National Institute for Health and Care Excellence

Medical Technologies Evaluation Programme

MT271 Spectra Optia Apheresis System for automated red blood cell exchange in patients with sickle cell disease

Consultation Comments table

MTAC date: 17 December 2015

There were 46 consultation comments from 9 consultees (7 NHS professionals, 1 manufacturer and 1 patient expert). The comments are reproduced in full, arranged in the following groups – (venous access, factual accuracy, evidence, editorial and general). The draft responses to the 46 comments are based mainly on expert advice.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			Venous access	
1	3. Health Professional (within NHS, Expert Adviser)	2.1	Automated erythrocytapheresis by Spectra Optia can also be performed via a permanent indwelling line (port-a-cath) or via arterio-venous fistula.	Thank you for your comment. The Committee decided to change section 2.1 to further clarify that venous access for the Spectra Optia can be made using peripheral or central veins. Other references to venous access in sections 2.7, 2.8 and 3.21 have also been changed to reflect this.
2	6. Health Professional (within NHS)	general	Dear Sir or Madam, I have read with great interest the proposed guidelines regarding 'Spectra Optia for automated red blood cell exchange in patients with sickle cell disease'. I am a Senior Staff Nurse for Apheresis and work at University College London Hospitals (UCLH). We implemented automated red cell exchange (aRCEx) in 2008 (using Cobe Spectra then; Spectra Optia now) and provide now the biggest aRCEx programme in the UK (to my knowledge) with currently more than 100 patients on the programme having regular aRCEX. In our experience peripheral access should be the first choice for vascular access: Peripheral access can be established using 18 gauge or 20 gauge cannulas, in rare circumstance even a 22 gauge cannula has proven to be feasible (especially in children) providing adequate inlet blood flow rates. Below is a copy for a presentation displaying the vascular access	Thank you for your comment. Please see the response to comment 1.

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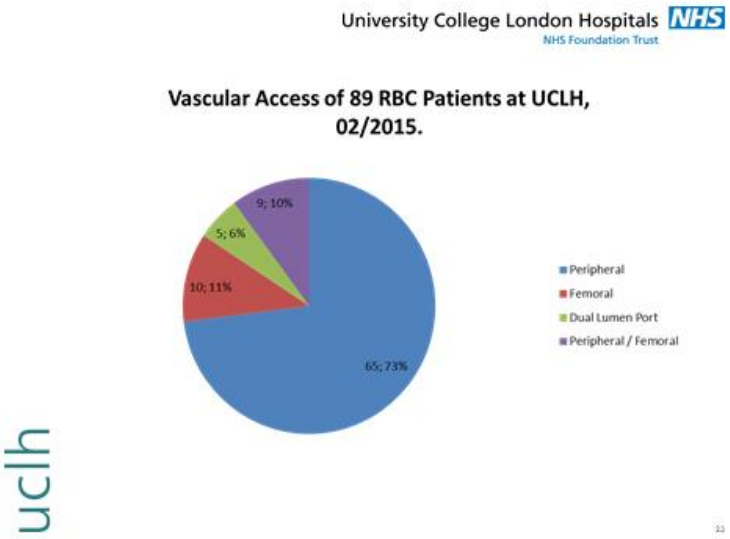
			choices at our trust for patients on regular aRCEx (although this data set is from February 2015, it is unlikely that the percentages of patients having peripheral access will have changed significantly by November 2015). Additionally, using an Ultrasound device for peripheral deep vein cannulation will help to avoid central vascular access (i.e. femoral line). The purpose of my email is to highlight that central venous access for aRCEx procedures is one option, albeit it should not be regarded as the first choice of access as the vast majority of aRCEx can be done successfully via peripheral access. Kind regards [redacted]  	
3	8. Manufacturer	2.1	The phrase ‘large vein in the leg’ is ambiguous and	Thank you for your comment.

