Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)
Identification of Novel Psychoactive Substances (IONA)

1. Is your project research?

(●) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product

( ) Clinical investigation or other study of a medical device

( ) Combined trial of an investigational medicinal product and an investigational medical device

( ) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice

( ) Basic science study involving procedures with human participants

( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology

( ) Study involving qualitative methods only

(●) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)

( ) Study limited to working with data (specific project only)

( ) Research tissue bank

( ) Research database

If your work does not fit any of these categories, select the option below:

( ) Other study

2a. Please answer the following question(s):

a) Will you be taking new samples primarily for research purposes (i.e. not surplus or existing stored samples), including any removal of organs or tissue from the deceased?	(●) Yes ( ) No
b) Will you be using surplus tissue or existing stored samples identifiable to the researcher?	(●) Yes ( ) No
c) Will you be using only surplus tissue or existing stored samples not identifiable to the researcher?	(●) Yes ( ) No
d) Will you be processing identifiable data at any stage of the research (including in the identification of participants)?	(●) Yes ( ) No

3. In which countries of the UK will the research sites be located?*(Tick all that apply)*

- [x] England
- [x] Scotland
- [x] Wales
- [ ] Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- (•) England
- ( ) Scotland
- ( ) Wales
- ( ) Northern Ireland
- ( ) This study does not involve the NHS

4. Which review bodies are you applying to?

- [ ] HRA Approval
- [x] NHS/HSC Research and Development offices
- [ ] Social Care Research Ethics Committee
- [x] Research Ethics Committee
- [ ] Confidentiality Advisory Group (CAG)
- [ ] National Offender Management Service (NOMS) (Prisons & Probation)

For NHS/HSC R&D offices, the CI must create Site-Specific Information Forms for each site, in addition to the study-wide forms, and transfer them to the PIs or local collaborators.

5. Will any research sites in this study be NHS organisations?

(•) Yes ( ) No

5a. Do you want your NHS R&D application(s) to be processed through the NIHR Coordinated System for gaining NHS Permission?

(•) Yes ( ) No

If yes, you must complete and submit the NIHR CSP Application Form immediately after completing this project filter, before proceeding with completing and submitting other applications.

6. Do you plan to include any participants who are children?

(•) Yes ( ) No

7. Do you plan at any stage of the project to undertake intrusive research involving adults lacking capacity to consent for themselves?

(•) Yes ( ) No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

8. Do you plan to include any participants who are prisoners or young offenders in the custody of HM Prison Service or who are offenders supervised by the probation service in England or Wales?

(●) Yes ( ) No

9. Is the study or any part of it being undertaken as an educational project?

( ) Yes (●) No

10. Will this research be financially supported by the United States Department of Health and Human Services or any of its divisions, agencies or programs?

( ) Yes (●) No

11. Will identifiable patient data be accessed outside the care team without prior consent at any stage of the project (including identification of potential participants)?

( ) Yes (●) No

NOTICE OF SUBSTANTIAL AMENDMENT

Please use this form to notify the main REC of substantial amendments to all research other than clinical trials of investigational medicinal products (CTIMPs).
The form should be completed by the Chief Investigator using language comprehensible to a lay person.

Details of Chief Investigator:

	Title	Forename/Initials	Surname
	Prof	Simon	Thomas
Work Address	Medical Toxicology Centre		
	Newcastle University		
	Newcastle		
PostCode	NE2 4HH		
Email	simon.thomas@ncl.ac.uk		
Telephone	01912606180		
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Full title of study:	Identification and characterization of the clinical toxicology of novel psychoactive substances (NPS) by laboratory analysis of biological samples from recreational drug users.
Lead sponsor:	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Name of REC:	North East - Newcastle and North Tyneside 2
REC reference number:	15/NE/0023
Name of lead R&D office:	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Date study commenced:	23/3/2015
Protocol reference (if applicable), current version and date:	Protocol V2 (6th January 2016)
Amendment number and date:	Amendment No 1 (6th January 2016)

Type of amendment

(a) Amendment to information previously given in IRAS

(●) Yes ( ) No

If yes, please refer to relevant sections of IRAS in the "summary of changes" below.

(b) Amendment to the protocol

(●) Yes ( ) No

If yes, please submit <u>either</u> the revised protocol with a new version number and date, highlighting changes in

bold, or a document listing the changes and giving both the previous and revised text.

(c) Amendment to the information sheet(s) and consent form(s) for participants, or to any other supporting documentation for the study

(●) Yes ( ) No

If yes, please submit all revised documents with new version numbers and dates, highlighting new text in bold.

Is this a modified version of an amendment previously notified and not approved?

