–28. Mass

analysis involves "mass selection, fragmentation and subsequent mass analysis steps [that] can be achieved with multiple mass analyzers used in series." *Id.* at 2:21–23. Whitehouse discloses:

> Multiple mass analyzers, such as triple quadrupoles, which are used to achieve selective CID [Collison Induced Dissociation] collision have been commercially available for some time and hence the term MS/MS has become commonly used to mean a mass selection step followed by an[] ion fragmentation step, followed by a mass analysis step of the fragment ions.

Id. at 2:24–30.

Whitehouse's multiple mass analyzer is depicted in Figure 1, which is reproduced below.

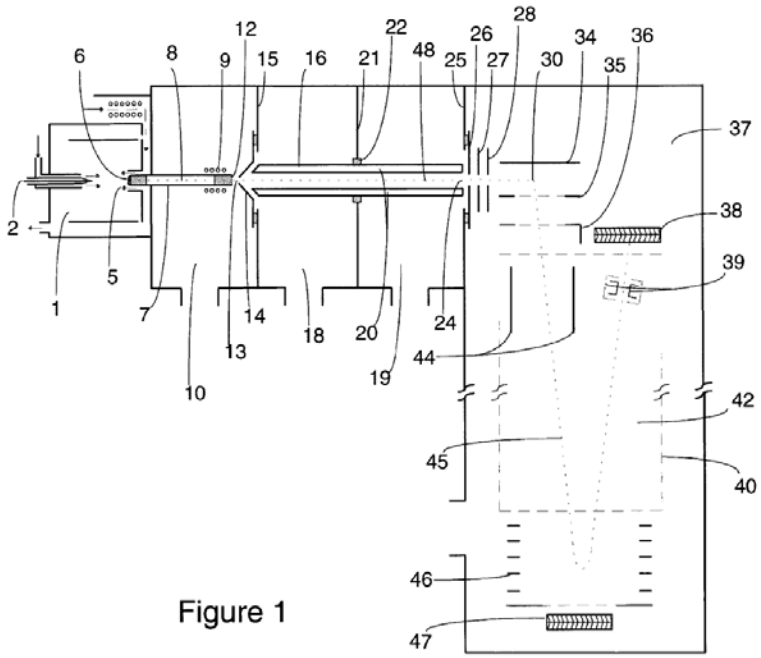


Figure 1

Figure 1 of Whitehouse is a schematic illustration of a multiple mass analyzer that includes Electrospray ion source 1, multipole ion guide 16 in vacuum chambers 18 and 19, electrostatic lenses 34–36, and TOF mass analyzer 42/47. *Id.* at 9:61–65, 11:6–9, 11:21–24, 11:62–12:5. Multiple ion guide 16 can be a quadrupole. *Id.* at 11:50–52.

Whitehouse discloses that various Atmospheric Pressure Ion (API) sources can be "interfaced to mass analyzers include Electrospray, nebulizer assisted Electrospray, Atmospheric Pressure Chemical Ionization, Inductively Coupled Plasma (ICP) and Glow Discharge ion sources." *Id.* at 10:36–40. Whitehouse further discloses that "[o]ne or more vacuum pumping stages have typically been used with various API/MS designs," and that "[t]ypically API/TOF mass spectrometer instruments include three or more vacuum pumping stages to remove background gas exiting from the API source orifice into vacuum." *Id.* at 10:50–52, 10:55–58. Whitehouse also discloses its "vacuum stage partitions and ion optics . . . are designed to provide an efficient means of transporting ions in the mass analyzer . . . while neutral background gas is pumped away." *Id.* at 10:45–50.

5. Tanner

Tanner relates to a "method and apparatus for resolving ion signals for an analyte ion from ion signals caused by isobaric and non-spectral interferences." Ex. 1036, 1:9–11. Isobaric and spectral interferences are ions that have "the same nominal mass-to-charge (m/z) value" or that "have an m/z value which cannot be resolved from that of the analyte ion by the mass spectrometer being used." *Id.* at 1:17–22. Tanner discloses "[s]uch interferences are common in many types of mass spectrometers," including those that use plasma, glow discharge, electrospray, and ion spray sources. *Id.* at 1:22–27.

Tanner discloses several embodiments of an apparatus for removing isobaric interferences, including embodiments depicted in Figures 1 and 21. *Id.* at 2:45–46, 3:37–38. Figure 21 of Tanner is reproduced below.