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	(sponsor)		slightly misleading. Some centres use central venous access for automated exchange, but this is not always the femoral vein. If lay terms are to be preferred then we suggest this is changed to 'large veins in the groin or neck'.	Please see the response to comment 1.
4	8. Manufacturer (sponsor)	2.7	It is understood that top-up transfusions are commonly used in children because they are unlikely to be iron overloaded and the small catheters used are more suitable for paediatric venous access. The larger catheters and ports used for manual and automatic exchange may be unsuitable for some children. However, please note, that exchange transfusion does not always require a larger catheter and/or port – please see http://www.evelinalondon.nhs.uk/resources/patient-information/simple-top-up-transfusion-information-forparents.pdf	Thank you for your comment. Please see the response to comment 1.
5	8. Manufacturer (sponsor)	2.8	Exchange transfusions require larger lines and higher flow rates compared with top-up transfusions, which may make venous access more challenging. – We do not agree that central venous access 'is most commonly required with Spectra Optia' and suggest that this is a misinterpretation of the evidence. Some centres routinely use central access, but this is an organisational decision and is not a requirement of the use of the device (Please refer to the Terumo BCT Spectra Optia Apheresis System Red Blood Cell Exchange Procedure Guide (TerumoBCT Procedure Guide RBCx.pdf), page 20). For example, we understand	Thank you for your comment. Please see the response to comment 1.

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			that Guy's and St Thomas is in the process of transitioning from a central to a peripheral access service. Additional training can improve the use of peripheral veins. Please see: Sandhu et al, (2004) Br. J. Anaesth.p292; National Infusion and Vascular Access Society (NIVAS) 2015 conference report (http://www.nivas.org.uk/images/uploads/misc/NIVAS_Conference_Report_Final_Version_20.07.15.pdf).	
6	8. Manufacturer (sponsor)	3.20	For clarity Terumo BCT does not agree central venous access 'is most commonly required with Spectra Optia' and suggest that this is a misinterpretation of the evidence. Some centres routinely use central access, but this is an organisational decision and is not a requirement of the use of the device (Please refer to the Terumo BCT Spectra Optia Apheresis System Red Blood Cell Exchange Procedure Guide (TerumoBCT Procedure Guide RBCx.pdf), page 20). For example, we understand that Guy's and St Thomas is in the process of transitioning from a central to a peripheral access service. Additional training can improve the use of peripheral veins. Terumo BCT are willing to collaborate to bring the "centres of excellence" together, who achieve >90% success rates for peripheral cannulation for SCD patients. Occasionally hand held ultrasound devices are used for guided deep vein cannulation. This still keeps the procedure a peripheral procedure. Please see: Sandhu et al, (2004) Br. J. Anaesth.p292; National Infusion and Vascular Access Society (NIVAS) 2015 conference report (http://www.nivas.org.uk/images/uploads/misc/NIVAS_Co	Thank you for your comment. Please see the response to comment 1.

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			nference_Report_Final_Version_20.07.15.pdf)	
7	9. Health Professional (within NHS)	Page 9	It is very rare we find someone without adequate venous access, maybe 1 person the 150 procedures we would do in a year.	Thank you for your comment. Please see the response to comment 1.
Factual accuracy				
8	3. Health Professional (within NHS, Expert Adviser)	2.6	25% of patients being unable to tolerate hydroxycarbamide is probably an over-estimate. More commonly patients tolerate hydroxycarbamide but it is not effective in preventing symptoms. Hydroxycarbamide may not be suitable in 15-25% because it is not tolerated or it is not effective (there is limited data on this). Hydroxycarbamide is currently the only licensed drug for use in SCD	Thank you for your comment. Due to the lack of published evidence available this value was based on expert opinion. The Committee decided to change the wording of section 2.6 to: up to 25% of people cannot have or choose not to have it, based on expert advice received during the Committee meeting.
9	3. Health Professional (within NHS, Expert Adviser)	2.7	This paragraph implies that transfusion therapy is only used where hydroxycarbamide is not effective/not tolerated. This is not so, transfusion therapy is first line recommended treatment in primary or secondary stroke prevention (ie in patients who are at high risk of stroke because of high trans-cranial Doppler blood flow or because of previous stroke). Ie long term transfusion therapy is indicated in patients with increased stroke risk or patients with chronic complications which are not	Thank you for your comment. The Committee decided to change section 2.7 to further clarify the reported use of transfusion as a first-line treatment in primary or secondary stroke prevention in patients at high-risk of stroke.

