Clinical Evaluation Report for

Neonatal Resuscitation Circuit

According to

MEDDEV. 2.7.1 Rev.3

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Three Lions Limited

1. General details

1.1 Manufacture

Name: Three Lions Limited

Address: No. 21 Qunyi Industrial Park, Heng Shan Road, Kunshan, Jiangsu P.R. China, 215300

1.2 Verification Team

Item	Name
Technician	Vincent Chou
Q.C. Dept.	Swallow Ou
Production Dept.	G. Zhang, Michael Liu
Management Representative	Stephen Shan

1.3 Product Information

Product Category: Neonatal Resuscitation Circuit

Product Type: Single Use

2. Description of the device and its intended application

2.1 Abstract

This clinical evaluation report summarized the performance information for Three Lions Limited (hereinafter referred to as 3L) Neonatal Resuscitation Circuit (hereinafter referred to as Neo.) in order to demonstrate the clinical safety and effectiveness. We reviewed from directions, the compliance to harmonized standard, and equivalence comparison to marketed product, literature, and internal raw data. It is concluded that 3L Neonatal Resuscitation Circuit is able to perform the intended use and does not compromise patient or other user's safety.

3. Intended therapeutic and/or diagnostic indications and claims

3.1 Intended Use

3L Neo.is indicated as an accessory to add positive end expiratory pressure breathing capability. The valve is designed into the breathing circuit T-Piece with a standard fitting for face mask, laryngeal mask or endotracheal tube.
The 3L Neo. is a disposable breathing circuit for the transmission of breathing gases from a breathing gas source to the newborn patient in labor and delivery environments. It is suitable for newborn patients from birth to 1 month of age. It is intended exclusively for use in combination with the Resuscitaire Radiant Warmer.

3.2 Biological Aspect

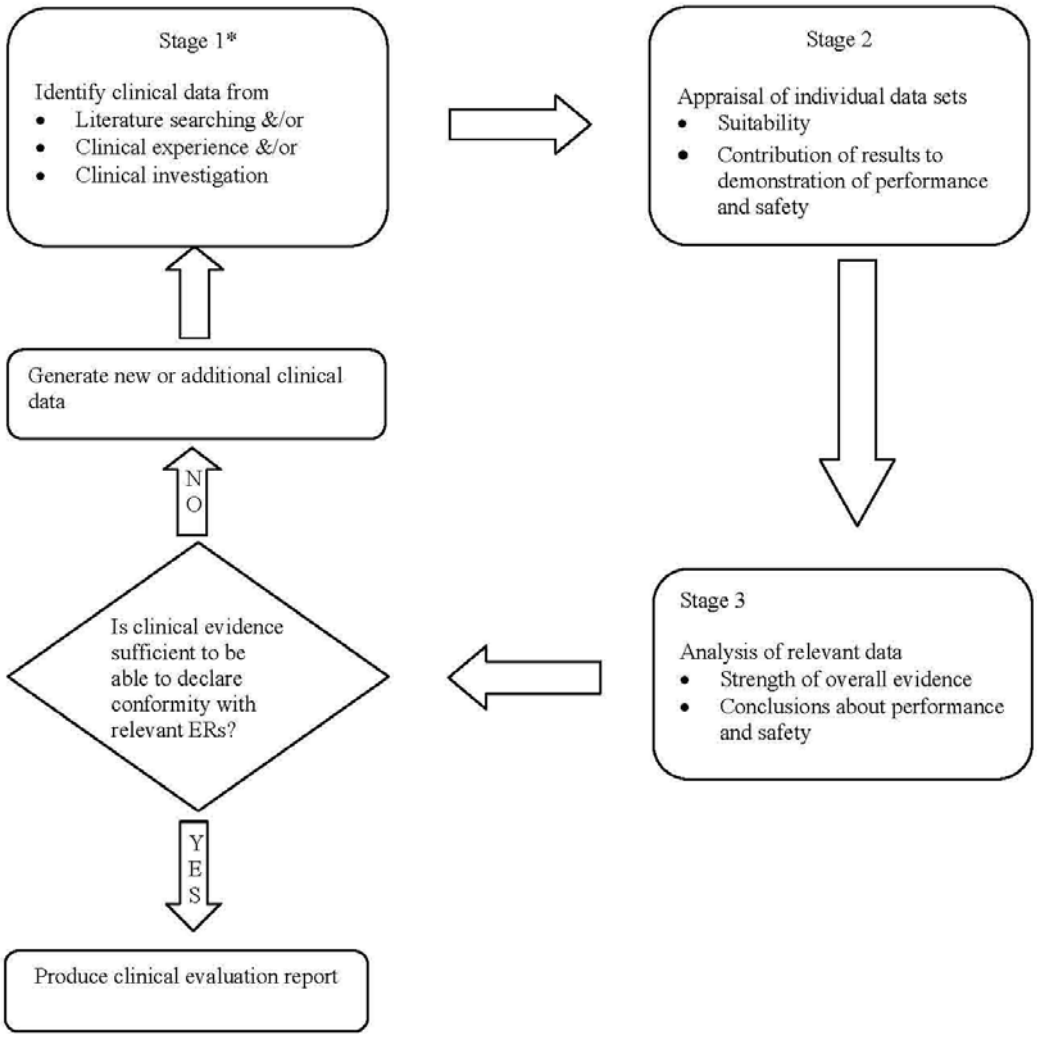
3L Neonatal Resuscitation Circuit had been tested according to the EN ISO10993-1 for the evaluation and conduct the EN ISO10993-5, -10 test. The result is confirmed to meet the requirement.

