Confidentiality Advisory Group

Minutes of the meeting of the Precedent Set Review Sub Committee of the Confidentiality Advisory Group held on *29 September 2023* via correspondence.

Present:

Name	Capacity	Items
Professor William Bernal	CAG Alternate Vice Chair	2.1
Dr Pauline Lyseight-Jones	CAG Lay Member	2.1
Dr Harvey Marcovitch	CAG Expert Member	2.1

Also in attendance:

Name	Position (or reason for attending)
Mr William Lysé	HRA Approvals Administrator
Ms Caroline Watchurst	HRA Confidentiality Advisor

1. DECLARATIONS OF INTEREST

There were no declarations of interest.

2. NEW PRECEDENT SET REVIEW APPLICATIONS FOR CAG CONSIDERATION

2.1	**23/CAG/0148**	**Aspirin Esomeprazole Chemoprevention Trial – EXtension Long-term Clinical Study : A cohort follow up of a phase III randomised study of**

		Aspirin and Esomeprazole Chemoprevention in Barrett's Metaplasia
	Chief Investigator:	Professor Janusz Jankowski
	Controller:	University College London
	Application type:	Research

The Group reviewed the above application in line with the CAG considerations.

Summary of application

This application from University College London (UCL) set out the purpose of medical research that aims to collect the health status of previously consented AspECT participants (alive and deceased), to confirm if aspirin and proton pump inhibitor (PPI)s effectiveness increases long term, to see if aspirin effectiveness increases, and to see if any complications from PPI use occur over a longer period of follow up.

AspEXT EXceL is a follow up trial to the original AspECT consented trial which tested 2 drugs – a high and low dose PPI, with and without aspirin in patients with Barrett's oesophagus (a condition which can develop into oesophageal cancer many years later), with the aim of investigating the benefits in reducing the risk of cancer in these patients. The results from the original trial showed that high dose PPI significantly reduced the occurrence of cancer. In addition, high dose PPI with aspirin appeared to be more effective than when used alone. However, the trial was not long enough to determine whether conversion to oesophageal cancer was significant for each/both drugs.

Most of the patients will be alive, and data collection will be undertaken with consent, and is not relevant for 's251' support. Some of the patients, however, may have died and will therefore not be able to consent. Participating sites will be asked to provide as much information as possible regarding oesophageal adenocarcinoma diagnosis, date and cause of death and PPI and Aspirin use prior to death using hospital notes, and this will be entered into an electronic case report form (eCRF) called OpenClinica (hosted by Amazon Web Services). 's251 support is required for this.

Where this information is missing, sites will send confidential patient information (AspECT ID, NHS number, date of birth and sex at birth) regarding deceased participants to the UCL Data safe haven (DSH). 's251 support is also required for this.

If the participating sites cannot provide the NHS number or date of birth, then UCL will request this information from the original AspECT sponsor (Oxford Clinical Trials Unit) using AspECT ID. 's251' support is also required for this flow and the flow back, as the pseudo-ID will be used to re-identify the patient, and provide confidential patient information to UCL. UCL will in turn disclose NHS number and date of birth to NHS England, in order for NHS England to link to the listed datasets, and return the data back to UCL for analysis. Once in UCL-DSH, the data will be linked back to clinical data from the original AspEXT trial, using the using AspECT ID, that will have been separately disclosed to UCL.

Confidential information requested

Cohort	1587 AspECT participants in total (alive and deceased) (across all of UK) 's251' support only relevant regarding the deceased patients on England and Wales, however the applicant cannot yet estimate how many people this is relevant for.
Data sources	1. 20-35 Participating Aspect sites in England and Wales – (high recruiting AspECT sites with at least 20 participants) a. AspECT screening/enrolment logs b. medical records 2. University of Oxford a. original AspECT database 3. NHS England a. Hospital Episode Statistics (HES) b. Admitted Patient Care (APC) c. Emergency Care Data Set (ECDS) d. Civil Registrations (Deaths) data set
Identifiers required for linkage purposes with original AspECT trial	1. original AspECT trials ID number (to identify NHS number and date of birth if missing from trust data, and to link to AspECT data)
Identifiers required for linkage purposes with NHS England	1. NHS number 2. Date of birth 3. sex
Identifiers required for analysis purposes	1. Date of death 2. CAG form states date of birth – it is not clear from query responses if this is modified for analysis. 3. sex Cause of death, diagnosis of oesophageal cancer or dysplasia at time of death, date of diagnosis and PPI and Aspirin use prior to death will also be provided back to the applicant.
Additional information	The identifiable patient data will be held separately to the clinical data. This separation happens at the point of data entry at a site/trust level. OpenClinica will hold the clinical data which will contain the clinical data including full date of death, and UCL DSH will hold confidential patient information

	The data retained by OpenClinica will contain full date of death and therefore should not be considered pseudonymized, as this is also confidential patient information.

