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MSAC Secretariat through HTA Access Point
Australian Government Department of Health and Ageing
Level 9
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4 July 2012

Private and confidential

Dear Sir/Madam

Sirtex Medical Limited - Consultation decision analytical protocol 1242
Our ref: **TRP:PAC:1856**

Introduction

- 1 We act for Sirtex Medical Limited (**Sirtex**).
- 2 Sirtex has reviewed the 'Consultation Decision analytical protocol (**DAP**) to guide the assessment of the use of Y90-microspheres in patients with hepatic primary and secondary cancers' number 1242 which was released for public comment on 28 May 2012 (**DAP 1242**).
- 3 We understand that the preferred response date for public comment on DAP 1242 is 5 July 2012. Given that the content and purpose of this letter does not lend itself to the registration procedure for public comment, we are sending it to MSAC to inform MSAC of Sirtex's current position and to request that further time be allowed for Sirtex to complete its investigations and confirm its position.
- 4 Sirtex otherwise reserves its position pending MSAC's response to this letter.
- 5 If MSAC has any queries regarding the content of this letter or it wishes to discuss any aspect of it, please let us know.

The proposal and related documents

- 6 DAP 1242 refers to:
 - 6.1 an application requesting the MBS listing of yttrium-90 microspheres by Sirtology Pty Limited (**Sirtology**) received by the Department of Health and Ageing in December 2011¹; and
 - 6.2 a covering letter to the application making certain requests².

¹ See page 5 paragraph 1 of DAP 1242

² See page 5 paragraph 3 of DAP 1242

- 7 Whilst DAP 1242 summarises in part and makes reference to these documents, they do not appear to have been released or be otherwise available.

Sirtology and Dr Gray

- 8 Sirtology (variously described in DAP 1242 as the 'applicant' and the 'sponsor') is owned and controlled by Dr Gray and entitles or persons with whom he is connected. A copy of company searches for Sirtology and Pine Ridge Holdings Pty Limited is **enclosed** (see Tab 1 of the enclosed bundle).
- 9 We also note that DAP 1242 refers to Dr Gray as the principal of Sirtology (see the twelfth bullet point of paragraph 5 on page 6 of DAP 1242 – see paragraph 11 below).

MBS listing for SIR-spheres

- 10 Paragraph 2 on page 5 of DAP 1242 states:

'This proposal relates to a new Intervention; however, selective Internal radiation spheres (SIR-Spheres) have been Interim listed on the MBS since May 2006 (items 35404, 35404, and 35408). This interim listing was due to expire in May 2011 but it has been maintained. SIR-Spheres are made by a separate manufacturer but are identical to Y90-microspheres in all physical respects.'

- 11 Paragraph 5 on pages 5 and 6 of DAP 1242 states:

'SIR-Spheres have been Interim-listed on the MBS since May 2006. The application states that the resin-based yttrium-90 microspheres produced by Sirtex Medical Limited (SIR-Spheres™) and Sirtology Pty Ltd (Y90-Microspheres™) are identical. Both products are also the same product that was described by Bruce Gray in 1983 and first used in patients in 1986. Similarities include:

- The raw microspheres from which both products are made are the same (4% cross linked polystyrene divinylbenzene copolymer).
- The raw microspheres used to produce both products are sourced and manufactured identically by the same company (BioRad Laboratories in Hercules California USA via the subsidiary BioRad Laboratories Pty Ltd in New South Wales). BioRad also obtains the raw starting materials for both products from the same source.
- Both microspheres products contain the same isotope; yttrium-90.
- Both Sirtex Medical Limited and Sirtology Pty Ltd obtain the yttrium-90 from the same source; Perkin Elmer in USA.
- Both products are designed to treat patients with advanced liver cancer that is not amenable to surgical resection or regional ablation.
- Both products rely on the same clinical trial evidence. The Australian randomised clinical trial data are owned and controlled by Bruce Gray.
- Both products are delivered to the patients by the exact same technique of SIRT (also called radio-embolisation).
- Both products are manufactured using the same wet chemistry processes that were first described by Bruce Gray in 1983 and using the exact same input materials.
- The quality inspection processes during manufacture for both products are the same.
- Both microspheres products are spherical and are the same size; mean diameter 32-33µ.
- Both microspheres products are the same density (SG ~1.6).
- The reaction cells used for production for both products are manufactured by Gray Surgical, a private medical device company of the principal of Sirtology Pty.Ltd.
- Both products use identical ancillary devices for delivery of the radioactive microspheres to the patient; V-Vial, V-Vial Holder, Delivery Set and DeliveryBox [sic].

