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 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 review bodies are you applying to?

- [x] NHS/HSC Research and Development offices
- [ ] Social Care Research Ethics Committee
- [x] Research Ethics Committee
- [ ] National Information Governance Board for Health and Social Care (NIGB)
- [ ] 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 NIGB Ethics and Confidentiality Committee 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

Integrated Research Application System
Application Form for Research limited to working with human tissue samples and/or data

NHS Health Research Authority

Application to NHS/HSC Research Ethics Committee

The Chief Investigator should complete this form. Guidance on the questions is available wherever you see this symbol displayed. We recommend reading the guidance first. The complete guidance and a glossary are available by selecting Help.

Please define any terms or acronyms that might not be familar to lay reviewers of the application.

Short title and version number: (maximum 70 characters - this will be inserted as header on all forms)
Identification of Novel Psychoactive Substances (IONA) - (Scotland)

Please complete these details after you have booked the REC application for review.

REC Name:
Scotland A

REC Reference Number:
15/SS/0047

Submission date:
06/03/2015

PART A: Core study information

1. ADMINISTRATIVE DETAILS

A1. Full title of the research:

Identification and characterization of the clinical toxicology of novel psychoactive substances (NPS) by laboratory analysis of biological samples from recreational drug users (Scotland).

A3-1. Chief Investigator:

	Title	Forename/Initials	Surname
	Prof	Simon	Thomas
Post	Professor of Clinical Pharmacology and Therapeutics		
Qualifications	BSc, MBBS, MRCP, MD, FRCP, FRCPE		
Employer	Newcastle Hospitals NHS Foundation Trust		
Work Address	Medical Toxicology Centre Newcastle University Newcastle		
Post Code	NE2 4HH		
Work E-mail	simon.thomas@ncl.ac.uk		
* Personal E-mail			
Work Telephone	01912606180		

* Personal Telephone/Mobile	
Fax	01912820288

** This information is optional. It will not be placed in the public domain or disclosed to any other third party without prior consent.*
A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application.

A4. Who is the contact on behalf of the sponsor for all correspondence relating to applications for this project?
This contact will receive copies of all correspondence from REC and R&D reviewers that is sent to the CI.

	Title	Forename/Initials	Surname
	Mr	Sean	Scott
Address	The Newcastle upon Tyne Hospitals NHS Foundation Trust		
	Newcastle Joint Research Office		
	Level 6, Leazes Wing, Royal Victoria Infirmary		
Post Code	NE1 4LP		
E-mail	Sean.Scott@nuth.nhs.uk		
Telephone	0191 282 5490		
Fax			

A5-1. Research reference numbers. *Please give any relevant references for your study:*

Applicant's/organisation's own reference number, e.g. R & D (if available):	07312
Sponsor's/protocol number:	
Protocol Version:	1.4
Protocol Date:	13/02/2015
Funder's reference number:	HPRU-2012-10076
Project website:	

Additional reference number(s):

Ref.Number Description	Reference Number
England and Wales REC reference	15.NE.0023
England and Wales IRAS number	168706

Registration of research studies is encouraged wherever possible. You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you have registered your study please give details in the "Additional reference number(s)" section.

A5-2. Is this application linked to a previous study or another current application?

(●) Yes ( ) No

Please give brief details and reference numbers.
This study has also been considered by an English REC which has provided a favourable opinion (ref 15.NE.0023). A split application is required because of differences in English and Scottish law relating to adults with incapacity. There are also small differences in the inclusion criteria and laboratory arrangements used for Scottish research sites. This allows people with less severe toxicity to have samples sent to the Scottish Police Authority Forensic Services (Edinburgh) for analysis.

2. OVERVIEW OF THE RESEARCH

To provide all the information required by review bodies and research information systems, we ask a number of specific questions. This section invites you to give an overview using language comprehensible to lay reviewers and members of the public. Please read the guidance notes for advice on this section.

A6-1. Summary of the study. *Please provide a brief summary of the research (maximum 300 words) using language easily understood by lay reviewers and members of the public. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, this summary will be published on the website of the National Research Ethics Service following the ethical review.*

Recreational drug use has been common for many years, but a major recent change in epidemiology has been the increasing use of new recreational drugs, sometimes termed Novel Psychoactive Substances (NPS) or 'legal highs.' These substances are numerous and associated with significant acute toxicity including increasing hospital presentations and fatalities. The effects of chronic exposure are usually unknown.