4. Context of the evaluation and choice of clinical data types

The same product has been sale for more than 100,000 per year on the medical device market in Europe, and has been used by many healthcare facilities in Europe. There is no advisory notice, recall to be active after the post marketing
Therefore, nasopharyngeal airway technology is very mature, nasopharyngeal airway research and evaluation and analysis of documentation, and device-related adverse event

information should be informative. Illustrates nasopharyngeal airway safety and efficacy in clinical applications.

4.1 Stages of clinical evaluation in accordance with the following flowchart:



*Conformity to harmonized performance standards may be sufficient to demonstrate compliance to relevant Essential Requirements (ERs)

4.2 LITERATURE SEARCH

Scope of the literature search:

Such as documents covered of Neonatal Resuscitation Circuit had in the security, performance and adverse event information.

4.3 Methods

(i) Date of search :2012.05.10
(ii) Name of person(s) undertaking the literature search: Vincent Chou
(iii) Period covered by search :
Nearly 5 years on the Neonatal Resuscitation Circuit had of security, poor performance and event information.
(iv) Literature sources used to identify data:

- scientific databases – bibliographic (e.g. MEDLINE),
- adverse event report databases (e.g. US FDA's **M**anufacturer **A**nd **U**ser Facility **D**evice **E**xperience database)
- reference texts

Include justification for choice of sources and describe any supplemental strategies (e.g. checking bibliography of articles retrieved, hand searching of literature) used to enhance the sensitivity of the search.

(v) Database search details:
- search terms: "Neonatal", "Resuscitation Circuit had ", "performance", and their relationships Boolean logic.
- medium used : Online, Attach copy of downloaded.