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			responsive to hydroxycarbamide.	
10	3. Health Professional (within NHS, Expert Adviser)	2.9	Chelation therapies can cause other side effects in addition to gastrointestinal side effects including renal dysfunction, liver dysfunction, arthropathy and decreased white blood cell count	Thank you for your comment. The Committee decided to change section 1.9 to further describe the side effects of chelation therapy.
11	3. Health Professional (within NHS, Expert Adviser)	3.19	Infusion pump chelators are administrated 5-7 nights a week NOT 3-weekly as stated	Thank you for your comment. The Committee decided to change section 3.20 to further clarify the frequency of administration of chelation therapy.
12	3. Health Professional (within NHS, Expert Adviser)	4.5	My understanding is that donor blood may be removed by both manual and automated procedures.	Thank you for your comment. The Committee decided the change section 4.5 to remove the incorrect statement.
13	8. Manufacturer (sponsor)	4.5	...“only sickle cells are removed by the Spectra Optia...” The Spectra Optia does not remove only sickle cells. The Optia removes red blood cells and cannot discern between sickle red blood cells. However, donor cells are infused at a different access site to that where the blood is venesected.	Thank you for your comment. Please see the response to comment 12.

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14	8. Manufacturer (sponsor)	2.1	Please correct the company name to 'Terumo BCT'.	Thank you for your comment. The company name was updated.
15	8. Manufacturer (sponsor)	4.5	'The committee noted that automatic exchange with Spectra Optia uses more packed red blood cell units than manual exchange.' It should be noted that the depletion/exchange protocol on the Optia allows for more efficient utilisation of donor packed red cells thereby using fewer units per procedure (Trompeter, et al. (2015b). Red cell depletion in automated red cell exchange: a safe and effective method of exchange transfusion whilst reducing blood usage. Br J Haem, 169:91).	Thank you for your comment. The depletion/exchange protocol has not been covered in detail as the guidance focuses on automatic exchange as this was judged to be the most relevant protocol for long-term exchange programmes. The study by Trompeter et al. (2015) was included in the company submission; please see section 3.5.4 of the EAC assessment report for further information.
16	9. Health Professional (within NHS)	2.1	We have seen some patients faint or become unwell 30-50 minutes after the procedure, I would not recommend children leave immediately after the procedure to continue with normal activities. We advise an hour of rest post procedure. Some patients after regular exchanges may be considered on an individual basis to be discharged earlier.	Thank you for your comment. The Committee considered this comment carefully but not to change section 2.1 because it was advised that a post-procedure rest period is common practice for any transfusion treatment.
17	9. Health Professional (within NHS)	Page 9	I would not recommend a band 5 as appropriate to carry out a procedure like this (in paediatrics), in a disease like	Thank you for your comment. In the model presented by the company, it

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			sickle cell which can have it's own complications. We have had some patients suffer emergency events during an exchange and in paediatrics even calling upon my junior members of staff (band 5s) for assistance in these situations they are very nervous. I fear that in complex cases or emergency incidents if a band 5 were carrying out the procedure it would be an unfair amount of responsibility to put on someone with so little experience. If you state senior band 5 the wording becomes very subjective and again I feel that persons too junior would be asked to carry out what is such an autonomous procedure and would be unfairly burdened with such responsibility. I also feel it may affect your retention of nurses in the field of paediatric apheresis.	was assumed that a nurse of staff grade 5 could undertake automated exchange and top up transfusion, but more experienced staff were needed for manual exchange. The EAC accepted this assumption based on clinical expert advice. It is assumed that if an emergency arose during elective procedures, more experienced staff would intervene, but this possibility was not modelled. If the model assumed a higher staff grade was required for automated exchange, this would increase its procedural cost slightly relative to manual and top up exchange. However, sensitivity analysis performed by the EAC indicates this difference is small (£6 difference in staff costs per hour) and will not affect the direction of results in any scenario. Further expert advice (see appendix 1) has stated that this depends greatly on the training and experience of the individual band 5 nurse. Some units are staffed by band 6 and 7 nurses who may be more experienced in different methods of venous access. The Committee decided to change section 4.2 to state that 1 appropriately trained nurse should operate the device.