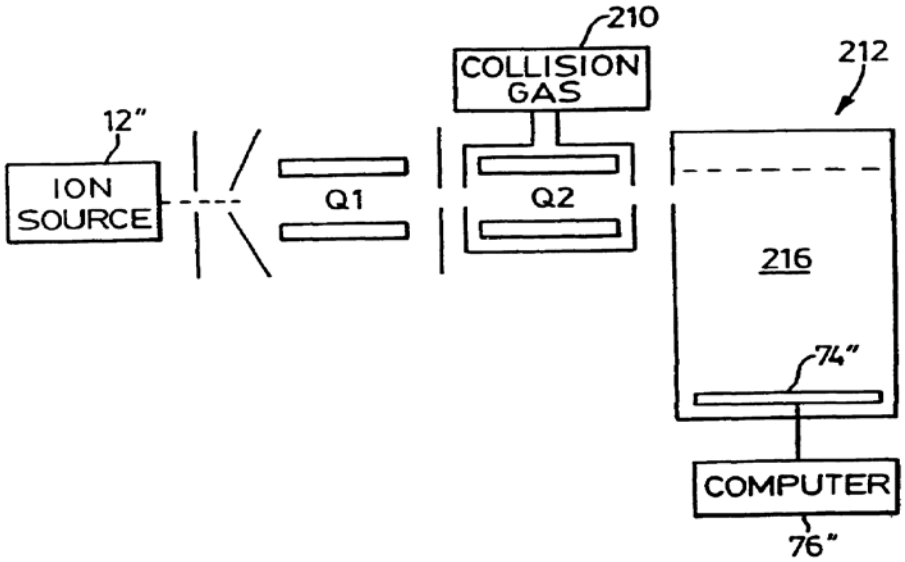


Figure 21 of Tanner is a schematic illustration of a mass spectrometer used to remove isobaric interferences. *Id.* at 3:37–38. The mass spectrometer includes ion source 12″, resolving mass spectrometer Q1, collision cell Q2, and TOF mass spectrometer 212. *Id.* at 11:54–67. Ion source 12″ can be "a conventional inductively coupled plasma source, glow discharge source, or any other type of well-known ion source." *Id.* at 3:57–59, 11:52–54. Mass spectrometer Q1 and collision cell Q2 "are typically . . . quadrupole mass spectrometers." *Id.* at 11:60–62. Collision cell Q2 is "supplied with collision gas from source 210." *Id.* at 11:60. The collision gas can be, for example, a mixture of hydrogen and helium. *Id.* at 10:67–11:1.

When in operation, Tanner's ion source 12″ "provides a stream of ions for analysis into . . . resolving mass spectrometer Q1," which "selects parent ions of interest" and injects them into "standard collision cell Q2." *Id.* at 11:55–60. Collision cell Q2 fragments the parent ions into "daughter

ions, which are injected into a conventional time-of-flight (TOF) mass spectrometer 212 for detection" and subsequent analysis. *Id.* at 63–67.

Tanner discloses the "[f]ragmentation of polyatomic ions in the collision cell can give rise to further or enhanced isobaric (spectral) interferences." *Id.* at 1:39–40. Additionally, "[r]eaction of plasma ions with the collision gas . . . may also give rise to spectral background interference, as can contaminant species from the collision cell or vacuum chamber or . . . collision gas." *Id.* at 1:39–45. Tanner describes those reactions in the collision cell that can give rise to isobaric interferences as "varied and complex" but discloses the collision cell can be operated in a manner that "reject[s] precursor or intermediate ions . . . before the reaction sequence produces ions which form isobaric interferences." *Id.* at 6:34–40. In particular, Tanner discloses operating the collision cell as a bandpass filter because "the intermediate ions to be rejected tend to occur both below and above the desired mass to be observed." *Id.* at 6:65–7:3. The width or window of this bandpass filter is "chosen with respect to the chemistry involved in each particular case" and depends on such factors as "the masses of the desired ions to be observed, the type of collision cell used, and the masses of the interfering ions which could create isobaric interferences either themselves or by subsequent reactions." *Id.* at 8:3–9

Another embodiment of Tanner's mass spectrometer is shown in Figure 1 of Tanner, which is reproduced below.