(vi) Selection criteria used to choose articles

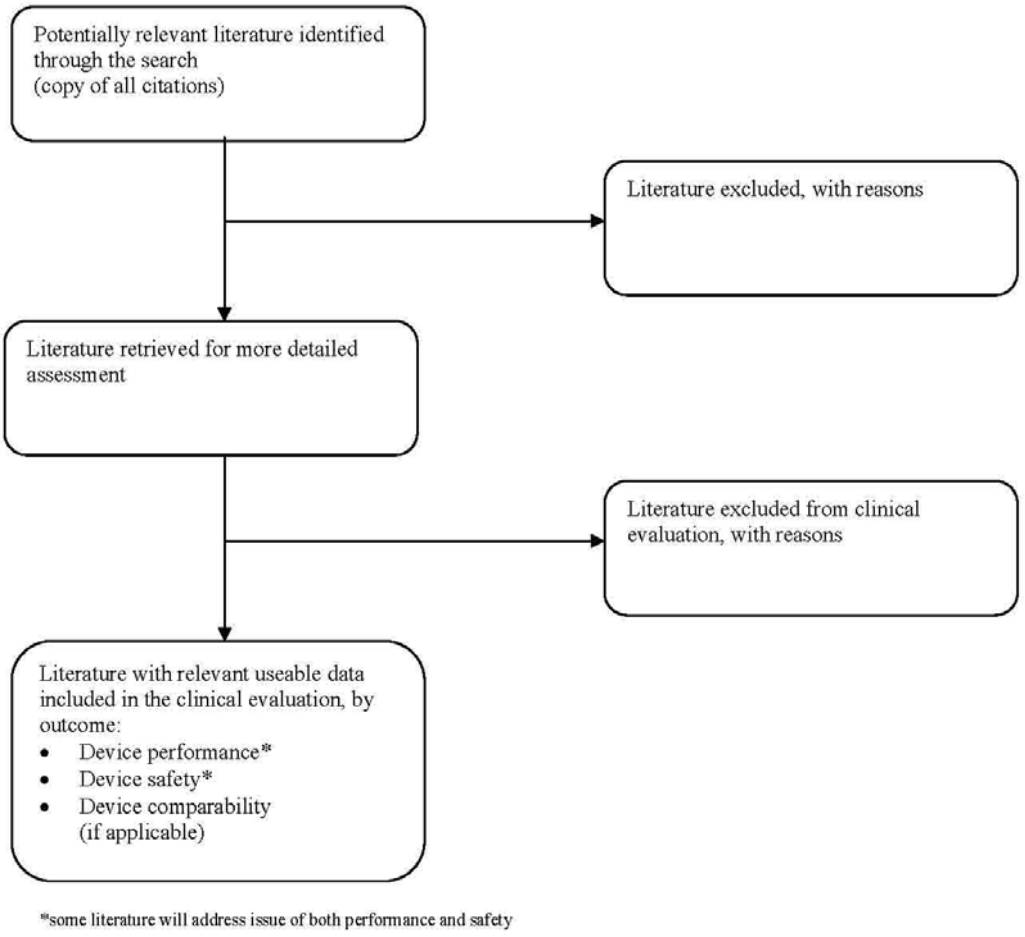
4.4 Outputs

(i) Attach copy of literature citations retrieved from each database search

(ii) Data selection process

Attach flow chart and associated tables showing how all citations were assessed for suitability for inclusion in the clinical evaluation.

Documenting the screening and selection of literature within a literature search report



*some literature will address issue of both performance and safety

5. Summary of the clinical data and appraisal

Associated with the content of the proposed assessment of retrieved documents as follows:

1. Arch Dis Child Fetal Neonatal Ed. 2007 September; 92(5): F421.

   Free-flow oxygen delivery using a T-piece resuscitator

2. Resuscitation. 2002 Jul;54(1):63-7.

   Improvement in timing and effectiveness of external cardiac compressions with a new non-invasive device: the CPR-Ezy.

   Boyle AJ, Wilson AM, Connelly K, McGuigan L, Wilson J, Whitbourn R.

   Source **:** Department of Cardiology, Cardiac Investigation Unit, St. Vincent's Hospital, Princes St., Fitzroy 3065, Melbourne, Australia. boylea@svhm.org.au

3. Arch Dis Child Fetal Neonatal Ed. 2009 Nov;94(6):F461-3. Epub 2009 Apr 8.

   Potential hazard of the Neopuff T-piece resuscitator in the absence of flow limitation.

   Hawkes CP, Oni OA, Dempsey EM, Ryan CA.

   Source : Department of Neonatology, Cork University Maternity Hospital, Wilton, Cork, Ireland.

4. Resuscitation. 2008 Nov;79(2):230-3. Epub 2008 Aug 8.

   Variation in inspiratory time and tidal volume with T-piece neonatal resuscitator: association with operator experience and distraction.

   McHale S, Thomas M, Hayden E, Bergin K, McCallion N, Molloy EJ.