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18	8. Manufacturer (sponsor)	3.2	In our submission we reported that we identified 33 studies, not 43 (see p38 of 230 in the sponsor's submission). All 33 were presented in our submission; 29 of these for clinical outcomes and 4 for adverse events. (Note that on p38 we erroneously reported this as 3 relating solely to adverse events.)	Thank you for your comment. Section 3.2 has been changed to correct the error in the draft, which should state 33 studies, not 43. This has been corrected in section 3.2.
			Evidence	
19	3. Health Professional (within NHS, Expert Adviser)	5.1	The Haemoglobinopathy Registry Report is not relevant information as it does not refer to regularly transfused patients only. All patients who are on regular top up transfusions for 2-5 years will become ironloaded	Thank you for your comment. The National Haemoglobinopathy Registry, although subject to some biases, was judged to be the best source of data for the estimate of the proportion of patients undergoing chelation therapy as a consequence of prior top-up transfusions in years 2 to 5 of the model. The figure used by the EAC was specifically for patients undergoing regular transfusion (derived from Table 4 page 25, and estimate from Figure 6.6, page 14). There is an assumption that those requiring chelation will be on regular transfusions. This issue was also addressed in a response to a company comment during the fact check process for the Assessment Report. The EAC stated that "This

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				highlights a limitation of the model, in that patients cannot move between treatment subgroups. Whilst the EAC accepts that most patients receiving top up therapy would need chelation after approximately 2 years of treatment, in reality a proportion of these would move to other treatment modalities such as RBCx. Therefore the EAC considers that, for the purpose of the model, an estimate of 75% on chelation, derived from published sources (with acknowledgement of the limitations described) is a reasonable estimate." The Committee considered this comment and decided not to change the guidance.
20	8. Manufacturer (sponsor)	5.3	The first sentence suggests that no published evidence was used in the company's economic model. For clarification please see 'The clinical parameters used in the company's model (table 1) which were based on data from published studies (Adams 1996, Carrara 2010, Dedeken 2014, Hilliard 1998, Kalff 2010, Masera, 2007, and Sarode 2011 (please see section 9.2 of the 'submission of evidence by sponsor' for further clarification), clinical expert opinion, extrapolations from the clinical evidence and data from UK registries and NHS audits.'	Thank you for your comment. The EAC has stated that it would be correct to say that none of the clinical outcomes were directly derived from clinical studies on Spectra Optia. Data on complications and stroke were extrapolated from published studies, but these were not specific to automated exchange and for the reasons described in the Assessment Report the EAC did not consider these reliable. Data on chelation requirements were not directly reported in the published

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				studies mentioned, but were heavily extrapolated, as described in section 5.3 of the MTCD. The Committee considered this comment and decided changed section 5.3 to further clarify the relevance of the clinical studies from which parameters were drawn.
			Editorial	
21	3. Health Professional (within NHS, Expert Adviser)	Not stated by consultee	The second and third sentences here do not fit in with the first.	Thank you for your comment. The MTEP team sought clarification from the consultee as to which section this comments relates but no response was received.
22	8. Manufacturer (sponsor)	2.1	The first sentence is potentially misleading. The Spectra Optia Apheresis System is a multi-purpose device, of which only one intended purpose is examined in this guidance.	Thank you for your comment. The Committee decided to change section 2.1 to further clarify the description of Spectra Optia.
23	8. Manufacturer (sponsor)	2.2	As per our first comment, the Spectra Optia Apheresis System is a multi-purpose device which is used for cell harvesting as well as therapeutic apheresis. As this is made clear in the final sentence of this paragraph we	Thank you for your comment. Please see the response to comment 22.