( ) Yes (●) No

Summary of changes

Briefly summarise the main changes proposed in this amendment. Explain the purpose of the changes and their significance for the study.
If this is a modified amendment, please explain how the modifications address the concerns raised previously by the ethics committee.
If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given (or enclosed separately). Indicate whether or not additional scientific critique has been obtained.

BACKGROUND

The IONA study is collecting blood, urine and oral fluid samples from people presenting to UK hospitals with severe toxicity suspected to be related to use of novel psychoactive substances (sometimes called 'legal highs'). Sample analysis is being performed to identify the substances involved and to link these with clinical features of toxicity experienced by the participant. The study currently involves 11 study sites in England and Wales and 1 site in Scotland. Because the study can involve adults with incapacity, separate ethical approval was requited in England and Wales (15/NE/0023) and Scotland (15/SS/047).

This is a request for some substantive amendments to be made in the light of experience gained over the first 8 months of the study. Some non-substantial amendments are also notified.

SUBSTANTIAL AMENDMENTS REQUESTED

1. Participant and exposure details

We have been asked by the Home Office to seek more detailed information about drug exposures in cases of severe toxicity, including data on the source of recreational drugs involved. We would therefore like to ask participants where they obtained these, with options being internet, shop, dealer, friend, relative or other. Participants can decline to provide this information if they prefer. Note that details of individual suppliers would not be sought. To allow this the structured data collection form has been amended and a copy is attached. Reference to this additional data has been added to the protocol (p36) and the collection of this information is also now explained in the revised participant information sheet (V2, 6th January 2016), which now includes the following in 'What will happen to me if I take part?' (P3).

'The researcher will also record information about you including your age, sex and details about your recent drug use. They will also ask you what drugs(s) or substances you think you may have taken, when this happened and where the substances came from.'

The following is also included in 'What do I have to do?'

'Other than answering questions about recent drug use and providing the blood and urine specimens, you do not have to do anything. Note that you can decline to answer any questions if you prefer.'

Because the information sheet has been changed, other documents that refer to this have also been updated to include the current information sheet version and date as follows

Consultee declaration form (England and Wales) V2, 6th January 2016
Consultee Information Sheet, V2, 6th January 2016

Participant informed consent form, V2, 6th January 2016
Consent form (Person previously included when they did not have capacity), V2, 6th January 2016

2. Sample transfer arrangements

Most hospitals are asking for batching of samples to reduce administrative and transport costs. This means that there are further delays until the results of sample analysis are known. This is now explained to participants in the information sheet as follows:

'Samples may be sent to the research laboratory in Newcastle in batches every few weeks and this means that it will take longer for results to be available.'

3. Consent process

The original ethical application specified that consent would be taken by an 'appropriately trained doctor in hospital' (Section A18). However, it is difficult for some of the research sites to arrange that and we would like to modify the arrangement so that consent may be obtained by any appropriately trained staff member, with the decision on appropriate training made by the employing NHS Trust and with this delegation of responsibility recorded in the local delegation log.

4. Telephone consent

There have been isolated instances where samples have been secured in advance of consent when potential participants were lacking capacity, but the potential participant left hospital before formal consent could be obtained. In at least one case inclusion had been authorised by a designated consultee, but the participant has left hospital before it was possible to ask them to sign the 'Consent form for persons previously included when they did not have capacity'. It should be noted that people can recover quite quickly from severe toxic effects and it is common for them to be discharged or take their own discharge at very short notice and often outside normal working hours.

We would therefore like to have mechanisms in place for obtaining consent from people who have left hospital but who were previously included on the basis of advice from a consultee when they did not have capacity. The process we are seeking authorisation for is that

(a) The patient is contacted by telephone to explain why they were entered in the study and asked if they would consent to the research team sending them an information sheet and the relevant consent form (These would be sent by post or email depending on expressed preference. A stamped addressed/freepost envelope will be included for postal returns of signed forms if this is the person's preference. Note however that we anticipate that it will be unusual for postal returns of consent forms to be used by participants.

(b) A further telephone call is made to the participant a few days after the forms have been sent by the local researcher. (allowing at least 4 days for consideration and return of posted forms). For those willing to discuss consent by telephone, options given in the 'Consent form for persons previously included when they did not have capacity' (1- remain in the study', 2 - consent to data/samples collected so far to be used for research' and 3 - do not consent to data/samples collected so far to be used for research) would be explained to the potential participant and their views recorded on the form by the person taking consent. This method of telephone consent has been used in other emergency department-based studies (e.g. Protocolised Management In Sepsis -ProMISe). The person taking consent would sign a declaration added to this consent for as follows:

I certify that the participant has been sent a copy of the information sheet. I have explained the options available and answered all questions asked. I have recorded accurately on this form the wishes of this participant as discussed with me by telephone.

