

MHRA

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United Kingdom

[I/S]

Sadler Building
The Oxford Science Park
OX4 4GE
UK

17 November 2017

Our ref: CI/2017/0044

Dear [I/S]

CLINICAL INVESTIGATION: NO OBJECTION

Manufacturer : Oxehealth Limited
Model Name : Oxecam
Your notification dated : 08/08/2017
Protocol version number : Version 1.1 dated 07 August 2017
Title of the study : Assessing the clinical performance and accuracy of the
Oxecam medical device

Further to your emails of 12/10/2017 and 30/10/2017 replying to the Conditional No Objection letter of 4/10/2017, I hereby notify you that the UK Competent Authority is of the opinion that the conditions have been met and therefore MHRA has no grounds for objection to the commencement of your clinical investigation in the UK.

Competent Authority Comments

- a. Please ensure that all requirements listed in the appendix to this letter are understood and adhered to, especially the requirements set out below for reporting adverse events to the UK Competent Authority. In addition, please submit quarterly summary SAE reports.
- b. We note your application was premature, because it was submitted before all testing was complete, this was despite your declaration in the application form stating the testing was complete and the device met the Essential Requirements apart from the one(s) under investigation. For future applications, please be aware MHRA will object to the commencement of any study if applications are submitted prematurely and/or manufacturers are making incorrect declarations. This may also lead to rejection of applications as being invalid.

- c. We also note, according to the information you have submitted, you appear to have started enrolment and some testing on the subjects before MHRA issued the final no objection letter confirming the conditions have been met. This is also despite several reminders from MHRA stating the study must not start in the UK until written confirmation had been given.

We would point out that using a non-CE-marked device on subjects without Competent Authority approval is in breach of the Medical Devices Regulations and as such is illegal. We are considering whether this matter needs to be brought to the attention of your academic institution.

- d. The device is indicated for use in adolescents as per the IFU. The data generated from this study will not demonstrate safety and performance of the device in an adolescent population and further information will be required to demonstrate this. The Manufacturer states they will provide additional data to evidence the use of the device in adolescents during the CE marking submission.

Yours sincerely

[I/S]

[I/S]

| (on behalf of the Competent Authority)

Tel:

[I/S]

| Email:

[I/S]

Appendix

Before commencing the clinical investigation

You should ensure that you have the following in place before commencing the study in the UK:

- Favourable REC opinion letter (required for all studies)
- Signed contract/agreement with participating NHS organisation(s)
- NHS Permission Letter (for studies conducted in the NHS in Northern Ireland, Scotland and Wales)
- HRA Approval letter (for studies conducted in the NHS in England)

	Studies conducted in England	Studies conducted in Northern Ireland, Scotland and Wales	Provide to MHRA when available	Keep available for MHRA
Favourable REC opinion letter	x	x	x	
Signed contract/agreement with participating NHS organisation(s)	x	x		x
NHS Permission Letter		x		x
HRA approval letter	x			x

If not already provided as part of the notification to MHRA, please provide us with a copy of the ethics committee favourable opinion letter as soon as it becomes available. The clinical investigation must not commence at any UK centre until the relevant ethics committee favourable opinion is obtained.

Each individual site in this clinical investigation must have confirmed management permission. NHS organisations in England provide this by confirming that they have the capacity and capability to take part in the study. In Northern Ireland, Scotland and Wales NHS organisations provide a letter of NHS Permission. Non-NHS organisations should confirm their management permission and receive a favourable Site-Specific Assessment from the Research Ethics Committee. Please note that this clinical investigation must not commence in any UK site until you have received the relevant confirmation for that individual site.

In addition, this clinical investigation must not commence in any NHS site in England until it has received HRA Approval.

Full details can be obtained from the Health Research Authority website (<http://www.hra.nhs.uk/>) or by emailing hra.queries@nhs.net. When seeking advice from the Health Research Authority you should make it clear that the investigation involves a non-CE marked medical device.

Labelling

The device(s) must be labelled “*exclusively for clinical investigations*”.

Following commencement of this clinical investigation:

Adverse Event Reporting

You are reminded that Regulation 16(10)(a) of the Medical Devices Regulations 2002 (SI 618) and Annex X of the Medical Devices Directive 93/42 require you to record fully all adverse events and report all serious adverse events occurring in all participating centres to the Competent Authority.

Such reports should be made to the MHRA (devices) Adverse Incident Centre and should include all serious adverse events, whether initially considered to be device related or not, that have occurred in all participating centres, whether European or non-European.

A “serious adverse event” is an adverse event that:

- a) led to a death, injury or permanent impairment to a body structure or a body function.
- b) led to a serious deterioration in health of the subject, that either resulted in:
 - a life-threatening illness or injury, or
 - a permanent impairment of a body structure or a body function, or
 - in-patient hospitalization or prolongation of existing hospitalization, or
 - in medical or surgical intervention to prevent life threatening illness
- c) led to foetal distress, foetal death or a congenital abnormality or birth defect.

