PATENT COOPERATION TREATY

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INTERNATIONAL SEARCHING AUTHORITY

To:

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2018/039548	26.06.2018	30.06.2017

International Patent Classification (IPC) or both national classification and IPC
INV. C12N15/10 B01L3/00 G01N33/49 B01L9/00 ADD. G01N1/40 C12M3/06 C12M1/12

Applicant
BOSTON SCIENTIFIC SCIMED, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	see form PCT/ISA/210	Ruiz-Echarri Rueda Telephone No. +31 70 340-0

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed.

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43*bis*.1(a))

3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:

   a. ☐ forming part of the international application as filed:

      ☐ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	5, 8, 10, 11
	No:	Claims	1-4, 6, 7, 9, 12-15
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-15
Industrial applicability (IA)	Yes:	Claims	1-15
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

1 **Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1.1 Reference is made to the following documents:

D1 US 2015/330879 A1 (MAI JUNYU [US]) 19 November 2015 (2015-11-19)

D2 WO 2013/059526 A1 (UNIV COLUMBIA [US]; SAQI ANJALI [US]; YEAGER KEITH [US]) 25 April 2013 (2013-04-25)

D3 CN 103 323 590 A (SHANGHAI YUNZE BIOTECHNOLOGY CO LTD; SHANGHAI GENEXT MEDICAL TECHNOLOG) 25 September 2013 (2013-09-25)

An automatic machine translation into English of document D3 is provided as "Enclosure 1". References are made to such translation ("enclosure 1").

1.2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-15 is not new and/or inventive in the sense of Article 33(2)-(3) PCT.

1.3 All the technical features of claim 1 are disclosed in D1 in the following passages. D1 discloses in [0027]-[0029], [0042]-[0043] and in Figs.1, 3A-D:

A cell filtration assembly (cf. D1, Fig.3C) comprising:
a filter support member (cf. D1, fig.3C, assembly of 8x1 strips (100)) including a sample well (30);
a filter membrane extending across the sample well (10);
the filter support member (assembly of 8x1 strips (100)) and/or the filter membrane (10) configured to be sectioned (cf. Fig.3C, wherein the assembly is sectioned in as many portions as number of strips (100));
a protective element (60) disposed over at least a portion of the filter support member (assembly of 8x1 strips (100)).

1.4 Furthermore, D2 also discloses all the technical features of claim 1 in [0047] and in figs.1-4 and 9A-B. D2 discloses a "*sectionable*" cell filtration assembly (120) (cf. D2, [0047]) comprising a filter support member (124) including a sample well, a "*sectionable*" filter membrane (122) and a protective element disposed over the filter support member (124) (cf. D2, [0047] "*In some embodiments, the filter membrane includes sidewalls formed of paraffin, paraform, plastic, rubber or foam*").

1.5 All the technical features of independent claim 1 are also disclosed by D3 in the following passages: (cf. D3, enclosure 1 p.3, l.13-23 and p.4, l.14-30 and in figs. 1a-b): See furthermore: cell filtration assembly (cf. D3, Fig.1(a)), a filter support member (1) including a sample well (cf. D3, figs.1a-c, cavity formed in (1)), a filter membrane (2) extending across the sample well, ("millipore filter") and a protective element (3).

1.6 The subject-matter of claim 1 is therefore not novel over D1-D3 under Article 33(2) PCT.

1.7 Furthermore, the passages of D1-D3 cited against the novelty of claim 1 disclose all the technical features of claims 2 and 4.

1.8 Regarding claim 12 (see Re Item VIII), the cell filtration assembly of D1 (cf. D1, Fig.3C) is adapted to capture cells from a biological sample (cf. D1, [0007]-[0008] and [0027]), it comprises a "*sectionable*" base member (cf. D1, fig.3C, assembly of 8x1 strips (100)). Furthermore, the protective element (60) is understood to be a shell (similar objection applies mutatis mutandis to claim 3, wherein a shell is claimed).
Also D3 discloses the cell filtration assembly (cf. Fig. 1a-b (1)+(2)+(3)) adapted to capture cells from a biological sample (cf. D3, p.5, l. 49 - p.6, l.5), wherein the protective element (3) is understood to be a shell.