5. Measurement of biomarkers for muscle toxicity

There is evidence that some NPS can cause muscle toxicity. Researchers in Edinburgh wish to use aliquots of blood/plasma samples provided to the study to measure potential miRNA biomarkers for muscle toxicity and correlate these with clinical data provided to the study such as creatine kinase, temperature etc. We have included background (P14) and methods (P39) for this in the protocol and an explanation of this in the participant information sheet as follows (in 'What will happen with any samples?')

'Research is also being performed at the University of Edinburgh measuring substances in the blood ('microRNA') that may be early indicators of adverse effects of drugs on muscle. A small amount of your blood sample will be sent from Newcastle to Edinburgh for this purpose.

All samples will only be labelled with your unique study code rather than your personal details. This means that the

research teams in Newcastle and Edinburgh will not be able to identify who you are.'

NON-SUBSTANTIAL AMENDMENTS

We would also like to notify the REC about the following amendments that we consider to be non-substantial.

6. Inclusion criteria

We have clarified in the inclusion criteria (Protocol P26) that the study involves people with 'suspected novel psychoactive substance exposure' (previously 'suspected recreational drug exposure') to be consistent with other parts of the protocol.

Also, following feedback from research sites, we wish to include participants who have (i) severe behavioural disturbances, even if not prolonged, (ii) myocardial infarction and (iii) acidosis as evidenced by a venous bicarbonate < 20 mmol/L (as some patients do not have arterial blood gases performed). Also, as most Emergency Departments are not familiar with the Poisoning Severity Score, relevant features indicating 'severe toxicity' (PSS3) using this scale have been included separately in the main list (Protocol P27). We would also like to allow local principle investigators to include patients if they have other manifestations of toxicity that they can justify as severe, because it is hard to predict all possible severe toxic effects that could result from exposure to novel psychiatric substances. (Protocol P26 and 27).

In order to verify that included participants meet these criteria, the data collection sheet now asks what severity criteria have been used when including the participant. Explanatory notes have also been provided to ensure more complete and consistent data collection. A copy is attached as follows (also in protocol as Appendix 2)

IONA data collection sheet, V2, 6th January 2015

7. Consistency between protocols in England and Wales and Scotland

There has been a separate updated protocol for Scotland where separate ethical approval has been required. A revised UK protocol covering the England & Wales and Scotland elements has been produced to ensure consistency in arrangements as far as possible. Changes that have been made are tracked into the protocol.

8. Other administrative protocol changes

Information sheets and consent forms have been removed from the appendices, as these have been updated. Details of research partners have been updated (Protocol P4). The recruitment algorithm has been corrected to remove a minor error (Protocol P35). Participant numbers have been updated in the Schedule of Events (P36) and in the estimated sample sizes (Protocol P 41) to be consistent with the Scottish ethical approval (Figures for England and Wales are not affected).

9. Start date

As ethical and other approvals were received more rapidly than anticipated, the study entered the first participant (with all approvals in place) on 23rd March 2015, in advance of the original estimated start date of 1st April 2015.

Any other relevant information

Applicants may indicate any specific issues relating to the amendment, on which the opinion of a reviewing body is sought.

The REC's attention is drawn in particular to the following part of the amendment proposed:

4. Telephone consent.

We have considered if it is necessary to have a separate witness to the lelephone consent and we would welcome the REC's opinion on that. Our preference would be to avoid that requirement as it will sometimes not be easy to implement, especially in smaller sites. We are informed that other studies using telephone consent arrangements do not have this requirement. We would, however, follow the advice of the REC.

List of enclosed documents

Document	*Version*	*Date*
Notice of substantial amendment - Amendment 1	V1	06/01/2016
Participant information sheet	V2	06/01/2016
Participant informed consent form	V2	06/01/2016
Consultee declaration form (England and Wales)	V2	06/01/2016
Consultee Information Sheet	V2	06/01/2016
Consent form (Person previously included when they did not have capacity)	V2	06/01/2016
Protocol (England and Wales) tracked	V2	06/01/2016
Protocol (England and Wales) clean	V2	06/01/2016

Declaration by Chief Investigator

1. *I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.*
2. *I consider that it would be reasonable for the proposed amendment to be implemented.*

This section was signed electronically by Prof Simon Thomas on 22/01/2016 16:33.

Job Title/Post:	Consultant
Organisation:	NUTH
Email:	simon.thomas@ncl.ac.uk

Declaration by the sponsor's representative

I confirm the sponsor's support for this substantial amendment.

This section was signed electronically by Andrew Johnston on 25/01/2016 13:59.

Job Title/Post:	RM&G Manager
Organisation:	NUTH-FT
Email:	andrew.johnston@nuth.nhs.uk