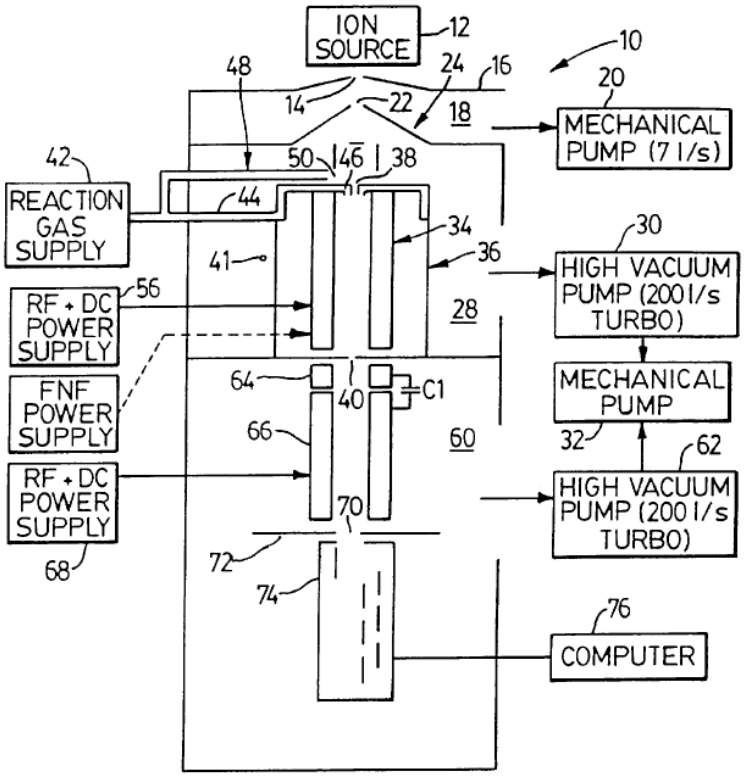


Figure 1 of Tanner is a schematic illustration of a mass spectrometer used to remove isobaric interferences. *Id.* at 2:45–46. The spectrometer includes ion source 12, orifice 14, first vacuum chamber 18, orifice 22, vacuum chamber 28, turbo pump 30, collision cell 41 (consisting of quadrupole 34 and can 36, and supplied with a reactive collision gas), orifice 40, vacuum chamber 60, turbo pump 62, and mass analyzer 66 (e.g., a quadrupole, TOF spectrometer, sector instrument, or ion trap). *Id*. at 3:55–4:10, 4:25–32.

6. Rowan

Rowan is a research paper entitled "Attenuation of Polyatomic Ion Interferences in Inductively Coupled Plasma Mass Spectrometry by Gas-Phase Collisions." Ex. 1033, Title.[6] The paper evaluates "[a] double

[6] All references to the page numbers in Rowan refer to the original page numbers in the lower left- or right-hand corner of each page in Exhibit 1033.

quadrupole arrangement to remove polyatomic ions by collision with an added target gas." *Id.* at 976 (Abstract). Rowan's mass spectrometer is shown in Figure 1, which is reproduced below.

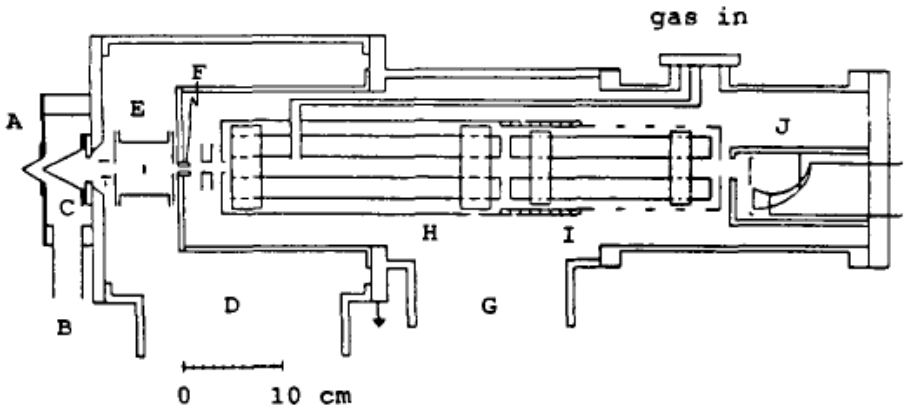


Figure 1 of Rowan is a schematic illustration of a mass spectrometer, absent its ICP source. *Id.* at 976–977. The spectrometer includes sampler cone A, expansion stage B, skimmer C, vacuum chamber D, Bessel box E, orifice F, vacuum chamber G, quadrupole H, mass filter I, and detector J. *Id.* at 977. Regarding the analysis done with this mass spectrometer, Rowan states "[i]t is important to note that the ion beam was not mass analyzed before the collisions occurred. Thus, a mixture of analyte ions and all the usual background ions (Ar^+, ArH^+, O^+, H_2O^+, etc.) was injected into the collision cell." *Id.* Rowan subsequently suggests improving future instruments by "readily incorporat[ing] features such as (1) mass analysis of the reactant ions before the collision cell, (2) differential pumping between the collision cell and mass analyzer, (3) a 'bent' collision cell, and (4) better kinetic energy resolution." *Id.* at 980. Rowan also discloses different mechanisms for removing interfering ions in the collision cell, including CID, and "chemical reactions between the polyatomic ions and the neutral collision gas." *Id.* at 979.

