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?

- [ ] IRAS Form
- [x] NHS/HSC Research and Development offices
- [ ] Social Care Research Ethics Committee
- [x] Research Ethics Committee
- [ ] Confidentiality Advisory Group (CAG)
- [ ] Her Majesty's Prison and Probation Service (HMPPS)

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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Telephone	01912606180		
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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:	Version 7, 6th March 2020
Amendment number and date:	6, 6th January 2020

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.

Revised protocol -V7, 6th January 2020

(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.

Revised Participant information sheet -V5, 6th January 2020

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 has been 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 previously called 'legal highs') or non-pharmaceutical opioids. The latter, including heroin, are included so that the involvement of unlicensed fentanyl analogues in episodes of severe toxicity can be monitored. 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 is funded via the NIHR Health Protection Research Unit (HPRU), but this funding ends in March 2020. The research is considered sufficiently important for public health surveillance in the UK that Public Health England issued a competitive tender for similar research to be continued, but with some modifications, as described in this amendment application. Newcastle University was successful in winning that tender and this provides additional funding for the period January 2020 to March 2021, with the option of renewing the research on an annual basis subject to the success of the research and resources being available.

This substantial amendment application covers the extension of the study to March 2021, the recruitment of additional participants over this period, changes to the study inclusion criteria to match PHE's current drug misuse surveillance priorities and changes in laboratory arrangements for sample analysis.

There are currently 29 research sites (emergency departments) who are recruiting to the IONA study until the end of March 2020, 26 in England, 1 in Wales and 2 in Scotland. Four sites (all in England) have indicated that they will not continue beyond that date, but 25 sites have confirmed their willingness to continue. Further sites will be sought as needed to ensure adequate participant recruitment and geographical coverage. 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) and similar but separate substantial amendment requests are being made to each research ethics committee.

AMENDMENTS REQUESTED

(a) Increase in participant numbers
The current ethical approval (following previous protocol amendments) is for recruitment of a grand total of 850 participants, 670 recruited in England and Wales and 180 recruited in Scotland, with recruitment starting in March

2015 and ending on 31st March 2020.

The new funding from PHE provides additional resource (over and above the NIHR grant) for the 2019-20 financial year and new funding for 2020-21. The additional funding allows recruitment of additional participants as follows:

2019-20. An additional (over and above the current NIHR target recruitment) 60 patients in England and Wales by the end March 2020 (total 730) and an additional 20 in Scotland (total 200), giving an overall total of 930.

2020-21. A further 180 participants in England and Wales by the end March
2021 (total 910) and an additional 40 in Scotland (total 240). This gives an overall total of 1150 participants by that date.

IONA is an observational study with no specific statistical comparisons planned. It does not subject participants to additional intervention-based risks. We are requesting additional recruitment numbers to allow further monitoring of the substances involved in episodes of toxicity associated with drug misuse, including exposure to new psychoactive substances, rather than for any specific statistical comparison. The larger sample size allows more information to be obtained, giving more accurate and longer-term information on temporal trends and geographical variations in substances identified. The sample size is limited by the potential costs of processing and analysing samples, which is expensive for the types of mass spectrometry analysis used. The new grant awarded by PHE allows additional sample numbers to be analysed, enabling additional participant recruitment during the financial year 2019/20 and previously unplanned recruitment during 2020/21.
These revised recruitment targets are reflected in the updated schedule of events (England and Wales Protocol V7, 6th January 2020, pages 34-35 of the clean version; Scotland Protocol V5, 6th January 2020, pages 32-33 of the clean version).

(b) Extension of study end date
The additional funding from PHE allows the study to be extended for an additional year and we are therefore seeking approval for a revised end date for recruitment of 31st March 2021 and a final end date of 20th September 2021 (all analysis completed). If further funding is available beyond 2020/21, a further substantial amendment request will be made.

(c) Alteration to the inclusion and exclusion criteria.
Currently the IONA study is recruiting participants with severe toxicity (according to specific criteria) where there is clinical suspicion of exposure to a new psychoactive substance (NPS) or non-pharmaceutical opioid (e.g. heroin). The latter group was added in 2017 so that involvement of new fentanyl analogues in episodes of heroin toxicity could be identified. The recruitment has been restricted to these groups because of limited capacity for laboratory analysis of samples to identify the substances involved and the need to concentrate on those groups where NPS use was most likely. However, this does not give an accurate picture of the contribution of NPS to all drug toxicity presenting to emergency departments. NPS are also sometimes detected in people who believe they have only used traditional drugs of misuse and vice versa.

PHE have therefore made the resource available to extend the recruitment criteria to include all people presenting to hospital with toxicity (of any severity) related to misuse of any drug. This provides a less biased picture of the drugs of misuse causing emergency department presentations, including traditional drugs of misuse as well as NPS. It therefore provides a more comprehensive picture of the contribution of NPS to drug toxicity. It also simplifies the entry criteria and this is helpful for the research sites.

We are therefore seeking approval to alter the inclusion and exclusion criteria to cover this as detailed below. These changes require minor alterations to the data collection sheet and a revised copy is enclosed with this application (IONA Data collection sheet V4 06Jan2020).

Inclusion criteria - current
• Patient with suspected novel psychoactive substance exposure
OR
• Patient with severe or unexpected toxicity from non-pharmaceutical opioid misuse1
AND
• Presence of severe acute toxicity (See text)
AND
• Patient consent (immediate or retrospective)

Inclusion criteria – proposed (this amendment)
• Patient attending an emergency department with toxicity as a result of suspected drug misuse
• Patient consent (immediate or retrospective)

Exclusion criteria - current
• Refusal of consent
• No clinical suspicion of novel psychoactive substance or non-pharmaceutical opioid exposure
• Absence of severe toxicity
• Children and young people <16 y Samples collected for investigation of suspected non-accidental injury

Exclusion criteria - proposed (this amendment)
• Refusal of consent
• No clinical suspicion of drug misuse
• Children and young people <16 y
• Samples collected for investigation of suspected non-accidental injury

(d) Change in laboratory arrangements
Following the conclusion of the NIHR grant, it is no longer possible to maintain the mass spectrometry required for the study at Newcastle University. Arrangements have therefore been made to out-source this work to a commercial forensic laboratory (LGC Group, Fordham). This laboratory is highly competent at performing these analyses and does this routinely in the investigation of forensic cases for coroners and the courts. We have previously compared results for the same samples between the Newcastle laboratory and LGC and found a high level of agreement. The relevant Participant information sheet has therefore been altered to take this change in laboratory into account and copies with tracked changes are attached.

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*
Protocol	V7	06/01/2020
Participant information sheet	V5	06/01/2020
IONA Data collection sheet	V4	06/01/2020

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 13/01/2020 10:06.

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 Miss Sinead Magorrian on 13/01/2020 10:25.

Job Title/Post:	R&D Officer
Organisation:	NuTH
Email:	sinead.magorrian@nhs.net