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) - (Scotland)

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 applications do you require?

IMPORTANT: If your project is taking place in the NHS and is led from England select 'IRAS Form'. If your project is led from Northern Ireland, Scotland or Wales select 'NHS/HSC Research and Development Offices' and/or relevant Research Ethics Committee applications, as appropriate.

- [ ] IRAS Form
- [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 in Northern Ireland, Scotland and Wales the CI must create NHS/HSC Site Specific Information forms, for each site, in addition to the study wide forms, and transfer them to the PIs or local collaborators.

For participating NHS organisations in England different arrangements apply for the provision of site specific information. Refer to IRAS Help for more information.

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		
Fax	01912820288		

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 (Scotland).
Lead sponsor:	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Name of REC:	Scotland A
REC reference number:	15/SS/0047
Name of lead R&D office:	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Date study commenced:	9/11/2015
Protocol reference (if applicable), current version and date:	Version 2, 25th April 2016
Amendment number and date:	Amendment 1, 25th April 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.

Anticipated recruitment numbers for Scotland have been adjusted (Section A59, reduction from 400 to 200 over 4 years).

(b) Amendment to the protocol

(●) Yes ( ) No

If yes, please submit either 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.

Protocol (Version 2, 25th April 2016) attached with changes tracked. Changes also described in the notice of substantial amendment.

(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.

The following documents are affected (revised versions attached)
- Participant Information Sheet and consent form (V2, 25/4/2016)
- Participant Information Sheet and consent form (Nearest Relative/Guardian or Welfare Attorney) (V2, 25/4/2016)
- Consent Form (Person previously included when they did not have capacity)(V2, 25/4/2016)

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 (second site in set-up). 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 to the IONA-Scotland protocol in the light of initial experience gained. Some non-substantial amendments are also notified. Note that unless stated as specific to the Scottish protocol, similar changes have also been subject to a protocol amendment application for England and Wales.

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 (V2, 25th April 2016, p36) and the collection of this information is also now explained in the revised participant information sheet and consent form document (V2, 25th April 2016), which now includes the following in 'What will happen to me if I take part?'

'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.'

Similar changes have been made to the Participant Information Sheet and Consent Form (Nearest Relative/Guardian or Welfare Attorney) document (V2, 25th April 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 in the information sheets as follows:

'Samples may be sent to the research laboratories in Newcastle or Edinburgh 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 form 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 (P14-15) and methods (P40) for this in the updated 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 at Newcastle University, the University of Edinburgh and the Scottish Police Authority Forensic Science Laboratory will not be able to identify who you are.'

6. Participant numbers in Scotland

Original estimates of participant numbers in Scotland were made on the basis of rates of presentation to the Royal Infirmary of Edinburgh during 2014-5. However, presentation rates have fallen following successful local actions to reduce the sales and use of NPS. There may also be a further reduction in presentation rates when the new Psychoactive Substances Act comes into law. It is therefore appropriate to revise downwards the estimated numbers of participants from Scotland from the original figure of 400 to 200 (severe or non-severe toxicity) over 4 years. While this will reduce the amount of data available, it will not compromise the ability of the study to meet its aims.

7. Transfer of drug/product samples in Scotland.

Discussions have taken place between the PI in Edinburgh, Prof Eddleston, and the Scottish Police about appropriate methods for transporting samples of drug product (NPS packets/powders etc) that may be provided by participants alongside blood and urine samples. These drug product samples are extremely useful as they are easier to analyse for content than biological samples and once NPS have been identified in the product it is easier to confirm or exclude its presence in the biological samples. The issue is that these samples may contain substances controlled under current legislation (which may not be known by the user or clinician) and will almost always contain psychoactive substances the supply of which will be illegal when the Psychoactive Substances Act comes into law. The police have advised that these product samples can be sent to the Scottish Police Authority Forensic Science Laboratories with the biological samples covered by a memorandum signed by the local PI and the SPA FSL. A copy of the memorandum is provided with this application.

IONA-S Memorandum – NPS packets V1.0, 4th April 2016

NON-SUBSTANTIAL AMENDMENTS

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

8. 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 define severe toxicity as 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 whether included participants meet these criteria, the data collection sheet now asks what severity criteria are present when including the participant. (Note that for the Scottish protocol (unlike in England & Wales), severe toxicity is not one of the inclusion criteria). 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) and is the same form as currently used in England and Wales.

IONA data collection sheet, V2, 6th Jan 2016

9. Consistency between protocols in England and Wales and Scotland

There is a separate protocol for England and Wales where separate ethical approval has been required. The protocol for IONA-Scotland has been revised to ensure consistency in arrangements as far as possible. Changes that have been made are minor (other than those described above) are tracked into the protocol.

10. Other administrative protocol changes

Details of research partners have been updated (Protocol P2-4). The recruitment algorithm has been corrected to remove a minor error (Protocol P32). 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).

Any other relevant information

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

List of enclosed documents

Document	*Version*	*Date*
Notice of substantial amendment	V1	25/04/2016
PIS and consent form	V2	25/04/2016
PIS and consent form (Nearest Relative/Guardian or Welfare Attorney)	V2	25/04/2016
Consent Form (Person previously included when they did not have capacity)	V2	25/04/2016
Memo re Collection of NPS Packets	V1	25/04/2016
Protocol	V2	25/04/2016
Data collection sheet	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 25/04/2016 14:16.

Job Title/Post:	Consultant
Organisation:	Newcastle UNiversity
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 09/05/2016 08:18.

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