7. Kishi

Kishi is an article published in the Hewlett Packard Journal, entitled "A Benchtop Inductively Coupled Plasma Mass Spectrometer." Ex. 1034, Title.[7] Figure 1 of Kishi depicts the mass spectrometer and is reproduced below.

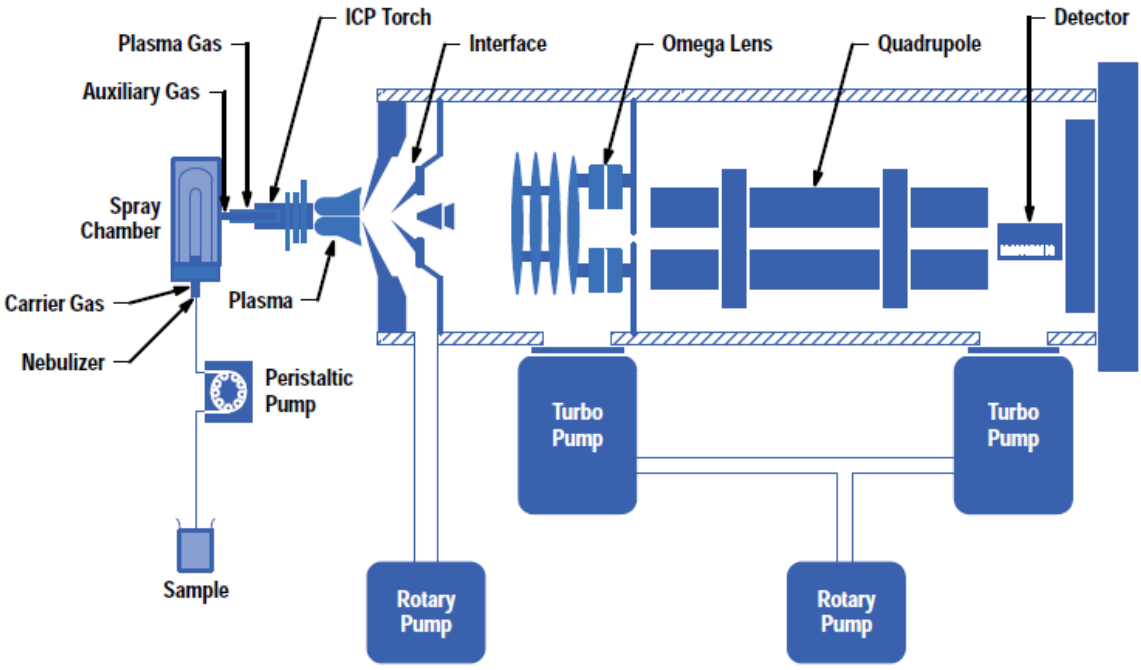


Figure 1 of Kishi is a schematic illustration of a mass spectrometer having an ICP torch or source, an ion expansion chamber evacuated by a rotary pump, an Omega or ion lens in a vacuum chamber evacuated by a turbo pump, and a quadrupole mass analyzer and detector in a vacuum chamber evacuated by a second turbo pump. *Id.* at 1.

A more detailed illustration of a portion of Kishi's mass spectrometer is shown in Figure 3(a), which is reproduced below.

[7] All references to the page numbers in Kishi refer to the original page numbers in the bottom right-hand corner of each page in Exhibit 1034.