   Source : Department of Neonatology, National Maternity Hospital, Holles Street, Dublin 2, Ireland.

Sample Appraisal Criteria for Suitability

The data suitability criteria can be considered generic to all medical devices, however the actual method used will vary according to the device considered.

Sutability Criteria	Description	Grading System	
Appropriate device	Were the data generated from the device in question?	D1 D2 D3	Actual device Equivalent device Other device
Appropriate device application	Was the device used for the same intended use (e.g., methods of deployment, application, etc.)?	A1 A2 A3	Same use Minor deviation Major deviation
Appropriate patient group	Where the data generated from a patient group that is representative of the intended treatment population e.g., age, sex, etc.) and clinical condition (i.e., disease, including state and severity)?	P1 P2 P3	Applicable Limited Different population
Acceptable report/data collation	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	R1 R2 R3	High quality Minor deficiencies Insufficient information

Sample Appraisal Criteria for Data Contribution

To assess the data contribution criteria of the suitable data, the evaluator should sort the data sets according to source type and then systematically consider those aspects that are most likely to impact on the interpretation of the results

Data Contribution Criteria	Description	Grading System	
Data source type	Was the design of the study appropriate?	T1 T2	Yes No
Outcome measures	Do the outcome measures reported reflect the intended performance of the device?	O1 O2	Yes No
Follow up	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	F1 F2	Yes No
Statistical significance	Has a statistical analysis of the data been provided and is it appropriate?	S1 S2	Yes No
Clinical significance	Was the magnitude of the treatment effect observed clinically significant?	C1 C2	Yes No

There is scope for the evaluator to determine what types of issues are most important in relation to the nature, history and intended clinical application of the device.

6. Data analysis

6.1 Performance

Content of the proposed assessment	Reference literature	Source	Description	Grading System
Appropriate device application	Free-flow oxygen delivery using a T-piece resuscitator	Bibliographic (NCBI: The National Center for Biotechnology Information)	Was the device used for the same intended use ?	■A1 Same use ☐A2 Minor deviation ☐A3 Major deviation
	Improvement in timing and effectiveness of external cardiac compressions with a new non-invasive device: the CPR-Ezy.	Bibliographic (NCBI)	Was the device used for the same intended use ?	■A1 Same use ☐A2 Minor deviation ☐A3 Major deviation
	Potential hazard of the Neopuff T-piece resuscitator in the absence of flow limitation.	Bibliographic (NCBI)	Was the device used for the same intended use ?	■A1 Same use ☐A2 Minor deviation ☐A3 Major deviation
	Variation in inspiratory time and tidal volume with T-piece neonatal resuscitator: association with operator experience and distraction	Bibliographic (NCBI)	Was the device used for the same intended use ?	■A1 Same use ☐A2 Minor deviation ☐A3 Major deviation

Section 5th applicability evaluation and clinical application of evaluation component retrieving documents, marked Nasopharyngeal Airway performance recognition can prove that devices complete performance, clinical application of these information from hospitals, scientific research and its application analysis, so the documentation has statistical significance, clinical importance and consistency of results.

6.2 Safety

The same product has been sale for more than 100,000 per year on the medical device market in Europe, and has been used by many healthcare facilities in Europe. There is no advisory notice, recall to be active after the post marketing. Neonatal Resuscitation Circuit has been introduced into the market for more than 10 years and distributed in and to areas mainly of European. does not compromise patient or other user's safety.

6.3 Product Literature and Instructions for Use

The basis of the relevant standards and regulations, and in the light of the content of related files and their associated adverse events, the 3L Neonatal Resuscitation Circuit series manual, labeling files, such as the preparation and analysis into the risk management evaluation.

7. Conclusions

Based on the above analysis and evaluation, 3L Neonatal Resuscitation Circuit safety and performance has met the company claimed that the intended use of the product. And risk evaluation and clinical evaluation of weighing devices in patients with another when the risks associated with the apparatus used is acceptable. It was concluded that 3L Neonatal Resuscitation Circuit is substantially equivalent to CE MDD cleared products, functions as intended, and without significant safety concerns. The assessment of user benefit to health from use as intended are much higher than the probable risks of injury or illness.