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			suggest that 'intended for use in therapeutic apheresis' is deleted from the first sentence.	
24	8. Manufacturer (sponsor)	2.1	Suggest that 'the selected components of blood' is replaced with 'the patient's red blood cells'. Also, suggest adding a following sentence: 'The rest of the blood components (plasma and other cells) are returned to the patient along with the donor red blood cells'.	Thank you for your comment. The Committee decided to change Section 2.1 in line with the consultee's suggestion.
25	8. Manufacturer (sponsor)	5.2	We suggest that 'complications of SCD' is clarified as including secondary stroke, painful crises, acute chest syndrome and priapism.	Thank you for your comment. The Committee decided to change section 5.2 in line with the consultee's suggestion.
26	8. Manufacturer (sponsor)	5.3 Table 1	The table is not very clear. Could the information from the first 2 rows be presented separately, as per Table C4.2 and C4.4 in the sponsor's submission? It is currently unclear that the first row is the percentage of patients without initial iron loading who then become iron loaded on a chronic transfusion regime, and the second row is the percentage of patients with initial iron loading who can cease chelation therapy on a chronic transfusion regime. Could the rest of the table be reformatted as per table C5 in the sponsor's submission (p172 of 230). Should the table should also include the starting proportions of patients with initial iron overload who are on chelation therapy: 90% for automated exchange and top-up transfusion and 80% for manual exchange?	Thank you for your comment. The Committee considered this comment but decided not to change section 5.3 because the change would not improve the clarity of presentation and because the full information is presented elsewhere.

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27	8. Manufacturer (sponsor)	5.4	For clarification, the cost of a stroke in the base case was determined assuming that the stroke occurring at 2 years and 6 months, therefore incurring 3 months of acute costs and 2 years and 3 months of ongoing care costs over the 5 year time horizon. It is an overall cost for the duration of the model. It should also be made clear that only secondary strokes were included in the company's model as there was no data to support a difference in the rates of primary stroke between transfusion modalities.	Thank you for your comment. The Committee decided to change section 5.2 to clarify that the complications considered included secondary stroke. Please also see response to comment 25.
28	8. Manufacturer (sponsor)	5.5	Results of the sensitivity analysis were not reported with tornado diagrams. Tornado diagrams were used by the company to identify which variables influenced the rankings of the 3 treatment options, but were not presented in the submission.	Thank you for your comment. The Committee decided to remove the incorrect reference to tornado diagrams.
29	8. Manufacturer (sponsor)	5.7	For clarification, the Spectra Optia System the base case analysis showed that the largest cost component over 5 years was the red blood cell units. For top-up transfusion the largest cost component was chelation costs. For manual exchange chelation costs were also significant, but this modality had the highest staff costs. The one-way sensitivity analysis showed that the rankings of the three transfusion modalities were most often dependent on the number of red blood cell units per procedure and the number of procedures per year. We suggest reporting the base case component costs and the sensitivity analysis results in separate paragraphs to improve clarity.	Thank you for your comment. The medical technologies consultation document summarises the conclusions drawn from the economic submission and assessment. The Committee decided not to change section 5.7 because it judged that the guidance was clear and because full details of the cost modelling are described in the assessment report and assessment report overview.

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30	8. Manufacturer (sponsor)	5.9	As a reminder, the company's base case made no assumptions about the attribution of the device costs as these were not included in the model. The text suggests that we did not consider these costs, however the effect of capital and maintenance costs were investigated separately from the de novo model due to the variety of options for these costs to be incurred (as identified in this paragraph). We demonstrated that even the largest UK SCD transfusion centres could have spare device capacity, enabling its use for other procedures and earning additional tariffs. We calculated a worst case scenario where all device costs were attributed to 5 SCD patients, which demonstrated that, in most cases, this would not outweigh the savings due to reduced chelation and staff costs. We consider that the description of the EAC's device capacity modelling is unclear and suggest the following amendment based on our understanding of the assessment report and EAC's additional information: "The EAC determined that treating 30 SCD patients per year would only incur 50% of the Spectra Optia capacity, and 15 patients would equate to 30% capacity. They therefore included scenarios in which 30 SCD patients incurred 100% and 50% of the capacity (capital and maintenance costs), and 15 patients incurred 100% and 30% of the capacity."	Thank you for your comment. The Committee decided not to change section 5.9 because full details of the cost modelling are available in the company submission, assessment report and assessment report overview, and because the description is simplified for clarity in the context of guidance.
31	8. Manufacturer (sponsor)	5.1	Monitoring costs for chelation therapy were included in the company's model (see p177 of 230). The value of £1540 per year was taken from Cherry et al (2012) and included	Thank you for your comment. The Committee decided not to change