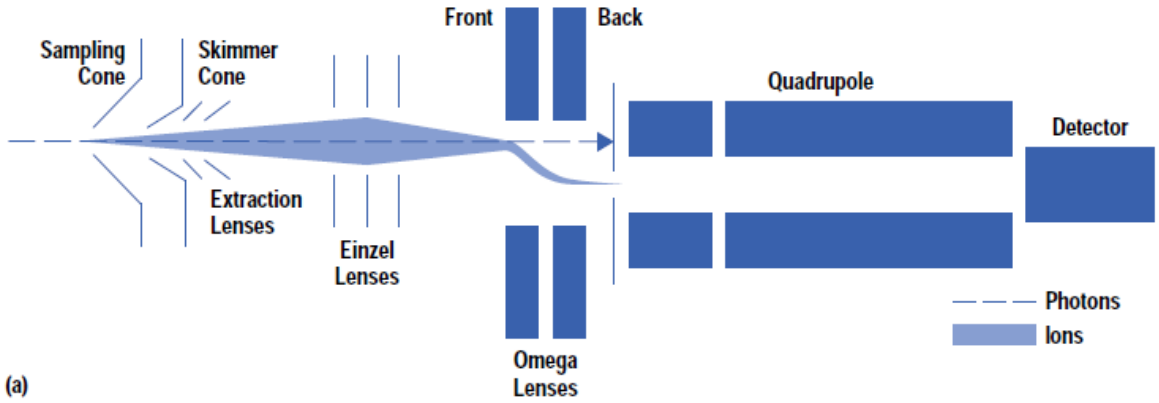


Figure 3(a) of Kishi is a more detailed illustration of a portion of Kishi's mass spectrometer, showing its sampling and skimmer cones and orifices, extraction, Einzel and Omega ion lenses, and offset axial alignment between these components and the quadrupole mass analyzer and detector. *Id.* at 2.

E. Patentability of claims 13, 15–17, 28–32, 34, 37, 38, 40, 41, and 47–50 over Douglas and Johnston

Petitioner argues claims 13, 15–17, 28–32, 34, 37, 38, 40, 41, and 47–50 are unpatentable over the combination of Douglas and Johnston. Pet. 32–45. For purposes of determining whether to institute, we focus on Petitioner's contentions with respect to claim 28.

1. Reasons to combine Douglas and Johnston

Petitioner's analysis for this ground relies on a combination of Douglas and Johnston and is based on modifying the way Douglas's TQMS is used to perform elemental analysis—namely, by scanning Douglas's first and third quadrupoles at the same mass-to-charge ratio (as taught by Johnston) rather than with an offset mass-to-charge ratio. *See* Pet. 33, 37; Ex. 1004 ¶¶ 61, 68.

Petitioner contends that both Douglas and Johnston teach using a TQMS "where both the first and third [quadrupoles] are operated in mass selective mode, and scanned together with a set mass offset, with a collision cell in between the two quadrupoles." *Id.* at 33 (citing Ex. 1022, 1; Ex. 1029, 48). Relying on the testimony of Dr. Yost, Petitioner argues that a person skilled in the art would have understood "that this mass offset can be set to any number, including zero as disclosed in Johnston." *Id.* at 37 (citing Ex. 1004 ¶ 68; Ex. 1022, 2). According to Dr. Yost, persons skilled in the art at the time the '386 patent was filed "were performing experiments using positive, negative, or zero offsets" and would have been motivated to use Douglas's TQMS "to perform an offset of zero experiment to detect atomic ions which do not undergo fragmentation or reaction in the collision cell." Ex. 1004 ¶ 68.

Patent Owner argues Petitioner's proposed combination of Douglas and Johnston is deficient because Petitioner has failed to provide sufficient reasoning to combine these references, especially as to *why* a person skilled in the art would have combined their teachings, and has failed to allege a reasonable expectation of success. Prelim. Resp. 40–41, 45–47. Patent Owner further argues the different goals of Douglas and Johnston undermine Petitioner's reason to combine these references because Douglas's goal was to observe reaction products produced in a collision cell, whereas Johnston's

goal was to observe "stable species [that] pass through the collision cell intact." *Id.* at 46 (citing Ex. 1022, 2; Ex. 1029, 48).[8]

At this stage of the proceeding, we are persuaded that Petitioner has provided sufficient reasoning to combine the teachings of Douglas and Johnston. First, the fact that Douglas and Johnston have different goals and perform different types of experiments does not, by itself, preclude a person of ordinary skill in the art from combining their respective teachings. As the U.S. Supreme Court has stated, "[a] person of ordinary skill is also a person of ordinary creativity, not an automaton," and in many cases can "fit the teachings of multiple patents together like pieces of a puzzle." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 420–421 (2007); *see also In re Heck*, 699 F.2d 1331, 1333 (Fed. Cir. 1983) ("The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned.").

