National Institute for Health and Care Excellence

IP1252– Insertion of a subretinal prosthesis system for retinitis pigmentosa

Consultation Comments table

IPAC date: Thursday 15 October 2015

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 2: Specialist adviser	**4 & 5**	A critical recent reference has recently been published - Subretinal Visual Implant Alpha IMS - Clinical trial interim report. Stingl K, Bartz-Schmidt KU, Besch D, Chee CK, Cottriall CL, Gekeler F, Groppe M, Jackson TL, MacLaren RE, Koitschev A, Kusnyerik A, Neffendorf J, Nemeth J, Naeem MA, Peters T, Ramsden JD, Sachs H, Simpson A, Singh MS, Wilhelm B, Wong D, Zrenner E. Vision Res. 2015 Jun;111(Pt B):149-60. This reports trial outcomes in 29 patients receiving the first generation IMS alpha subretinal device, which is now CE Marked.	**Thank you for your comment** Stingl (2015) was not published at the time when the initial literature search was performed. The study was identified during the update search and is due to be included in table 2.

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2	Consultee 2: NHS Professional	**4 & 5**	Dear Members of the Interventional Procedures Advisory Committee, I am [redacted], at the [redacted]. I have been involved in Retinal Implant trials for many years, and I found the guidance Guidance IP 1252 factually incorrect and missing information published in the peer reviewed literature. I feel that it is very important that the committee considers the following comments : 1. The publication #1 cited in IP 1252 “Stingl K, Bartz-Schmidt KU, Besch D, et al. (2013) Artificial vision with wirelessly powered subretinal electronic implant alpha-IMS. Proceedings of the Royal Society of Biological Sciences 280 (1757): 20130077. doi: 10.1098/rspb.2013.0077.” is missing reference to the “Electronic Supplementary Material to the publication of K. Stingl et al.: Artificial Vision with Wirelessly Powered Subretinal Electronic Implant Alpha IMS. Proc.R.Soc.B (2013)”. This publication is here : http://rspb.royalsocietypublishing.org/content/royprsb/suppl/2013/02/18/rspb.2013.0077.DC1/rspb20130077supp1.pdf and also attached to this email with highlighted important sentences.	**Thank you for your comment** The supplementary material was not made available to the IP team when the paper by Stingl (2013) was received. This supplementary material has now been obtained. Relevant outcomes reported in the supplement will be added to table 2 of the overview.

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3	Consultee 2: NHS Professional	**4 & 5**	**(Comment 2 continued)** This study shows that of nine implanted patients: a. Three suffered from a device failure caused by a cable defect “This issue led to an intraorbital cable break in three subjects (S2, S3, S4), resulting in functional failure of the implant after three to nine months.” b. Three suffered from a device failure caused by a hermeticity “A second problem was caused by the quality of the chip’s hermetic seal. Corrosion of the IMS chip periphery was observed in three implants after approximately 250 days in situ. As a result, the chip gradually lost function and the patients opted for explantation (S1, S6, S7).” c. One patient suffered from a surgical complication “In the first subject (S1), an intraoperative touch of the optic nerve head by the tip of the implant occurred and resulted in failure of light perception via the implant.” d. My understanding is that of 9 patients implanted, 7 suffered a catastrophic failure that required explantation after 3-9 months.	**Thank you for your comment** Please refer to the response to comment 2.

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4	Consultee 2 : NHS Professional	**4 & 5**	e. Several British patients reported similar failures with this system (though its unclear whether they are part of this study, or another one): i. http://www.robinmillar.org.uk/bionic_retina.htm ii. http://www.bbc.com/news/uk-england-wiltshire-22009235	**Thank you for your comment** The first website is a blog reporting the personal experience of one patient. The device failed 2 months after implantation. Device failure is reported in the electronic supplement of the Stingl (2013) study which is due to be added to the overview. The second website is a newspaper article highlighting implant failure and loss of residual vision in one patient. Loss of residual vision has already been identified as an adverse event in the overview. Information from both websites would not normally be included in the overview.
5	Consultee 2 : NHS Professional	**4 & 5**	f. It is likely that 77% of patients had device failures in the past, and continue to have device failures.	**Thank you for your comment**

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6	Consultee 1: Specialist Adviser	**4 & 5**	It is important to distinguish between the unpowered subretinal chip (Chow et al., 2004) developed in the USA 10 years ago and the newer subretinal prosthesis under ongoing development by Retina Implant AG in Germany (Stingl et al., 2013). The former has to my knowledge been discontinued - there was no evidence of efficacy from the published papers. This was to be expected as the maximum power possible from a photo-electric diode capturing photons of light at the back of the eye would not be sufficient to activate the retinal circuits. This is why a powered device is needed. The consultation should relate to the powered subretinal implant only.	**Thank you for your comment** The IP programme produces guidance on procedures rather than individual devices. The IP team has determined that the company which produced the unpowered subretinal implant, evaluated in Chow (2004), has ceased production but is currently being restructured with the intention of continuing research. The Committee amended section 6.2 to state: “The Committee noted that the evidence included studies of different devices, some of which are no longer used. The committee recognised that the technology of subretinal prostheses and related devices is evolving and that further developments may result in substantial changes to outcomes which may influence patient selection in the future.”

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7	Consultee 2 : NHS Professional	**4 & 5**	2. The publication #4 cited in IP1252 “Geruschat DR, Bittner AK, Dagnelie G. (2012) Orientation and mobility assessment in retinal prosthetic clinical trials. Optometry and vision science 89 (9): 1308-15. doi: 10.1097/OPX.0b013e3182686251.” is not relevant as it was conducted with a totally different medical device, which was entirely contained in the subretinal space, and therefore would be expected to have a radically different safety and efficacy profile as the one covered by this guidance. a. This publication should not be cited in this guidance	**Thank you for your comment** Please refer to the response to comment 6.

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8	Consultee 2 : NHS Professional	**4 & 5**	3. The publication #5 cited in IP1252 “Chow AY, Chow VY, Packo KH, et al. (2004) The artificial silicon retina microchip for the treatment of vision loss from retinitis pigmentosa. Archives of Ophthalmology 122(4):460-9.” is not relevant as it was conducted with a totally different medical device, which was entirely contained in the subretinal space, and therefore would be expected to have a radically different safety and efficacy profile as the one covered by this guidance. a. This publication should not be cited in this guidance Many thanks in advance for taking into consideration the facts raised above. Please do not hesitate to contact me at any time if you would like to discuss this further.	**Thank you for your comment** Please refer to the response to comment 6.

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9	Consultee 1: Specialist adviser	**Note**	I have implanted and tested 6 patients so far with the IMS implant and the device has provided some degree of additional vision for all of them. The usefulness of the vision is variable and often depends on how independent the patients are with their sight loss. Most patients are able to navigate with the implant switched on and some could recognise faces . One could identify different bus shapes when waiting at the bus stop; another could see cars moving outside the window; another could walk along the side of the road by identifying double yellow lines. I am currently leading an NIHR i4i Award sponsored clinical trial to assess the next generation AMS-alpha implant. This has many improvements based on experience gained in the first clinical trial.	**Thank you for your comment** The Committee made a comment, noting that the procedure is intended for patients with end-stage disease who have no useful sight and no other treatment options. It recognised that even minor improvements in vision may help these patients, but it wanted evidence that any changes in metrics of vision result in improvements in quality of life and activities of daily living.