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			monthly creatinine and weekly neutrophil counts.	section 5.1 because the monitoring costs added by the EAC referred to additional diagnostic monitoring costs of organ damage associated with iron overload, for instance MRI scans of the liver. This was not included by the company in its submission.
32	8. Manufacturer (sponsor)	5.14	We suggest an amendment for clarity, to distinguish this modelling from that described in 5.9/5.12.: "The EAC incorporated the 90% chelation treatment rate for manual exchange into scenarios in which 30 SCD patients used 100%, 50% and 0% of the device capacity. The latter represents centres that already have the device but do not use it for red blood cell exchange."	Thank you for your comment. Please see the response to comment 29.
33	8. Manufacturer (sponsor)	5.6	The lowest cost for treatment from the company's base case is £34,538 for Spectra Optia in children with no iron overload, not £48,093.	Thank you for your comment. The value of £48,093 is the lowest cost of treatment for adult patients; section 5.6 has been changed to further clarify that this cost is for adults.
34	8. Manufacturer (sponsor)	2.4	'increased patient compliance and efficiency of the procedure'.	Thank you for your comment. This has been updated.

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			General	
35	5. Patient/carer organisation	general	Dear Sir/Madam, Re- Consultation on the evaluation of MT271 Spectra Optia Apheresis device for automated red blood exchange in patients with Sickle Cell Disorder (SCD) Thank you for sharing the NICE Medical Technologies Programme consultation on the above. We have been pleased to work with the NICE team on this important evaluation. We are particularly pleased that the opinion of the Sickle Cell Society and individual expert patients living with SCD have also been taken in to account and acknowledged alongside the contribution from clinical experts. The Sickle Cell Society welcomes this consultation document, which sets out clearly the case for the provisional recommendation of Spectra Optia apheresis device for automated red blood cell exchange. Please refer to the Society's previous written comments about the importance of this technology for patients living with SCD, much of which has been addressed in the consultation document. The NICE Advisory Committee is particularly interested in receiving comments on 4 areas set out in the consultation document. The Society's comments on these are as follows; 1. Has all of the relevant evidence been taken in to account We believe most of the evidence has been taken in to account. However we are aware from clinicians and from some patients that the costs associated to travelling for automated red cell exchange, for example from Birmingham to London, can be a deterrent for some	Thank you for your comment. In the cost analysis, costs are considered from a NHS and personal social services perspective and do not therefore include patient travel costs. However, the Committee considered this comment carefully and noted expert advice that that there was inequity of care for people with sickle cell disease in the UK which is described in section 4.6. Further information may be included in the NICE adoption and impact resource. Section 5.9 describes the evidence on, and approach to, modelling the shared use of Spectra Optia between indications.

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			patients on low income. This is relevant to the point in the consultation document about inequity and lack of consistency for patients who live with SCD. We believe that the NHS England Specialised services policy is that appropriate travel costs for specialised treatment is reimbursable. This therefore, in our view, is relevant evidence consideration for the NHS system, particularly the responsibilities of commissioners and providers. Whilst it is fair to say that the majority of patients with SCD are black or from minority ethnic groups, the demographics in areas of high concentration is far more mixed and diverse than that which (2.11) in the document implies. 2. Are the summaries of clinical effectiveness and resource savings a reasonable interpretation of the evidence. We believe that the summaries of clinical effectiveness and resource savings are a reasonable interpretation of the evidence, with one exception. It is clear from the evidence that these devices are already used in the NHS system for conditions other than SCD. Has this been taken into account for this calculation? 3. Are the provisional recommendations sound and a suitable basis for guidance to the NHS We believe that the provisional recommendations are sound and a suitable basis for guidance to the NHS. However we believe that the section on NHS Considerations must be strengthened because, as the evidence shows, SCD treatment is inconsistent and inequitable. Commissioners/providers have a responsibility to implement any NICE guidance. Unless rapid progress is made by commissioners on establishing designated SCD designated centres, particularly in the current context of challenging NHS financial performance,	