Further, Dr. Yost testifies that persons skilled in the art at the time of invention were "performing experiments using positive, negative, or zero offsets" between the first and third MSs of a TQMS. Ex. 1004 ¶ 68. At this stage of the proceeding, we find this testimony credible because it is consistent with the disclosures in Douglas and Johnston. For example, Douglas discloses scanning the third MS at a positive offset from the first MS to detect the reaction product (CeO^+) of ions (Ce^+) that gain mass because they *chemically react* with gas in a collision cell. *See* Ex. 1029, 48.

[8] Patent Owner cites to Douglas by referring to the page numbers stamped at the bottom right-hand corner of each page in Exhibit 1029. We cite to the page numbers of Douglas printed in the top left-hand or right-hand corner of each page in Exhibit 1029.

Johnston discloses scanning the third MS at a negative offset from the first MS to detect ions that lose mass that "corresponds to the mass of the neutral moiety" that is produced when the ions *fragment upon collision* with gas in the collision cell. Ex. 1022, 1, Fig. 3. Johnston also discloses scanning the third MS at zero offset from the first MS to detect ions that *do not fragment* upon collision with gas in the collision cell. *Id.* at 2, Fig. 4. In view of these disclosures, we are persuaded, for purposes of this Decision, by Dr. Yost's testimony that a person skilled in the art would have known that Douglas's TQMS could have been operated with the mass offset between the first and third MSs "set to any number, including zero as disclosed in Johnston." Ex. 1004 ¶ 74. Moreover, for purposes of this Decision, we are persuaded that Dr. Yost has provided sufficient reasoning to explain why a person skilled in the art would have run Douglas's TQMS with zero mass offset—namely, "to detect atomic ions which do not undergo *fragmentation or reaction* in the collision cell." *Id.* (emphasis added).

Moreover, at this stage of the proceeding, we do not find Petitioner's 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. In *KSR*, the Supreme Court 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 Douglas's TQMS can be modified to synchronously scan the first and third quadruples at a zero mass offset (as taught by Johnston), rather than at a fixed mass offset (as taught by Douglas). Indeed, Johnston teaches doing exactly that—synchronously scanning the first and third quadrupoles of a TQMS at either a fixed or zero offset. *Compare* Ex. 1022, 1 (disclosing a "neutral loss" mode in which "both mass analyzers are scanned in parallel. . . . however, the first analyzer is offset from the second analyzer by a selected mass") *with id*. at 2 (disclosing a "neutral loss of zero" mode in which "both mass analyzers must be scanned over the *same* mass range") (emphasis added); *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 Douglas discloses an ICP triple quadrupole mass spectrometer that includes an ICP ion source that generates both analyte ions and interfering ions at the same mass-to-charge ratio. Pet. 37 (citing Ex. 1029, 46–48). We are persuaded, at this stage of the proceeding, that the combination of Douglas and Johnston teaches this limitation.

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 both Douglas and Johnston disclose this limitation in the form of the first quadrupole of a TQMS that mass selects ions having a first mass-to-charge ratio. Pet. 37 (citing Ex. 1022, 2; Ex. 1029, 47).[9] We are persuaded, at this stage of the proceeding, that the combination of Douglas and Johnston 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 both Douglas and Johnston disclose this limitation, with Douglas disclosing a collision cell that removes interferences via dissociation or reaction ion chemistry, and Johnston disclosing a collision cell that removes interferences via dissociation (fragmentation). Pet. 38 (citing Ex. 1022, 2; Ex. 1029, 47). We are persuaded, at this stage of the proceeding, that the combination of Douglas and Johnston teaches this limitation.

[9] We note Petitioner incorrectly cites to Ex. 1006 at page 37 of the Petition. Because this asserted ground is based on the combined teachings of Douglas and Johnston (not Tanner), we presume this is a typographical error, and we correct the citation here.

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 argues both Douglas and Johnston teach this limitation because both references teach the first quadrupole selects and allows only ions have a selected mass-to-charge ratio to enter the collision cell. Pet. 38–39 (citing Ex. 1022, 2; Ex. 1029, 48). As a result, Petitioner argues, "[a]ny new product ions formed inside the collision cell through reaction or dissociation would necessarily have an m/z other than the m/z selected by the first quadrupole." *Id.* at 39; *see also* Ex. 1004 ¶ 72 (providing an example to explain the same argument).

Patent Owner argues Petitioner's argument is an inherency argument and fails because "neither Petitioner nor Dr. Yost explain why selecting a particular m/z ratio upstream of a collision cell ***necessarily*** minimizes the formation of interfering ions having the same mass ratio." Prelim. Resp. 42.