Clinical evaluation checklist for Notified Bodies			
Ref	**Requirement**	**Fulfilled**	**Comment**
0	**Conformity without Clinical Data**		
0.1	Any demonstration of conformity without clinical data (Annex 7.1.5 of 90/385/EEC and Annex X.1.1d of 93/42/EEC) must be adequately justified and based on • the output of the risk management process • viewed in the context of the device-body interaction • the intended clinical performance • the claims of the manufacturer. Adequacy of demonstration of conformity based on performance evaluation, bench testing and pre-clinical evaluation in the absence of clinical evaluation must be duly substantiated. The notified body must review the manufacturer's justification, the adequacy of data presented and whether or not conformity is demonstrated. • Is the manufacturer's justification adequate? • Is the performance evaluation, bench testing and preclinical evaluation adequate to demonstrate conformity to the Essential Requirements?	■ Yes ☐ No ☐ N/A	

1	**Clinical Evaluation, General**			
1.1	The manufacturer should include in the technical documentation a statement on the route(s) applied to retrieve the clinical data used to affix the “CE” marking. The statement should make clear whether that clinical data was obtained from the published literature or the results of clinical investigations or a combination of both and shall include an adequate justification of the route(s) selected and a demonstration of equivalency (technical, biological, clinical) and adequacy if clinical data from similar devices have been used.	■Yes ☐ No ☐ N/A	Clinical literature	V
			Published	
			Unpublished	
			Equivalence demonstrated	
			Clinical investigation	
			Combination of literature and investigation data Comment	
1.2	The Clinical Evaluation Report and the full clinical data used for CE marking should be included within the technical documentation	■Yes ☐ No ☐ N/A		
1.3	The manufacturer has clearly documented the objectives and the scope of the clinical evaluation and specified the clinical ER’s [e.g. clinical performance(s), safety, risks and favourable benefit/risk ratio related to intended use, target group(s) and indication(s)] to be met	■Yes ☐ No ☐ N/A		
1.4	The manufacturer has clearly outlined the performed steps and procedures of clinical evaluation according to this MEDDEV (specifically sections 5 to 9), adequate justification given for deviations	■Yes ☐ No ☐ N/A		
2	**Clinical investigation route**		**Not applicable**	
3	**Clinical literature data** A critical evaluation of relevant scientific literature that is currently available relating to safety, performance, design characteristics and intended purpose in the form of a written report			

3.1	**Methodology**		
3.1.1	A critical evaluation of relevant scientific literature has been presented	■Yes ☐ No ☐ N/A	
3.1.2	A search protocol for the identification, selection, collation and review of relevant publications should be written	■Yes ☐ No ☐ N/A	
3.1.3	The objective of the literature review should be clearly defined	■Yes ☐ No ☐ N/A	
3.1.4	The types of studies that are relevant to the objective of the literature review should be specified	■Yes ☐ No ☐ N/A	
3.1.5	Data should be taken from recognised scientific publications. Unpublished data should also be taken into account in order to avoid publication bias.	■Yes ☐ No ☐ N/A	
3.1.6	The literature review should state:		
3.1.6.1	sources of data, extent of the searches of databases or other sources of information	■Yes ☐ No ☐ N/A	
3.1.6.2	rationale for the selection/ relevance of the published literature	■Yes ☐ No ☐ N/A	
3.1.6.3	reasons for believing that all relevant references, both favorable and unfavorable, have been identified	■Yes ☐ No ☐ N/A	
3.1.6.4	criteria for exclusion of particular references together with a justification for this exclusion.	☐ Yes ☐ No ■ N/A	
3.1.6.5	detailed description of the different stages of literature search (including identification, appraisal, analysis and conclusion of hits)	■Yes ☐ No ☐ N/A	
3.2	**Relevance of data presented**		
3.2.1	A literature review should clearly establish the extent to which the literature relates to the specific characteristics and features of the device under consideration.	■ Yes ☐ No ☐ N/A	

