From: s22 [redacted]
To:
Cc: s22 [redacted] Devices Clinical
Subject: HP TRIM Document : R16/686595 : DA-2015-06850-1 - Clinical Round 2 - Wirion Embolic Protection System - MD Solutions Pty Ltd [SEC=UNCLASSIFIED]
Date: Friday, 9 September 2016 3:50:10 PM
Attachments: DA-2015-06850-1 - Clinical Round 2 - Wirion Embolic Protection System - MD Solutions Pty Ltd.tr5

---

s22 [redacted]

Please find the round 2 clinical assessment request attached to this email. If you have any questions at all, please do not hesitate to contact me.

Best regards,

s22 [redacted]

Medical Devices Branch
Therapeutic Goods Administration
devices@tga.gov.au

------< HP TRIM Record Information >------

Record Number:R16/686595
Title:DA-2015-06850-1 - Clinical Round 2 - Wirion Embolic Protection System - MD Solutions Pty Ltd

Australian Government

Department of Health

Therapeutic Goods Administration

Application Audit - Level 2
Clinical Assessment – 2nd Round

TRIM Reference: R16/686595

To be completed by DAVS Assessor:

Device UPI:	WIRION Embolic Protection System
Sponsor:	MD Solutions Australasia Pty Ltd
Manufacturer:	DA-2015-06850-1
Application ID:	Medtronic Australasia Pty Ltd
Submission ID:	DA-2015-06850-1
DAVS Assessor:	s22 [redacted]
Application TRIM	2015/027230 Round 1 clinical assessment data - DATA R15/716655
Sponsor's submission TRIM Ref.:	R16/684429 – for round 2 clinical assessment
Date submitted to TGA:	9/09/2016
Date Referred to Clinical Section:	9/09/2016
Screening for clinical data:	
Clinical Round:	For Round 2 Round 1 clinical assessor – Louise Brightman - R15/770692

To be completed by Clinical Assessor:

Does the submitted clinical data meet the requirements of essential principle 14 of Schedule 1 and Part 8 of Schedule 3 of the *Therapeutic Goods (Medical Devices) Regulations 2002?*	**☒YES / ☐NO**

Background

This is the 2nd Round Clinical Assessment for the WIRION Embolic Protection System (EPS), hereafter referred to as the subject device. Several deficiencies were highlighted in the 1st Round Clinical Assessment in the form of the bolded recommendations below.

TGA Recommendation 1: An explanation is required as to why this device was known by the previous names SCORPIO, GARDEX and GARDIA Medical EPD. Specifically, please confirm if there have been any manufacturing or device (material or mechanical) changes associated with the different names and if so, provide a discussion as to how these changes may or may not impact on the safety and performance of the WIRION System.

As per the S41JA response document, the applicant confirmed that of all the above-mentioned devices, there in only one commercially available, namely the WIRION EPS. The applicant provided the following text response and tabulated data (see table 1):

During the development of the WIRION system we had 3 generations that had different names. There were minor or no changes between those generations as can be seen in the table below describing the differences between the SCORPIO, GARDEX and the WIRION models. The change in the name was mostly driven from marketing reasons and not from changes in the device. Gardia Medical has only one commercial EPS system which is the WIRION system.

Table 1: Differences between the previously named devices and the subject device

Difference Description	SCORPIO	GARDEX	WIRION
Radiopaque markers on filter	Only on distal end	Only on distal end	On frame and distal end
Filter diameter range	3.5 – 5 mm	3.5 – 6 mm	3.5 – 6 mm
Retrieval catheter tip	Non retractable	Retractable soft tip	Retractable

In regards to the minor differences outlined in table 1, the S41JA response document stated that the differences do not alter the basic characterisation or functionality of the products. Whilst there was no specific reference to the safety implications of such differences within the S41JA response document, there is a clinical expert endorsement of the original clinical evaluation report (CER) and an overarching statement from the clinical expert regarding the safety of the subject device. Given that this particular non-clinical data is outside the scope of this clinical assessment, the clinical expert endorsement and statements regarding safety are considered acceptable in terms of adequately addressing TGA Recommendation 1.

TGA Recommendation 2: Given that the CER focused predominantly on the carotid application, and based on the insufficient clinical evidence to support the use of the WIRION System for cardiovascular interventions in general, please consider revising the proposed indication for use to include use within the carotid arteries only (note that this would be in line with the indication for use approved in the United States).

As per the S41JA response document, the applicant stated that the intended use as been revised to include use within the carotid arteries only. A draft IFU for the Australian market was supplied in an attachment (appendix 1) and upon review, the revised intended use was confirmed to be limited to use within carotid arteries. As such, TGA Recommendation 2 has been adequately addressed.

TGA Recommendation 3a: The provision of direct post-marketing data for the WIRION System is required including a breakdown of sales and complaints by geographical distribution, and a clinical expert discussion of any clinically relevant adverse events pertaining to the WIRION System.

Appendix 2 contained a Post-Market Surveillance Summary (revision 9.0) dated January 2016. A total of 80 subject devices were sold in 2015 and although the sales were no broken down according to jurisdictions, the sales were reported to have occurred in the United States (US), Europe and Israel (in addition to the carotid indication, it should be noted that the subject device has also been used in peripheral vasculature in Israel.

Of the 80 subject devices sold, one complaint was reported from the US in relation to intra-operative occlusion of the Internal Carotid Artery (ICA). Despite not being a reportable event, the case was investigated and deemed to be related to significant narrowing within the artery. The applicant highlighted that this is not a new or unknown clinical risk and that

spasm/occlusion are included in the subject device IFU. Upon review of the draft IFU for the Australian market, both vessel spasm and occlusion were listed as potential adverse events.