At this stage of the proceeding, we are persuaded that, by disclosing a first quadrupole of a TQMS that mass selects and transports to a collision cell only ions having a first mass-to-charge ratio, Douglas and Johnston both teach the first quadrupole minimizes the formation of artefact ions in the collision cell that have the first mass-to-charge ratio. Indeed, this is the only mechanism disclosed in the '356 patent for minimizing the formation of interfering artefact ions in the collision. The '356 patent discloses an ion optical device, acting as an auxiliary mass filter, selects ions having a first mass-to-charge ratio so that "[a]ny artefact ion that is formed in the collision cell *must* . . . be a reaction product from an ion of the m/e that is selected"

and, therefore, "*must* have a different m/e from that selected"). Ex. 1001, 5:4–12 (emphases added); *see also* Ex. 2029, 9 (Applicant admission that "[t]he advantage of the pre-collision mass filtering of the present application is that it removes any ions from the beam which might cause formation of new artefact ions in the collision cell.").

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 argues the combination of Douglas and Johnston discloses this limitation. *See* Pet. 39–40. In particular, Petitioner argues that both references teach receiving a portion of the mass selected ion beam from the collision cell and that Johnston teaches a "neutral loss of zero" mode in which "there is an offset of zero between the mass selecting at the first quadrupole and the third quadrupole, which would mean mass analyzing the ion beam at the same mass-to-charge ratio that was originally selected at the first quadrupole." *Id.* (citing Ex. 1004 ¶ 73; Ex. 1022, 2, Fig. 4; Ex. 1029, 48). Relying on the testimony of Dr. Yost, Petitioner further argues that Douglas teaches "mass analyzing the received beam at a constant offset," but "[a] person of skill in the art would [have understood] that this mass offset can be set to any number, including zero as disclosed in Johnston." *Id.* at 40 (citing Ex. 1004 ¶ 74; Ex. 1029, 48). Petitioner argues a person skilled in the art would have been "motivated to perform an offset of zero experiment to determine which ion source products (analyte ions) undergo

fragmentation or reaction in the collision cell." *Id.* (citing Ex. 1004 ¶ 74; Ex. 1022, 2).

Patent Owner presents two arguments alleging Petitioner has failed to show the combination of Douglas and Johnston teaches this limitation. First, Patent Owner argues that Petitioner's stated reason for combining the teachings of these references, which relies on Johnston's disclosure of a neutral loss of zero scan, is not supported by Johnston, which discloses that in neutral loss of zero scans only "ions which survive collisions are transmitted through the analyzer." Prelim. Resp. 44 (quoting Ex. 1022, 2 (caption of Fig. 4). Therefore, Patent Owner argues "it is not clear how this disclosure shows that an offset of zero experiment would allow the [person of ordinary skill in the art] to determine which ion products undergo fragmentation or reaction." *Id.* Next, Patent Owner argues running Douglas's TQMS at zero offset would not have allowed Douglas to work as intended because Douglas "was interested in observing what ions underwent reaction, which is the reason that he used an offset of 16 amu," and if "Douglas had run his experiment at a zero offset, as Petitioner suggests, he would not have been able to observe reaction products from collisions with oxygen." *Id.*

At this stage of the proceeding, we are persuaded that Petitioner has shown how and why a combination of the teachings of Douglas and Johnston teaches 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, as required by claim 28. We note Petitioner supports its reason to combine the teachings of Douglas and Johnston with a citation to

paragraph 74 of Dr. Yost's Declaration. *See* Pet. 40. According to Dr. Yost, the reason to combine is "to detect atomic ions which *do not undergo fragmentation or reaction* in the collision cell." Ex. 1004 ¶ 74 (emphasis added).[10] This is consistent with Johnston's teaching that in neutral loss of zero scans "only *unfragmented ions* may pass completely through the system," where they are subsequently detected. Ex. 1022, 2 (emphasis added).

Further, at this stage of the proceeding, we disagree with Patent Owner's contention that Petitioner's proposed combination of Douglas and Johnston would not have allowed Douglas's experiment to work as intended because Douglas's experiment was designed to detect analyte ion reaction products at a mass offset, and running the experiment with a zero mass offset would not have allowed the detection of the reaction products.

> The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference. . . . Rather, the test is what the combined teachings of those references would have suggested to those of ordinary skill in the art.

In re Keller, 642 F.2d 413, 425 (CCPA 1981).