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			we fear that that the inconsistency and inequality will simply be exacerbated. There is no evidence to suggest the plans for co-commissioning of specialised services between NHS England and local Clinical Commissioning Groups is having any impact on either improving services or reducing inequalities for SCD 4. Are there any equality issues that need special consideration and are not in the medical technology consultation document. Please see comments in 3 above. In addition, the fact that these devices can be located in Trusts for other conditions where they have a large sickle population, is evidence of inequality for SCD and in our view, is unacceptable. We believe the consultation document should therefore be more resolute on this point as part of its conclusions and in NHS system considerations. Yours sincerly [redacted] Sickle Cell Society	
36	3. Health Professional (within NHS, Expert Adviser)	General	Top up transfusion should have been a comparator (or could have been a comparator). Top up transfusions are often used as long term therapy, especially in children because of poor venous access. They are an appropriate option but will always cause iron loading and patients will need long term iron chelation. Therefore automated exchanges are preferred by many clinicians and patients as they do not cause iron loading. Some patients (particularly if they have poor venous access) may prefer long term top up and iron chelation and this is a valid and appropriate treatment if they are adherent to the iron chelation. Patient choice is an important factor in decision making. In my experience the majority of patients prefer	Thank you for your comment. Top-up transfusion was not included in the scope for this evaluation as it was judged that manual exchange transfusion was a more appropriate clinical comparator in terms of patient selection and indication. However, the Committee recognised that current practice is variable and that optimum treatment may require multiple treatment options. To reflect this, top-up transfusion was included as a comparator

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			exchange transfusion to top up transfusions and iron chelations. Sometimes long term top up therapy will not control the S% adequately and it is not appropriate for patients with relatively high Hb levels and these patients will need exchange transfusions.	in the economic modelling.
37	2. Health Professional (within NHS)	general	Optia Spectra is a very easily programmed automated exchange apheresis machine which we used at Homerton University Hospital where I worked before as Consultant Haematologist and Clinical Lead of Haematology Laboratory. Automated exchange programme is an lifesaving technology and we saved many lives by early and efficient exchange on ITU at Homerton University Hospital including pregnant clients with acute chest syndrome post-delivery. I hope NICE will review all literature and also will have at hand experience from Children Hospital of Philadelphia to approve Automated Exchange programme as mandatory for all UK centres looking after patients with sickle cell disease (n>100). Thanks [redacted]	Thank you for your comment. No relevant studies from the Children's Hospital of Philadelphia were identified through literature searches carried out for the company's submission or for the EAC's critique.
38	1. Heath professional (within NHS)	7 – cost evidence	Wholeheartedly agree with the comments made. We have a Spectra Optia in the department that is used for stem cell collection. We have several patients in Wales who would benefit from red cell exchange. The fact that automated exchange is not NICE approved inhibits the management and nursing staff from approving a business case to implement a programme in Wales.	Thank you for your comment.

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39	3. Health Professional (within NHS, Expert Adviser)	3.7	This shows that automated exchange results in an average decrease in ferritin whilst with partial exchange the ferritin increases	Thank you for your comment.
40	3. Health Professional (within NHS, Expert Adviser)	General	This provides useful evidence that patients on automated exchange programmes do not become iron loaded and that exchange transfusion can reduce iron load.	Thank you for your comment.
41	3. Health Professional (within NHS, Expert Adviser)	General	Spectra Optia is a good treatment option in patients with iron overload. It is not cost neutral over the first one-two years as patients will be treated with both the automated exchange process and with iron chelation. It will become cost neutral (and then of cost benefit) over several years as the iron burden will be decreased and then the iron chelation will be stopped. Therefore – if we take two patients who are beginning on long term transfusion and who have not been previously transfused (and are not iron loaded), automated pheresis will be cheaper than top up (and manual exchange) as there will be no additional iron chelation costs. If the patient has been commenced on top up transfusion and not treated appropriately with iron chelation they will become iron loaded (nb this should not happen with optimal iron chelation treatment). At this point the iron burden will need to be removed by iron chelation therapy. If they continue top up transfusions they will need to continue iron chelation for ever as they will continually be given iron. If they receive automated apheresis they will need iron chelation therapy to start with to reduce the	Thank you for your comment.

