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 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		
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For guidance on this section of the form refer to the guidance

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

Additional reference number(s):

Ref.Number Description	Reference Number

Name of lead R&D office:	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Date study commenced:	22nd March 2015
Protocol reference (if applicable), current version and date:	V4, 12th January 2017
Amendment number and date:	3, 12th January 2017

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 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.

(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 15 study sites in England and Wales and 1 site in Scotland. Because the study can involve adults with incapacity, separate ethical approval was required in England and Wales (15/NE/0023) and Scotland (15/SS/047).

This is a request for substantial amendments to be made to the study as follows:

SUBSTANTIAL AMENDMENTS REQUESTED

1. Adjustment of recruitment targets.

The originally approved recruitment targets for the IONA study were 200 patients with severe toxicity in England and Wales and 400 patients with any severity of toxicity in Scotland to be recruited before the study ends on 1st April 2019. The criteria differed between these two separately approved arms of the study because there was initially additional resource available in Scotland for analysis of Scottish samples.

The study has been recruiting in England and Wales since March 2015 and it has been comparatively straight forward to recruit study sites and participants with severe toxicity related to suspected NPS use. As of December 24th 2016 there were 179 patients in the England and Wales arm of the study.

Conversely, recruitment in Scotland has been slower than expected since the study commenced there in November 2015 with 34 participants recruited up to December 2016. There has been less interest from potential Scottish research sites than we had anticipated, with only 2 sites currently participating. Another important reason for slow recruitment has been actions taken in Scotland that have restricted the availability of NPS.

We would therefore like to adjust the balance of the study so that recruitment in England and Wales is increased from 200 to 400. At the same time we would like to reduce recruitment targets in Scotland to 200 patients. This would not change the total numbers of participants recruited across both arms of the study. Please also note that this is an observational study the success of which is not dependent on recruiting a specific number of patients.

2. Inclusion of patients with severe opioid toxicity

There is increasing concern about novel opioids emerging onto the scene in Europe. These have similar clinical effects to conventional opioids like heroin, but are often substantially more potent. Examples include fentanyl derivatives (acryloyl-,acetyl-, car-, thio-, 2-fluoro-, oc-, valeryl-, furanyl-, despropionyl-2-fluoro-fentanyl etc) and other novel opioids (e.g. AH-7921, U47,700, U49,900, MT-45, 4Cl-iBF, 4F-iBF). Because of their high potency, very small amounts can have severe or fatal effects and as a result there is a high risk of death if these are used as substitutes for heroin. Deaths have been reported in Europe, including the UK, where post-mortem toxicology has implicated novel opioids as the cause.

Currently the IONA study is unlikely to capture patients that might be affected by novel opioids as the clinical features they produce, being typical of opioid poisoning, are not likely to raise the suspicion of NPS use. We would therefore like to update the IONA study entry to include those with features consistent with severe opioid intoxication. These include rapidly developing unconsciousness, hypotension, pulmonary oedema, pinpoint pupils and response to the antidote naloxone. While many patients identified in this way will subsequently be confirmed by sample analysis as being intoxicated with conventional opioids like heroin, this will help estimate the proportion of UK patients with severe opioid toxicity where novel opioids are involved. It will also identify those substances most commonly involved.

3. Changes to participant data collection sheet

We would like to make some minor changes to the data collection sheet as follows:
(a) To clarify that the patient number needed (first box in section 1) is the IONA participant number rather than any local number
(b) to capture admission routine observations (pulse, BP, temperature, oxygen saturations, respiratory rate) and arterial blood gas results (pH, pCO2, pO2, Base excess).
(c) To allow the researchers to indicate that the patient has been included because of suspected severe opioid intoxication (section 1) and to report the administration of naloxone (Section 5).

4. Sharing of linked anonymised samples between laboratories

We are seeking approval to allow blood, plasma, urine and/or saliva samples (or the mass spectrometry data obtained from them) of some participants to be shared with other laboratories in the UK Forensic Early Warning System (FEWS) organised by the Home Office. This is to allow us to use the expertise in these laboratories to help identify NPS when necessary and to allow quality control of sample analysis by comparison of findings between labs. Shared samples or data would only be identifiable by study number and this can only be linked to the participant's identity by the local research site.

The participant information sheet has been adjusted to explain this (V 4, 12th January 2017) by inclusion of the following:

'Some samples (or analytical data obtained from them) may be shared with UK laboratories in Forensic Early Warning System (FEWS) organized by the Home Office, so that their expertise can be used to help identify substances that might be present and for quality control purposes.'

We would, however, like ethical approval to share linked anonymised samples from participants recruited using previous versions of the information sheet. We have considered obtaining further consent where needed, but this is likely to be very difficult for this population. Full anonymization of the samples before sharing would not allow any findings to be linked to the clinical data or eventually communicated back to the research site or participant.

Because there has been this change to the participant information sheet, the following documents have been updated so that they refer to this latest version (V4, 12th January 2017):

Participant informed consent form (V4, 12th Jan2017)
Consultee declaration form (England and Wales) (V4, 12th Jan2017)
Consent Form (England and Wales) - previous incapacity (V4, 12th Jan2017)

5. Updating of protocol

The protocol has been updated to
(a) include details of currently participating research sites and PIs (all previously dealt with as non-substantial amendments, pages 3-4)
(b) Include details of the proposed opioid NPS arm of the study (pages 11, 26)
(c) Detail numbers of participants intended for England and Wales and for Scotland and to update the schedule of events accordingly (p 33-34 and 39)
(d) Include the updated data collection sheet with its explanatory notes (p 49-52).

Protocol V4, 12th January 2017

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 3	V1	12/01/2017
Protocol	V4	12/01/2017
Data collection sheet	V3	12/01/2017
Participant information sheet	V4	12/01/2017
Participant informed consent form	V4	12/01/2017
Consultee declaration form	V4	12/01/2017
Consent form (Person previously included when they did not have capacity)	V4	12/01/2017

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 19/01/2017 15:37.

Job Title/Post:	Consultant
Organisation:	Newcastle Hospitals NHS FT
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 20/01/2017 14:53.

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