Petitioner does not propose modifying Douglas to scan the first and third quadrupoles at zero mass offset in order to *repeat* Douglas's ion reaction experiment and detect atomic ions that undergo reaction in the collision cell.

[10] Petitioner states that the reason to combine is "to determine which ion source products (analyte ions) *undergo fragmentation or reaction* in the collision cell." Pet. 40 (citing Ex. 1004 ¶ 74; Ex. 1022, 2) (emphasis added). At this stage of the proceeding, in view of Petitioner's citation to and the contents of paragraph 74 of Dr. Yost's Declaration, we understand the reason stated in the Petition to be a clerical mistake.

To the contrary, per the testimony of Dr. Yost, Petitioner proposes modifying Douglas to scan the first and third quadrupoles at zero mass offset in order "to detect atomic ions which *do not undergo fragmentation or reaction* in the collision cell." Ex. 1004 ¶ 74.

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 Douglas and Johnston.

F. Denial Under 35 U.S.C. § 325(d)

Petitioner acknowledges that Douglas is cited as admitted prior art in the Specification of the '386 patent and that Johnston and Rowan are cited on the face of the '386 patent, but Petitioner contends that all three references were not substantively discussed during the original or reissue prosecution. Pet. 32–33, 50; *see also* Ex. 1001, [56] (list of referenced cited). Petitioner acknowledges that Tanner was substantively discussed during prosecution of the parent of the '386 patent but contends it was not discussed during prosecution of the '386 patent itself. *Id.* at 50. Petitioner contends that Whitehouse and Louris are not cited on the face of the '386 patent. *Id.* at 45, 47. We note that Kishi is also not cited on the face of the '386 patent. *See* Ex. 1001, [56].

Patent Owner does not dispute Petitioner's contention that the Examiner did not substantively discuss the disclosures of Douglas, Johnston, or Rowan in the original or reissue prosecutions, or that Whitehouse and Louris are not cited on the face of the '386 patent. Nonetheless, Patent Owner argues we should exercise our discretion to deny the Petition under

35 U.S.C. § 325(d) because Petitioner "has not only filed a follow-on second petition for *inter partes* review of the '386 patent, [but] has done so largely based on prior art that was cited and considered during both original and reissue prosecution." Prelim. Resp. 34. Patent Owner further argues the following *General Plastic* factors favor denial: (1) Petitioner previously filed Case IPR2018-00298 challenging the same claims, (2) Petitioner knew of the prior art asserted in this petition when it filed Case IPR2018-00298, (5) Petitioner has failed to adequately explain the time elapsed between the filing of the Petition and the filing of Case IPR2018-00298, and (6) the finite resources of the Board. Prelim. Resp. 35–37 (citing *General Plastic Industrial Co., Ltd. v. Canon Kabushiki Kaisha*, Case IPR2016-01357, slip. op. at 16 (PTAB Sept. 6, 2017) (Paper 19).

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 deny institution of *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*, Paper 19, slip. op. at 18–19.

On the facts presented here, we decline to deny the instant Petition as an exercise of our discretion. Although the Office previously considered the patentability of some of the challenged claims over the combination of Tanner and Eiden,[11] the Office has not previously considered the

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patentability of the currently challenged claims as obvious over Douglas and Johnston, obvious over Douglas, Johnston, and Whitehouse, obvious over Douglas and Louris, obvious over Douglas, Louris, and Whitehouse, obvious over Tanner and Rowan, or obvious over Tanner, Rowan, and Kishi as set forth in the Petition. *See* Pet. 4.

Moreover, on the facts presented here, where Petitioner filed the instant Petition on December 14, 2017, a mere one day after filing the petition in Case IPR2018-00298, we do not find the *General Plastic* factors weigh in favor of declining institution. *General Plastic* recognizes that "there may be circumstances where multiple petitions by the same petitioner against the same claims of a patent should be permitted." *See General Plastic*, Paper 19, slip op. at 18. The *General Plastic* factors set forth certain considerations for weighing the competing goals of improving patent quality through the efficient use of post-grant procedures and protecting the patent owner from harassment through abuse of those procedures. *Id.* at 16–17. Although Petitioner raises numerous grounds in this Petition and in the petition in Case IPR2018-00298 filed one day earlier, we do not find the number of grounds raised to be so onerous that it is prejudicial to or constitutes harassment of the Patent Owner, especially given the number and scope of the challenged claims.

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 we 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").[12]

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

[12] 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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