Main issues considered, discussed and outcomes

The CAG noted that this activity fell within the definition of medical research and was therefore assured that the application described an appropriate medical purpose within the remit of the section 251 of the NHS Act 2006.

Having reviewed the application and considered the risks and benefits involved, the CAG was also assured that the proposed activity was in the public interest.

With regards to the patient and public involvement undertaken, the AspECT EXceL patient and public involvement group consists of 4 members; 2 Barrett's Oesophagus patients, 1 carer and 1 retired Oesophageal surgeon. However it appears they mainly reviewed patient facing documents which are not relevant for the CAG cohort, rather than the specific breach of confidentiality regarding the deceased.

The Sub-committee noted that whilst the membership of the patient and public involvement group is relevant and representative of the cohort, it is quite small with only 4 members. The patient and public involvement group do not appear to have taken part in addressing the use of identifiable data without consent. The Sub-Committee therefore felt that this patient and public involvement was currently insufficient, and that further consultation should be undertaken to specifically address the use of confidential patient information without consent and outside the direct care team, for the purposes described in this application. [**Action 1**]

The Sub-Committee were not clear on the exit strategy from ‘s251’ support. UCL CCTU will need to retain identifiable patient information for the duration of the study to facilitate data collection from NHS England (and equivalents) and participating sites. Following completion of data analysis, stored data will be safely destroyed. Following the final request for the dataset from NHS England there will no longer be the need for the NHS numbers and full dates of birth to be held by UCL CCTU. These identifiers will be deleted. It is not clear yet when this would be, as it depends on the speed of NHS England. It is not clear if full date of birth is required for analysis or not. It is not clear from the query responses. It is also not clear when full Date of death will be deleted by OpenClinica, or by UCL DSH.

The Members accepted that although the timepoint for deletion of the NHS number and date of birth (required for linkage) will depend on the speed that NHS England undertakes the linkage, an estimated timepoint for deletion of these identifiers should be specified. **[Action 2].** The Sub-Committee requested confirmation of whether full dates of birth and full dates of death are required to be retained for analysis, noting it was not clear why the applicant could not convert to age and days after inclusion or equivalent. If these are required for analysis in full format, this should be clearly

justified **[Action 3].** The applicant should also confirm a timepoint when full date of death will be deleted by OpenClinica, and also by UCL-DSH **[Action 4].**

The Sub-Committee would like confirmation, given the information in the protocol regarding Canadian co-applicants, that no confidential patient information will be disclosed outside of the UK? The applicant is to confirm that any data disclosed outside of the UK will be anonymised in line with ICO guidance **[Action 5].**

The Members also had some comments with regards to 'future-proofing' the consented arm of the study, although noted that the consented element is out of scope for CAG, and therefore this is provided as a recommendation only. If the applicants can foresee undertaking further linkage with this cohort in the future, (for example in five years time when they may have lost more of the original cohort to death), *(ref: protocol, p.21, para 6.4.3),* then the applicants should consider appropriate language in the current study consent documentation, as part of the consent process of the current alive population, in order for applicants not to have to re-visit this aspect, and potentially prevent the need for a future application to CAG **[Recommendation 1**].

<u>Confidentiality Advisory Group advice:</u> Provisionally supported

The CAG was unable to recommend support to the Health Research Authority for the application based on the information and documentation received so far. The CAG requested the following information before confirming its final recommendation:

Number	Action required	Response from the applicant
1	Please undertake further patient and public involvement to specifically address the use of confidential patient information without consent and outside the direct care team.	
2.	Please confirm an estimated timepoint for the deletion of identifiers required for linkage – NHS Number and data of birth.	
3.	Please confirm whether full dates of birth and full dates of death are required to be retained for analysis. If these are required for analysis in full format, this should be clearly justified, and a clear timepoint for deletion should be provided.	
4.	Please confirm a timepoint when full date of death will be deleted by OpenClinica, and also by UCL-DSH.	
5.	Please provide assurance that no confidential patient information will be disclosed outside of	

	the UK, and confirm that any data disclosed outside of the UK will be anonymised in line with ICO guidance.	

Recommendations

1.	If the applicants can foresee undertaking further linkage with this cohort in the future, then the applicants should consider appropriate language in the current study consent documentation, as part of the consent process of the current alive population, in order for applicants not to have to re-visit this aspect, and potentially prevent the need for a future application to CAG	

The Group delegated authority to confirm its final opinion on the application to the Chair and reviewers.

Professor William Bernal, CAG Alternate Vice Chair *06 October 2023*

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Signed – Chair *Date*

Ms Caroline Watchurst *05 October 2023*

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Signed – HRA Confidentiality Advisor *Date*