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			iron burden. However they will no longer be given excess iron every time they are transfused so that over time, as iron burden is reduced, the iron chelation therapy can be stopped and they will not need it again.	
42	4. Health Professional (within NHS)	general	There is currently inequity in access to automated exchange in England. Although there is a suggestion that London, Manchester and Birmingham (paediatric) have adequate access this is not the case. The reason is that most Apheresis services in London serve transplant haemato-oncology services, neurology, TTP and sickle services. This typically means that there has to be prioritisation so not all sickle patients access automated services every time and end up with manual exchange. Automated exchange is not always accessed as the tariff does not cover the costs so some centres use manual exchange as fewer units of blood may be used. The manual/top up processes means more iron loading. Iron loading is bad for health. Cardiac, liver and pancreatic toxicity. Chelation can be used but the cost is an issue but so is compliance. As a transplant physician some sickle cell patients may come to transplant and the literature is clear that iron loading with a ferritin > 1500 increases TRM. We should therefore try to reduce iron loading in any way we can! I do hope the appraisal will support this Optia assessment as this patient population is one of the most deprived and disadvantaged groups we deal with.	Thank you for your comment. The Committee was advised by clinical experts that provision of services for sickle cell patients were generally better in hospitals with a larger sickle cell population. However, the experts also stated that services were variable between centres in terms of the treatment delivered.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
43	7. Health Professional (other)	general	Dear NICE Thank you for the opportunity to comment on the evaluation documents for the above medical technology evaluation programme. I wish to confirm that the Department of Health has no substantive comments to make, regarding this consultation.	Thank you for your comment.
44	8. Manufacturer (sponsor)	5.4	As a reminder, adverse events and alloimmunisation costs were excluded from the company's model due to several characteristics; negligible costs, rarity and a lack of data suggesting different frequencies between transfusion modalities. Events related solely to the apheresis procedure were relatively common but mild and with negligible associated costs.	Thank you for your comment. The medical technologies consultation document summarises the conclusions drawn from the economic submission and assessment. Details of the company's economic model are fully described in the assessment report and assessment report overview.
45	8. Manufacturer (sponsor)	5.17	"local providers should take into account existing available devices..." We as an organisation are willing to collaborate and assist, where appropriate, with this. Utilising any device to its capacity would not only benefit the patients but the health system as a whole and we are fully supportive to drive health efficiencies.	Thank you for your comment.
46	8. Manufacturer (sponsor)	general	Thank you for inviting Terumo BCT to comment on the draft guidance. We felt that we had the opportunity to put our views forward during the establishment of the guidance and have no further comments to make at this	Thank you for your comment.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			stage, other than those mentioned above.	

"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or Advisory committees."

Appendix 1: Additional expert advice

1. ***Following treatment with Spectra Optia the patient (particularly children) may feel unwell/faint for 30-50 minutes following the procedure. Is this an important point that should be included in the guidance? Does your unit advise a post-procedure rest period?***

2. ***Some less experienced band 5 nurses may be too junior to supervise the auto exchange procedure, particularly for paediatric patients. The consulteer also states that 'senior band 5' is too subjective. Would you agree or disagree with this?***

Expert Adviser	*Comment*
Dr Gavin Cho	*1. I have not heard of this with regards to children in particular. The extracorporeal volume is going to be a proportionately larger part of the total blood volume for a child compared to an adult. Sometimes the apheresis machine is primed with donor red cells to start with in order to compensate for this.* *There is a post-procedure rest period to make sure the patient is OK but this is short (30 minutes?). We are not doing Paed patients at the moment in our unit.* *I am not sure in what part of the guidance this 'unwell/faint' comment should go.* *2. I agree that this is a little vague. It is hard to be prescriptive about this. It depends a lot on the actual person, there may be some very clever and competent Band 5 nurses who could learn the procedure but are fairly junior in years of experience. People in our unit have favoured a minimum of Band 6 to train up to operate the machine but I do not know if the decision was very scientific.*
Dr Sara Trompeter	*1. Yes 30 minutes adults and children. These are done as outpatient procedures and many patients go straight onto public transport.* *2. It needs to be a band 6 or 7. Band 5 have just been qualified and could work if they are not responsible for the venous access. This is why teams where there are band 5 doing this they have a high incidence of using central venous access. It needs to be a mix of 6 and 7.*