

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To: SINGH, MANISHA LEX ORBIS, 709-710, TOLSTOY HOUSE, 15-17, TOLSTOY MARG, NEW DELHI - 110001 INDIA			Date of mailing <i>(day/month/year)</i> 20-01-2020		
Applicant's or agent's file reference 1134W0496			FOR FURTHER ACTION See paragraph 2 below		
International application No. PCT/IB2019/058517	International filing date <i>(day/month/year)</i> 07-10-2019	Priority date <i>(day/month/year)</i> 06-10-2018			
International Patent Classification (IPC) or both national classification and IPC A61K9/20,A61K9/00 Version=2020.01					
Applicant JUBILANT GENERICS LIMITED					

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 43bis.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 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 notified the International Bureau under Rule 66.1bis(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/ Indian Patent Office Plot No. 32, Sector 14, Dwarka, New Delhi-110075 Facsimile No.	Date of completion of this opinion 20-01-2020	Authorized officer Dr. Kumar Karitkey Yadav Telephone No. +91-1125300200
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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

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Box No. I Basis of this 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 43bis.1(b)).
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 13ter.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 13ter.1(a)).
 - ☐ on paper or in the form of an image file (Rule 13ter.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:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 24

because:

☒ the said international application, or the said claims Nos. 24 relate to the following subject matter which does not require an international search (*specify*):

The subject matter of claim 24 relates to a method for treatment of the human or animal body which does not require an international search by the International Searching Authority in accordance with PCT Article 17(2)(a)(i) and [Rule 39.1(iv)].

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for said claims Nos. 24

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in the form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b).

☐ See Supplemental Box for further details.

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

1. Statement

Novelty (N)	Claims	<u>1-23, 25-28</u>	YES
	Claims	<u>NONE</u>	NO
Inventive step (IS)	Claims	<u>NONE</u>	YES
	Claims	<u>1-23, 25-28</u>	NO
Industrial applicability (IA)	Claims	<u>1-23, 25-28</u>	YES
	Claims	<u>NONE</u>	NO

2. Citations and explanations:

Reference is made to the following documents:

D1: Richard J. Kowalsky, Technetium Radiopharmaceutical Chemistry, The The University of New Mexico Health Sciences Center, College of Pharmacy, Albuquerque, New Mexico, 2006, Volume 12, Lesson 3, Pages 1-77; 31 December 2006;
https://pharmacyce.unm.edu/program_information/freelessonfiles/Vol12Lesson3.pdf.

D2: Mrinal K. Dewanjee, The Chemistry of 99mTc-Labeled Radiopharmaceuticals, Seminars in Nuclear Medicine, Vol. 20, Issue 1, 1990, Pages 5-27; 31 January 1990;
<https://www.sciencedirect.com/science/article/abs/pii/S0001299805801734>.

The subject-matter of instant claims 1-12 relates to the pharmaceutical composition of sulfur colloid comprising (a) a reducing agent; (b) a colloid support agent; and (c) a chelating agent. The pharmaceutical composition has a viscosity of about 1 cP to about 100 cP at a temperature of 2-25°C. The subject-matter of claims 13-18 defines all the three components of claim 1. Further, the subject-matter of claims 19-21 defines the radioprotectant. The subject-matter of claims 22-23 and 25-26 utilizes the said composition along with 99mTc-pertechnetate solution and utilizes them for performing reticuloendothelial imaging. The subject-matter of claims 27-28 defines the method for the preparation of said composition.

Novelty under Article 33(2) PCT:

The present application meets the criteria of Article 33(1) PCT, because the subject-matter of claims 1-23 and 25-28 is new in the sense of Article 33(2) PCT.

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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

1. Applicant had failed to cite any relevant prior art document in the background of the description (Rule 5.1(ii) PCT). Cited prior art documents D1-D2 should be identified in the background of the description and brief discussions about their disclosures should be provided therein.

2. Applicant had not provided sufficient experimental data for the synthesis of pharmaceutical composition of sulfur colloid and reconstitution with ^{99m}Tc-pertechnetate solution which is required to perform the invention by a person skilled in the art (Article 5 PCT).

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:

1. The subject-matter of independent claim 1 does not meet the requirements of Article 6 PCT because the components defined in claim 1 under sub-category a, b and c are very broad, vague, speculative in scope and unclear that do not have any specified meaning.

2. The approximate term "at least" used in claims 8-11, 22-25 and 27 leaves the reader in doubt as to the exact meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

3. The subject-matter of claims 5-11 does not meet the requirements of Article 6 PCT because the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved, namely in the form of viscosity duration, gel formation time, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Continuation of Citation and Explanation(Box5)

None of the cited documents D1-D2 disclose the pharmaceutical composition of sulfur colloid having a viscosity of about 1 cP to about 100 cP at a temperature of 2-25°C. Thus the subject-matter of claims 1-23 and 25-28 is new in the sense of Article 33(2) PCT.

Inventive Step under Article 33(3) PCT:

The subject-matter of claims 1-23 and 25-28 does not fulfill the requirements of Article 33(3) PCT in view of the cited prior art documents D1-D2 with common general knowledge.

The subject matter of independent claims 1 of the instant application is very broad in nature and lacks clarity. Document D1 discloses the composition of 99mTc-Sulfur Colloid (page 48, paragraph 3). 99mTc-sulfur colloid injection comprises of a colloidal dispersion of sulfur particles. The sulfur colloid comprises of a lyophilized mixture of anhydrous sodium thiosulfate (corresponding to the reducing agent), disodium edentate (corresponding to the chelating agent) and gelatin (corresponding to the colloid support agent) (page 48, paragraph 4). 99mTc-sulfur colloid is prepared by adding 99mTc-sodium pertechnetate to the said reaction vial (page 48, paragraph 5). Further D1 provides the information about the use of 99mTc-sulfur colloid in nuclear medicine, lymphoscintigraphy, liverspleen imaging, bone marrow studies and shunt patency evaluation, etc (page 49, paragraph 9).

Document D2 discloses the 99mTc-Labeled Colloids that is prepared by heating a mixture of 99mTc-pertechnetate and sodium thiosulfate in a boiling water bath for 5 to 10 minutes. The gelatin coating is used to stabilize the colloid size. Ethylenediaminetetraacetic acid (EDTA) is added in the reaction vial to chelate Al³⁺ ions and prevent aggregate formation by electrostatic interaction of negatively charged colloid and positively charged aluminum ions (Page 7, column 2). The sulfur atoms aggregate forming particles ranging in size from 0.1 to 1.0 µm. 99mTc-labeled compositions are used for imaging the resident-pool of macrophage in the reticuloendothelial system (Page 8, column 1).

Even though documents D1-D2 did not provide any information about the viscosity of the said composition, but these documents provides the same components of the pharmaceutical composition and discuss the preparation method and particle sizes of the colloids. Further, independent claim 1 lacks clarity and applicant had failed to provide any experimental data about the role of viscosity in the said pharmaceutical composition. Viscosity is a common term which is obtained through the routine experimentation by a person skilled in the art by involving common general

knowledge. Other components of the instant application are already disclosed by the prior art documents D1-D2. Therefore the subject-matter of claims 1-23 and 25-28 lacks inventive step criteria in the sense of Article 33(3) PCT.

Industrial Applicability under Article 33(4) PCT:

Claims 1-23 and 25-28 meet the criteria set out in Article 33(4) PCT, and thus have industrial applicability because the subject matter claimed can be made or used in the industry.