3.2.2	If the published studies do not directly refer to the device in question, the manufacturer must demonstrate equivalence with the device, which is the subject of the published reports.	☐ Yes ☐ No ■ N/A	
3.2.3	To be equivalent, the devices should have similarity with regard to the clinical, technical and biological parameters with special attention to the performance, principles of operation and materials; or if there are differences identified, an assessment and demonstration of the significance these might have on safety and performance must be set out[1]	■ Yes ☐ No ☐ N/A	
3.2.4	The manufacturer must be able to demonstrate the adequacy of the data in addressing the aspects of conformity set out in the objective	■ Yes ☐ No ☐ N/A	
3.3	**NB Assessment of clinical data** **The literature review should make clear the significance that is attached to particular references based on a number of factors. These include:**		
3.3.1	relevance of the author's background and expertise in relation to the particular device and/or medical procedure involved	■ Yes ☐ No ☐ N/A	
3.3.2	whether the author's conclusions are substantiated by the available data	■ Yes ☐ No ☐ N/A	
3.3.3	whether the literature reflects the current medical practice and the generally acknowledged "state of the art" technologies	■ Yes ☐ No ☐ N/A	
3.3.4	whether references are taken from recognised scientific publications and whether or not they have been reported in peer reviewed journals	■ Yes ☐ No ☐ N/A	
3.3.5	the extent to which the published literature is the outcome of a study/studies which have followed scientific principles in relation to design[2]	■ Yes ☐ No	

[1] Equivalence means:

Clinical: used for the same clinical condition or purpose, at the same site in the body, in similar population (including age, anatomy, physiology); have similar relevant critical performance according to expected clinical effect for specific intended use.

Technical: used under similar conditions of use; have similar specifications and properties e.g. tensile strength, viscosity, surface characteristics; be of similar design; use similar deployment methods (if relevant); have similar principles of operation.

Biological: use same materials in contact with the same human tissues or body fluids.

[2] For example in having demonstrable and appropriate endpoints, inclusion and exclusion criteria, an

		☐ N/A	
3.4	**Critical evaluation of the literature** **The literature review should contain a critical evaluation of the literature. This critical evaluation should:**		
3.4.1	be written by a person suitably qualified in the relevant field, and reviewed and approved by an expert knowledgeable in the “state of the art” and able to demonstrate objectivity	■ Yes ☐ No ☐ N/A	
3.4.2	contain a short description of the medical device, its intended functions, description of the intended purpose and application of use	■ Yes ☐ No ☐ N/A	
3.4.3	contain an analysis of all the available data considered, both favourable and unfavourable	■ Yes ☐ No ☐ N/A	
3.4.4	establish the extent to which the literature relates to the specific characteristics and features of the device being assessed, taking due account of the extend of similarity between the device(s) covered by the literature and the device under assessment	■ Yes ☐ No ☐ N/A	
3.4.5	demonstrate that those aspects of the use of the device, including performance, addressed in the clinical part of the risk analysis are met as claimed by the manufacturer, and that the device fulfils its intended purpose as a medical device	■ Yes ☐ No ☐ N/A	
3.4.6	analyse the identified hazards, the associated risks and the appropriate safety measures of patients, medical staff and	■ Yes ☐ No ☐ N/A	
3.4.7	contain a risk analysis relevant to the device design, materials and procedures involved, taking into account any adverse events, results of post-market surveillance studies, modifications and recalls (if known)	■ Yes ☐ No ☐ N/A	
3.4.8	contain a description of the methods of weighting of different papers and the statistical methods of analysis employed taking into account the assessment methods, the type and duration of study and the heterogeneity of the population included within the study	■ Yes ☐ No ☐ N/A	

appropriate and validated number of patients submitted, carried out for an appropriate duration, providing evidence and analysis of all adverse incidents, deaths, exclusions, withdrawals and subjects lost follow-up and identifying an appropriate statistical plan of analysis. Ideally, evidence should be generated from a clinical trial (controlled if appropriate), properly designed cohort/case controlled study, well documented case histories or sequential reports conducted by appropriate experienced experts, whether in relation to the device itself or an equivalent device. If unpublished data is being included in the assessment, the literature review will need to weigh the significance that is attached to each report.