The subject-matter of claims 3 and 12 is therefore also not novel over D1 and D3 under Art. 33(2) PCT.

1.9 Regarding claim 8 (see Re Item VIII). D1 differs in that the protective element (100) of D1 is a plate and not a protective coating element (cf. D1, [0043]). However, the technical effect of the plate (60) does not seem to differ from the technical effect of the coating element of claim 8 (see Re Item VIII) and therefore, this technical feature does not involve an inventive step over D1. Furthermore, D1 is silent about the material of the protective element (60) of D1. This technical feature is however not considered to involve an inventive step over D1 because its use and its technical effect is well known by the person skilled in the art as it is already anticipated in [0027] of D1: "*the well is made of a low fouling material such as a polymer or a copolymer, e.g., polypropylene or poly(methyl methacrylate) (PMMA) to minimize non-specific biomolecule adhesion*". Therefore the plate (60) is considered to be a mere alternative to the coating element of claim 8 and the subject-matter of claim 8 does not seem to involve an inventive step over D1 under Art. 33(3) PCT.

1.10 Moreover, D3 discloses in p.8, l.3-9 a protective coating agent cured on the bottom of the protective element (3). D3 is silent regarding the material of such agent. Polymeric material is however not considered to have a surprising technical effect over D3 and it is therefore also not considered to be inventive over D3.

1.11 These objections (see above 1.9 and 1.10) apply mutatis mutandis to claim 5.

1.12 Moreover, the technical features of claims 6 and 9 are not considered to be inventive over D1-D3 because the use of Paralyne as coating in a cell filtration assembly is well known by the person skilled in the art as it is exemplary disclosed in D4 and D5 (cf. D4, [0085]) and (cf. D5 [0014] and [0147]).

1.13 Furthermore, the technical features of claims 11 and 14 are disclosed in the following passages of D1, D2 and/or D3: claim 11: (cf. D1, in [0034], (e.g. "*filter membrane is a 0.3-0.7 mm thick, glassfiber disc filter with pore size range from 0.3 to 2.7 µm*")), (cf. D2, [0049]) and (cf. D3, p.3, l.45-53), and claim 14: (cf. D1, [0042] and fig.1 (15)).

1.14 Furthermore, the passages of D2 cited against the novelty of claim 1 also disclose all the technical features of claims 2-4, 7, 12 and 15 and take away the inventive step of claims 8, 10 and 11.

1.15 Moreover, D2 discloses in [0067] and in Fig 9A-B all the technical features of claim 15 (cf. D2, protective cap (530))

1.16 The subject matter of claims 1-15 are therefore not novel and/or inventive over D1, D3 and/or D2 under Art. 33(2)-(3) PCT.

Re Item VIII

2 **Certain observations on the international application**

2.1 Regarding the wording "configured to be sectioned" in claim 1: Under the meaning of "sectioned", as "divide into sections" (e.g, cut in several sections), any physical element is configured to be sectioned. This technical feature is does therefore not limit the subject-matter of the claim. This objection applies mutatis mutandis to all the claims claiming a "*sectionable* element".

2.2 The technical features of the protective element which are needed to "*protect the filter support... from tissue processing reagents*" are not clear. These technical features are therefore not considered to limit the subject-matter of the claim. Similar objection applies mutatis mutandis to claims 8 and 12.

Furthermore, the biological sample has not been previously anticipated in the claim. It is understood not to form part of the subject-matter of the claim and its technical features are unknown.

2.3 The present set of claims contain three independent claims from the same category (apparatus claims 1, 8 and 12) and therefore an objection under Rule 13.1 PCT arises. It seems however that such claims mainly differ in the wording of their technical features. It is therefore suggested to amend these claims in order to overcome this objection.