Whilst the complaint rate is currently 1.25%, it may be a result of the low sales to date and the learning curve effect. Whilst it would be expected that the complaint rate demonstrate a downward trend as use of the subject device increases, it is worth noting that the single complaint thus far was non-reportable and that the purpose of the device is to reduce risk of embolisation associated with the requisite vascular interventions. Seeing that no cases of embolisation were reported nor cases of death or serious injury, it would seem that the benefits outweigh the risks at this time. It would be advisable that the applicant continue to monitor post-market trends and notify regulatory agencies if there is an upward trend in complaint rates.

TGA Recommendation 3b: Please also provide a clinical expert discussion of the clinically relevant MAUDE reports for the FilterWire EZ and the AngioGuard RX devices, including whether these types of adverse events are expected with the WIRION System and whether the rates are acceptable when compared to the literature.

The S41JA response document provided tabulated MAUDE information for the clinically equivalent devices, namely the FilterWire EZ and the Angioguard RX. Complaint rates for these devices were compared to the subject device rates sourced from customer data (see table 2 below). A text discussion regarding the content of the table was also provided (see italicised excerpt below).

Table 2: Comparison of complaint rates (sourced from response document)

Report subject	FilterWire EZ	Angioguard RX	WIRION
Removal difficulty	50% (9/18)	50% (6/12)	50%(4/8)
deployment difficulty	11% (2/18)	8.3% (1/12)	-
Device/package damaged prior to use	5.5% (1/18)	8.3% (1/12)	12.5%(1/8)
Device damage during use	11% (2/18)*	-	25%(2/8)**
Filter unit damaged	11% (2/18)	8.3% (1/12)	-
Interference to blood flow	5.5% (1/18)	-	-
Catheter advancement/problem in crossing the lesion	5.5% (1/18)	25% (3/12)	12.5%(2/8)

The most common complaint pertaining for all 3 devices is filter removal (retrieval) difficulty (50%). The second most common complaint is device damage during use. In the WIRION it is damage in delivery catheter handle (25%) and in the predicate devices it is damage in the dedicated GW which was reported in 8.3-11% of the MAUDE reports. Additional reports in all three devices included catheter advancement/problem in crossing the lesion (5.5-25%) and device/package damage prior to use (5.5%-10%). It may be observed that while there were reports of catheter deployment difficulty (8.3%-11%) in the predicate devices, no such complaint was received for the WIRION.

Although the rates in the tables appear high, it should be noted that the rates are not based on a percentage of total sales but rather the proportion of total MAUDE reports for that particular device. As such, the most relevant information is the comparison of the percentages, particularly those that have potential for clinical complications such as removal and/or deployment difficulty, interference to blood flow and catheter advancement/issues crossing the lesion. As per the table 2, the rates of removal difficulty are the same between the clinically equivalent devices and the subject device. In contrast to the two clinically equivalent devices, no reports of deployment difficulty or interference to blood flow have been reported for the subject device (although it should be noted that the subject device is unlikely to have been used as frequently

as the other devices). Issues relating to catheter advancement and/or crossing the lesion were observed for both the clinically equivalent devices and the subject device, with the latter devices' rate falling between the two rates reported for the former devices.

Again, it is worth noting that none of the subject device complaints led to a reportable event. Given that no cases of embolisation were reported nor cases of death or serious injury, this data tends to suggest that the benefits of using the device outweigh the risks at this time. It would be advisable that the applicant continue to monitor post-market trends and notify regulatory agencies if there is an upward trend in complaint rates.

TGA Recommendation 4: It is expected that all of the clinical risks identified within the CER and IFU are appropriately incorporated into the Risk Analysis document either individually or as part of the broader category, for example, embolisation.

The S41JA response document stated that the risk analysis had been updated to incorporate all of the risks identified within the CER and IFU. The applicant referred to the most updated version of the risk analysis (revision 16 dated May 2016) as an attachment in appendix 4. Upon review of the updated risk analysis, the documentation appears to have incorporated additionally relevant clinical risks. For example, embolisation relating to various circumstances was identified with occurrence and severity ratings pre and post-mitigation strategies (with occurrence but not severity reducing to an acceptable level based IFU and training mitigation strategies).

TGA Recommendation 5: Evidence is required to demonstrate that a clinical expert (with experience in interventional cardiology and experience using similar EPDs) has reviewed and endorsed the content of the CER. Please ensure that a Curriculum Vita is provided for the clinical expert.

The applicant provided a signed letter from s22 [redacted]. The letter was dated September 2016 and confirmed that s22 [redacted] endorses (approves) the content and information provided of the CER, the risk management documentation and the post-market surveillance.

Upon reviewing the attached Curriculum Vitae, it was confirmed that Professor Rosenschein is an interventional cardiologist and the current director of cardiology at an Israeli hospital. Although not a vascular surgeon, Professor Rosenschein has a special research interest in EPD and is considered to be an appropriately qualified clinical expert.

Conclusion

Although the device has had a relatively small number of sales, it is relatively new to the market and the post-marketing data does not suggest any unexpected or reportable adverse events/complaints. Given that the subject device is intended to reduce or prevent the serious event of embolisation during intravascular (carotid) procedures and the associated (and potentially devastating) clinical sequelae, the absence thus far of embolic events, deaths and/or serious injury would suggest that the benefits outweigh the risks. No further information is requested from a clinical perspective at this time.

Is additional clinical data required?	**NO**

Name, date and signature of Clinical Assessor:

Name:	s22 [redacted]	**Date:**	29/09/2016
Signature:			