NOTE 1: Planned hospitalization for pre-existing condition, or a procedure required by the Clinical Investigation Plan, without a serious deterioration in health, is not considered a serious adverse event.

NOTE Device deficiencies that might have led to a serious adverse event where a suitable action had not been taken or an intervention had not been made or if circumstances had been less fortunate are handled under the serious adverse event reporting system.

Such adverse events should be reported as soon as possible. When reporting these events please include the total number of patients treated in the UK at the time of reporting.

MEDDEV 2.7/3 provides guidance on the requirements for reporting serious adverse events with timelines and provides a template form to use for this purpose. This document can be downloaded from: <http://ec.europa.eu/growth/sectors/medical-devices/guidance/>

In the case of a blinded control clinical investigation using a CE marked device as control, all adverse events should be reported to MHRA in line with the requirements above.

Where an un-blinded controlled clinical investigation is being carried out using a CE marked device as the control, adverse events involving the CE marked devices should be reported to the competent authority in line with vigilance guidelines.

Please use the MEDDEV 2.7/3 reporting Excel spreadsheet to report serious adverse events. Please email the complete spreadsheet to [I/S] quoting MHRA's CI reference number or upload through MORE <https://aic.mhra.gov.uk/> including the MHRA's CI reference number in the 'incident description' field. **Please ensure that sufficient information is included in the table to allow MHRA to understand what happened in each incident and that all fields are complete.** Failure to do so will result in further requests for additional information on each individual case, therefore please ensure the following:

- a. ALL sections are completed in FULL, especially sections where a decision is required as to whether or not the event is device / procedure related.
- b. Any deaths reported should have the cause of death recorded.
- c. Reports should be made in a timely manner as per regulatory requirements.

Please note that adverse events involving a medicinal product should also be reported to MHRA Medicines by the manufacturer of the medicine or sponsor of the study. Information on the requirements for reporting of such events can be found here <https://yellowcard.mhra.gov.uk/>

Summary reports

In addition to the reporting of individual serious adverse events as detailed above, please provide summary reports of all serious adverse events. Please refer to the Competent Authority Comments section at the top of this letter for details of the frequency required.

When providing these summaries please include in tabular format the following information broken down by event type:

- number of serious adverse events
- number of participants affected by those events
- percentage of the total number of enrolled participants affected by those events

Event type	Number of events	Number of participants affected	% of participants affected
e.g. Stroke			
e.g. Heart Failure			

Please also include a summary analysis of the serious events together with the manufacturer's conclusions. Please also ensure the following when submitting a table of adverse events:

- ALL sections are completed in FULL, especially sections where a decision is required as to whether or not the event is device / procedure related.
- Any deaths reported should have the cause of death recorded.

- Reports should be made in a timely manner as per regulatory requirements.
- Incomplete tables will not be assessed and will be returned to you.

Amendments

You must notify the Competent Authority of all proposed changes to this investigation and await our letter of no objection before you implement them. This includes changes relating to the device, study documentation including the clinical investigation plan, investigators or investigating institutions, and changes made upon the request of an ethics committee. Failure to notify us of proposed changes could result in the manufacturer being liable to prosecution.

When notifying changes, please provide the following information:

- the reference number shown at the top of this letter.
- In tabular format - a summary of each proposed change with the rationale and justification for each change.
- red lined and clean copies of all amended study documentation.
- a signed statement by or on behalf of the manufacturer that the proposed change(s) do not predictably increase the risk to the patient, user or third party.

Study deviations

You must notify the Competent Authority of all deviations to the study as soon as you have been made aware of them. Please provide details about the nature of the deviation, when it occurred, where it occurred, and any proposed corrective actions.

Final Report

Under Regulation 16(11) and 29(10) of the Medical Devices Regulations 2002 (SI 618), as amended by the Medical Devices (Amendment) Regulations 2008 (SI 2936), you are required to notify MHRA of the end of this clinical investigation. In the case of premature termination a justification for the premature termination is also required. A letter informing the Competent Authority of when the trial has been completed would be appreciated.

Under Regulation 16(10) and 29(9) of the Medical Devices Regulations 2002 (SI 618) the written report of a completed clinical investigation must be kept available for the Secretary of State if required. MHRA request that a copy of the written report is provided when available.

CE Marking

MHRA would be interested to know when the device under investigation is CE marked and would be most grateful for notification of this once completed.

We request that at the same time MHRA are also provided with a summary report of the clinical data from this clinical investigation that was used to support the CE mark.

MHRA actions

The assessors who assisted with the evaluation of your notification will be sent a copy of this decision, for information only and strictly "in confidence". Our decision will also be notified to the relevant ethics committee(s) and HRA if you have confirmed that you are happy for us to do this. If you have not then you may wish to advise them of this decision yourself.

We will retain all the documentation provided by you for one month from the date of this letter. After this time the documentation (except for one copy, retained for record purposes only) will be destroyed, unless you request its return.