- Both products are classified as Class-3 Active Implantable Medical devices.
 - Both products are shipped in Type-A registered Dangerous Goods packaging.
 - Neither product is patentable.
- 12 Whilst the passage quoted above does not make it entirely clear, we have assumed that the asserted similarities between the two products replicate the position of the applicant (Sirtology).
- 13 Whilst it is otherwise not clear as to whether or not the authors of DAP 1242 agree and adopt all or any of those assertions, the balance of DAP 1242 appears to proceed on an assumed or concluded basis that the two products are the same or relevantly similar.
- 14 Tables 1 – 5 (on pages 7-10 of DAP 1242) describe the current MBS Items as Items for SIR-Spheres as administered by Sirtex.
- 15 It appears that the application by Sirtology is founded on the proposition that MSAC can treat the Sirtology product and SIR-Spheres as 'the same' or as 'identical'. Sirtex does not accept that proposition and considers that neither the applicant nor MSAC is in a position to reach that conclusion. Without setting out exhaustively Sirtex's position, we note the following matters:
- 15.1 It would appear that the features of SIR-Spheres (relied upon by the applicant and/or MSAC) are derived either from information gained by Dr Gray during his employment with Sirtex which ceased in 2006 (see further below) or from Sirtex's application and interim funding obtained from MSAC in 2005. Given the significant lapse in time between those dates and the present and the nature of the information provided to MSAC in 2005, it is not possible for Sirtology or MSAC to determine whether or not the two products are as at today the same or identical;
- 15.2 as MSAC is aware, SIR-Spheres was first listed on the Australian Register of Therapeutic Goods by the Therapeutic Goods Administration (TGA) in 1998 and pursuant to that approval is the subject of ongoing auditing by TGA. Whilst we understand that the existence of the TGA approval was a prerequisite for MBS listing of SIR-Spheres;
- 15.3 It is noted on page 12 of DAP 1242 that:
[Sirtology] is in the process of submitting an application to the [TGA] for the registration of the Y90-microspheres. The anticipated date of submission to the TGA is March 2012 and the requested indication is 'treatment of non-operable liver cancer'.
- Whilst it does not appear that the contemplated TGA approval has been received (and we do not know whether an application has been submitted), it is otherwise not evident from DAP 1242 the extent to which Sirtology has provided MSAC with the necessary detail to allow a proper consideration of the features of its product to determine its similarity or otherwise to SIR-Spheres. In making this observation, we are not suggesting that Sirtology is obliged to provide such detail but merely pointing out that in the absence of such detail, no reliable conclusions as to similarity can be drawn;
- 15.4 Sirtex has been developing and administering SIR-Spheres in Australia since obtaining TGA approval in 1998 and in other jurisdictions for a number of years (Sirtex obtained United States Food and Drug Administration approval in March 2002). Those developments have included further clinical trials sponsored by Sirtex and other investigations including the investigations required by MSAC as a condition of the interim funding;
- 15.5 one difference between the products is that they would be manufactured at different facilities. Sirtex deploys quality and safety systems which control design and production of its products, and any question of comparison would need to have regard to these systems. Sirtex does not consider that it has

any obligation to disclose the details of its systems (which are confidential and commercially sensitive);

15.6 we also draw your attention to the matters raised below.

16 Moreover, Sirtex is concerned that:

16.1 DAP 1242 in its current form may be interpreted as an endorsement or an adoption by MSAC of the propositions of similarity in circumstances where, for the reasons outlined above, MSAC is not in a position and may never be able to be in a position to make the comparison urged by Sirtology that the two products are identical or the same as at the date of the publication of DAP 1242;

16.2 without clarification DAP 1242 may have unwittingly given support to an impression that the involvement of Dr Gray is a necessary and important link between the two products and their identity as at today, whereas that is not the case.

Sirtex and Dr Gray

17 There was a pre-existing and relevant relationship between Sirtex and Dr Gray. We draw MSAC's attention to the following matters.

18 The history of this relationship was considered by his Honour Justice French (as he then was) in *University of Western Australia v Gray (No 20)* (2008) 246 ALR 603 (**Judgment**) (copy **enclosed** at Tab 2).

19 Sirtex has reason to question the accuracy of the assertion recorded in DAP 1242 (as quoted in paragraph 11 above) that:

'Both products rely on the same clinical trial evidence. The Australian randomised clinical trial data are owned and controlled by Bruce Gray.' [emphasis added]

20 Sirtex has reason to believe that it may own or have an interest in the documents recording any clinical trial data, any copyright works in relation to that data and any confidential information that forms part of that data. Without setting out the basis of Sirtex's position in detail, the following observations are made:

20.1 DAP 1242 does not identify the clinical trial evidence or Australian randomised clinical trial data which is said to be owned and controlled by Dr Gray and upon which it is said both products rely. In respect of some of the historical clinical trial data (much of which was referred to in the publications the subject of Sirtex's application to MSAC), we draw MSAC's attention to paragraphs [420-434] and [910] of the Judgment;

20.2 on 1 May 1997, Dr Gray and an entity associated with him - Cancer Research Institute Inc. (**CRI**) - assigned various assets including intellectual property to Sirtex (then known as 'Paragon Medical Limited'). Relevantly, those assignments included:

(a) an Asset Purchase Deed from CRI to Sirtex (see paragraphs [1017-1024] of the Judgment. A copy of this Deed which was an exhibit in the proceedings is **enclosed** at Tab 3);

(b) an Assignment Agreement between Dr Gray and Sirtex (see paragraphs [1042]-[1045] of the Judgment. A copy of this Agreement which was an exhibit in the proceedings is **enclosed** at Tab 4);

20.3 Dr Gray was employed by Sirtex from 1 May 1997 to 23 January 2007 in various capacities including Medical Director, head of Research and Development, Chairman, Chief Executive Officer, consultant medical advisor (see paragraph [1324] of the Judgment);

20.4 Dr Gray was a director of Sirtex from 1997 to 23 January 2007 (see paragraph [1324] of the Judgment);

- 20.5 Sirtex, as part of its investigations, will be seeking the position of Sirtology and Dr Gray on these issues and therefore the matters set out above are subject to receipt and consideration of any response from Sirtology and Dr Gray;
- 20.6 since Dr Gray's relationship with Sirtex concluded, Sirtex has been involved in further clinical trials (including those mentioned above) which are relevant to SIR-Spheres and which have been done with no involvement of Dr Gray.
- 21 The interest of Sirtex in the clinical trial data and any other related intellectual property, information or documents relied upon by Sirtology to make its application is the subject of investigation by Sirtex. That investigation is likely to take some time and until it has been completed it is not possible for Sirtex to inform MSAC of its position definitively.
- 22 As part of Sirtex's investigation, we request MSAC please:
- 22.1 provide us with a copy of the application by Sirtology lodged in December 2011, any amendments to that application and any related correspondence including the covering letter referred to in paragraph 6.2 above;
- 22.2 confirm whether or not our assumption as to paragraph 5 on pages 5 and 6 of DAP 1242 (made in paragraph 12 above) is accurate and MSAC clarify (and explain the basis if necessary) the extent to which the authors of DAP 1242 have assumed or concluded the accuracy of the asserted similarities between the two products;
- 22.3 confirm whether in the consideration of DAP 1242, the authors have had any communication with Sirtology or Dr Gray involving consideration of the clinical trial data referred to in the application and, in particular, whether or not Sirtology has been asked to identify with precision the clinical trial evidence and clinical trial data referred to in DAP 1242;
- 22.4 confirm whether or not MSAC will be placing any reliance on the sixth bullet point in paragraph 5 on page 6 of DAP 1242 (namely that the two products rely on the same clinical trial evidence which is to be asserted to be owned and controlled by Dr Gray);
- 22.5 confirm whether or not MSAC's consideration of the application would be different if the statement in the sixth bullet point on page 6 of DAP 1242 was incorrect and, in particular, that the clinical trial data was not owned or controlled by Dr Gray;
- 22.6 note that depending on the answers to the above, Sirtex may wish to make specific submissions on this issue.

Patent applications

- 23 The passage from paragraph 5 on pages 5 and 6 of DAP 1242 contains the statement that:
- 'Neither product is patentable.'
- 24 We draw to your attention that the SIR-Spheres products manufactured by Sirtex are the subject of pending patent applications in Australia and a number of other jurisdictions.


Trademark

- 25 The passage quoted above from paragraph 5 on pages 5 and 6 of DAP 1242 says that the application states that:
- 25.1 'SIR-Spheres' is a registered trademark of Sirtex; and
- 25.2 'Y90-Microspheres' is a registered trademark of Sirtology.

- 26 An earlier paragraph on page 5 of DAP 1242 also says that 'Yttrium-90 Microspheres' is a registered trademark of Sirtology.
- 27 While SIR-Spheres is a registered trademark of Sirtex, our searches reveal that there was no registered trademark of Y90-Microspheres or Yttrium-90 Microspheres belonging to Sirtology or any other entity at the time the application was made.
- 28 Public comment and input is sought on the issues identified on page 4 of DAP 1242. One of those issues is:

 'Whether the term SIR-Spheres in the current MBS item descriptors represents the radioembolisation procedure or whether it refers to the trademarked SIR-Spheres product'
- 29 It is not clear from DAP 1242 precisely what is contemplated by the determination of this issue and the potential impact of any such determination on Sirtex's rights under the trademark. Sirtex is concerned that the process may (inadvertently) involve consideration of issues outside the authority and jurisdiction of MSAC. Sirtex requests that the intended inquiry in relation to this issue is explained with greater clarity and precision (mindful of Sirtex's concerns) so that Sirtex can consider the extent to which it should make any submissions on this topic.
- 30 As suggested above, if MSAC considers it would be useful to meet with Sirtex to explore these matters, Sirtex would be pleased to attend such a meeting.

Yours faithfully



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Encl.