3.4.9	include an analysis of the market experience of the same or similar devices, including the results of post-marketing studies, post-market surveillance and short- and long-term adverse events	■ Yes ☐ No ☐ N/A	
3.4.10	contain a list of publications appropriately cross referenced in the evaluation	■ Yes ☐ No ☐ N/A	
3.4.11	if the clinical data relates to an equivalent device, contain a statement that equivalence with all the relevant characteristics has been demonstrated	■ Yes ☐ No ☐ N/A	
3.4.12	include a conclusion[3] with a justification, including an assessment of any probable benefit to health from the use of the device as intended by the manufacturer, against probable risks of injury or illness from such use taking account of the "state of the art". The conclusions should make clear how the objectives of the literature review have been met and identify any gaps in the evidence necessary to cover all relevant aspects of safety and performance	■ Yes ☐ No ☐ N/A	
3.4.13	The critical evaluation should be signed and dated by the author	■ Yes ☐ No ☐ N/A	
3.5	**NB Assessment of the critical evaluation of literaturenpresented by the manufacturer**		
3.5.1	Are the manufacturers' conclusions valid?	■ Yes ☐ No ☐ N/A	
3.5.2	Is the data, taken together with the available pre clinical data, sufficient to demonstrate compliance with the essential requirements covering safety and performance of the device in question under normal conditions of use?[4]	■ Yes ☐ No ☐ N/A	
3.5.3	Are the claims made in the device labeling substantiated by the clinical data taken together with the pre-clinical data?	■ Yes ☐ No ☐ N/A	
3.5.4	Was the assessment performed in a critical and objective manner?	■ Yes ☐ No ☐ N/A	

[3] Conclusions should consider the claimed use - indications, contra-indications and instructions for use proposed by the manufacturer.

[4] If not, identify gaps in the demonstration of compliance with the relevant essential requirements or in the demonstration of equivalence that need addressing through the means of a specifically designed clinical investigation(s).

4	**Post-market clinical follow up – the notified body should check and review the manufacturer's post market clinical follow up plan:**		
4.1	Has the manufacturer presented an appropriate plan for post-market clinical follow up in line with appropriate guidance?	■ Yes ☐ No ☐ N/A	
4.2	If no post-market clinical follow up plan is presented, has this been adequately justified by the manufacturer?	☐ Yes ☐ No ■ N/A	
4.3	Has the manufacturer an adequate post-market surveillance system in place?	■ Yes ☐ No ☐ N/A	
4.4	Has the manufacturer committed to inform the NB of significant updates to their clinical evaluation arising from PMS/PMCF?	■ Yes ☐ No ☐ N/A	
5	**Notified Body Decision Making**		
5.1	**In reviewing the evaluation of clinical data submitted by the manufacturer the NB must decide whether the manufacturer has adequately**		
5.1.1	described and verified the intended characteristics and performances related to clinical aspects	■ Yes ☐ No ☐ N/A	
5.1.2	performed a risk analysis and estimated the undesirable side effects	■ Yes ☐ No ☐ N/A	
5.1.3	concluded on the basis of documented justification that the risks are acceptable when weighed against the intended benefits	■ Yes ☐ No ☐ N/A	
5.2	**NB assessment of benefit/risk presented in the clinical evaluation data**		
5.2.1	the listing and characterisation of the clinical performance of the device intended by the manufacturer and the expected benefits for the patient	■ Yes ☐ No ☐ N/A	
5.2.2	the use of the list of identified hazards to be addressed through evaluation of clinical data	■ Yes ☐ No ☐ N/A	
5.2.3	the adequate estimation of the associated risks for each identified hazard by: a) characterising the severity of the hazard; b) estimating and characterising the probability of occurrence of the harm (or health impairment or loss of benefit of the treatment) (document with rationale)	■ Yes ☐ No ☐ N/A	

5.2.4	the decision on the acceptability of risks in relation to each identified hazard	■ Yes ☐ No ☐ N/A	