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Type of Action	Pilot B
Project Title	An optical neuro-monitor of cerebral oxygen metabolism and blood flow for neonatology
Acronym	BabyLux
Project n.	620996

D5.3 APPROVAL BY LOCAL AUTHORITIES

Work Package	WP5
Lead Partner	RH-Neo
Contributing Partner(s)	ICFO, HemoPhotonics, IRCCS Ca' Granda, RH-Neo, PoliMi
Security Classification	CO (Confidential)
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Document history

Version	Date	Comments	Authors
1.0	27.01.2016	First draft	Bjørn Andresen, Gorm Greisen (RH)
1.1	30.01.2016	Second draft	A.Torricelli (PoliMi)

Statement of originality

This deliverable contains original unpublished work except where clearly indicated otherwise. Acknowledgement of previously published material and of the work of others has been made through appropriate citation, quotation or both.

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Table of Contents

1. Executive Summary

The manufacturer and clinical partners have compiled the application and accompanying documentation for submission to the national medical device agencies. Approval will be applied for in parallel in both Denmark and Italy.
The draft clinical protocol (D5.1 Definition of the Clinical Protocol) has been modified into a clinical investigation plan in compliance with ISO 14155:2011 “Clinical investigation of medical devices for human subjects – Good clinical practice”. Main changes are description of device accountability, monitoring plan, schedule and updated safety assessment based on a risk assessment according to ISO 14971: 2007. Changes to the protocol will be reported as an amendment to the research etichs comitees as required.
The BabyLux user manual and investigator’s brochure have been updated to comply with Annex B of ISO 14155:2011.

The applications Have been submitted in both Denmark and Italy on February 2016.

2. Introduction

The BabyLux demonstrator is a medical device intended for clinical investigation and not bearing CE mark.

This deliverable includes the application and accompanying documentation to the medical device agencies in both Denmark and Italy.

This procedure is required by the EU regulations on Medical Devices, in particular by three main Directives:

- Council Directive 90/385/EEC on Active Implantable Medical Devices (AIMDD) (1990)
- The Council Directive 93/42/EEC on Medical Devices (MDD) (1993)
- Council Directive 98/79/EC on In Vitro Diagnostic Medical Devices (IVDMD) (1998)

The BabyLux demonstrator is not “implantable, nor “in vitro”, therefore it is regulated by the “The Council Directive 93/42/EEC on Medical Devices (MDD) (1993)”

The latest consolidated version 11.01.2007 including amendment No. 5 (Directive 2007/47/EC) is attached in different languages:

- CELEX_01993L0042-20071011_DA_TXT.pdf, Danish
- CELEX_01993L0042-20071011_EN_TXT.pdf, English
- CELEX_01993L0042-20071011_IT_TXT.pdf, Italian
- CELEX_01993L0042-20071011_ES_TXT.pdf, Spanish

The main articles and annexes in the latest consolidated version of the 93/42/EEC MDD relevant to BabyLux are: Article 1, Article 3, Article 9, Article 15, Article 17, Annex I, Annex VIII, and Annex X.

Further information can be found on the website:
http://ec.europa.eu/growth/sectors/medical-devices/index_en.htm.

3. CONTENT

3.1 Fondazione IRCCS Ca' Granda Milan: Approval by Italian Ministry of Health

The procedure for starting a clinical investigation in Italy with a medical device not bearing a CE mark is described in the web pages of the Italian Ministry of Health at the following link: http://www.salute.gov.it/portale/ministro/p4_8_0.jsp?lingua=italiano&label=servizionline&idMat=DM&idAmb=SC&idSrv=ICPRE&flag=P

The documents prepared for the final application (see Appendix A) are:

- 01: Summary document for the notification of clinical investigation with medical device;
- 02a: Declaration of the sponsor;
- 02b: Declaration of the manufacturer;
- 03: Clinical Investigator's Brochure;
- 04: Risk analysis;
- 05: User manual;
- 06: Literature survey;
- 07: Clinical investigation plan;
- 08: Evaluation by the Ethical Committee;
- 09: List of the Italian sites;
- 10: Receipt of the credit transfer of 2.160,45 euro addressed to account BIC BPPIITRRXXX, IBAN IT24 F0760114500000060413416 in name of Tesoreria di Viterbo with reason "art. 5, comma 12, L. 407/90 – Indagine clinica con dispositivo medico- Ministero della Salute";
- 11: Declaration of the power of representation of the sponsor

3.2. RegionH, Rigshospitalet: Approval by the Danish Medicines Agency

The documents included in the final application to Medical Devices under the Danish Medicines Agency (Medicinsk Udstyr, Sundhedsstyrelsen) are (see Appendix B):

- Cover letter (*in Danish*)
- The Danish Medicines Agency's application form for clinical investigations (*in Danish*)
- The BabyLux Clinical Investigation Plan: "An optical neuro-monitor of cerebral oxygen metabolism and blood flow for neonatology" v. 4.0
- The BabyLux Investigator's Brochure (IB) v. 1.0
- Patient information and informed consent form for all three test settings as previously approved by the ethics committee (*all in Danish*):
    - Deltagerinformation til forældre pCO2 v. 3.0
    - Deltagerinformation til forældre brugervenlighed v. 3.0
    - Deltagerinformation til forældre sektio v. 3.0
    - Samtykke (S5) pCO2 v. 1.0
    - Samtykke (S5) brugervenlighed v. 1.0
    - Samtykke (S5) sektio v. 1.

- Letter of Authority, allowing the Danish Health Agency to access the subject's record (*in Danish*)

- Statement of Compliance by the manufacturer certifying that the device complies with the essential requirements of the Medical device directive 93/42/EEC apart from the aspects covered by the investigation
- The BabyLux User's Manual (UM) v. 1.0
- The BabyLux Risk Assessment v. 1.0
- A copy of the approval by the ethics committee (*in Danish*)

Pictures of the device are included in the investigator's brochure.

4. Conclusions and future work

The documents required for the application for use of the BabyLux device in clinical investigation has been prepared. Submission to the competing authorities is expected within February 2016. As approval has previously been obtained for both technologies integrated in the BabyLux device separately, we expect to get approval without delay.

Queries by the health authorities will be thoroughly and promptly answered, if any.

In final preparation for the clinical investigation, the Case Record Forms and Trial Master File will be compiled, and the data storage and management plan notified to the Data Protection Agency.

Appendix A

Italian application submitted to the Ministry of Health on 25 February 2016.

Appendix B

Danish application submitted to the Danish Medicines Agency on 12 February 2016.