Currently there is no systematic national UK data collection system linking analytically confirmed use of NPS with acute toxicity. This causes a delay before clinicians, public health teams, law enforcement and policy makers can define and mitigate the harms associated with specific NPS. There are typically no published data available on the pharmacology and toxicity of these substances as they emerge into recreational use, leaving healthcare professionals without evidence to guide patient management in the event of toxicity.

This research will help to address this gap by collating information about the acute toxicity of NPS in the UK via four inter-related studies using

(1) Anonymised aggregated data collected by the National Poisons Information Service (NPIS)

(2) Anonymised aggregated data available on positive samples from participating NHS toxicology laboratories

(3) Further laboratory analysis of linked-anonymised samples collected from patients with acute severe toxicity as part of usual clinical care and sent to participating NHS laboratories, where NPS use is suspected.

(4) Collection and analysis of samples from consenting patients presenting to participating emergency departments with toxicity associated with suspected NPS use.

Samples will be subjected to detailed toxicology analysis using state of the art methods, informed by the latest information on the NPS being encountered by clinicians in the UK.

The research will identify trends in enquiries and positive laboratory samples relating to NPS, identify NPS involved in episodes of acute toxicity presenting to UK hospitals and link specific substances with reported features of toxicity.

A6-2. Summary of main issues. *Please summarise the main ethical, legal, or management issues arising from your study and say how you have addressed them.*

Not all studies raise significant issues. Some studies may have straightforward ethical or other issues that can be identified and managed routinely. Others may present significant issues requiring further consideration by a REC, R&D office or other review body (as appropriate to the issue). Studies that present a minimal risk to participants may raise complex organisational or legal issues. You should try to consider all the types of issues that the different reviewers may need to consider.

The proposed research includes a suite of 4 linked studies and the main issues with each are summarised as follows:

Study 1. Analysis of fully anonymised National Poisons Information Service enquiry data. These data are collected routinely by NPIS as part of the clinical record of the patient. We believe that analysis of routinely collected aggregated anonymised data without specific consent is consistent with MRC guidance and does not present any ethical difficulties.

Study 2. Collation of fully anonymised data provided by participating NHS toxicology laboratories. Again, we do not believe that the analysis of routinely collected aggregated anonymised data presents any ethical difficulties.

Study 3. Further analysis of samples already collected as part of clinical care. For this study we propose to use blood, urine or oral fluid samples sent to participating toxicology laboratories as part of routine clinical care. Linked anonymised samples of interest (e.g. where severe unexplained toxicity had occurred in the context of recreational drug use) would be sent for further analysis in Newcastle University. The link to the patients identity would be held in the

NHS toxicology laboratory to allow additional important findings to be fed back to the patient and clinical team, but the research team in Newcastle would not be able to identify either. We believe that with these safeguards this is consistent with MRC guidance and the Human Tissue Act 2004 and is ethically justifiable, especially as further analysis is an extension of the drug screening that the sample was originally sent for. For further discussion please see Part B: Section 4, question 5.

Study 4. Collection of samples for research purposes from patients attending participating emergency departments. The great majority of samples and data will be provided with consent in place at the time of transfer to the research team. We would, however, also like to collect and save any residuals from blood/urine samples already taken for clinical reasons in patients lacking capacity to consent because of intoxication. These samples would be retained within the study site's NHS laboratory and only used for the study once the patient had recovered capacity and provided delayed consent. For those where recovery of capacity is delayed (at least 12h), we would like to use samples collected without consent. We are proposing arrangements to allow this by means of appropriate declarations from personal or nominated consultees (England and Wales) or consent from persons with relevant powers (Scotland). Participants subsequently regaining capacity will be able to consent for themselves at that time or withdraw their data and samples from the research.

We believe the approach we are using is ethically justifiable because of the importance in obtaining samples soon after recreational drug exposure in severely poisoned patients and because samples will only be sent and analysed after consent has been obtained or after approval/consent from consultees or persons with relevant powers.

3. PURPOSE AND DESIGN OF THE RESEARCH

A7. Select the appropriate methodology description for this research. *Please tick all that apply*:

- [ ] Case series/ case note review
- [ ] Case control
- [ ] Cohort observation
- [ ] Controlled trial without randomisation
- [x] Cross-sectional study
- [x] Database analysis
- [x] Epidemiology
- [ ] Feasibility/ pilot study
- [x] Laboratory study
- [ ] Metanalysis
- [ ] Qualitative research
- [x] Questionnaire, interview or observation study
- [ ] Randomised controlled trial
- [ ] Other (please specify)

A10. What is the principal research question/objective? *Please put this in language comprehensible to a lay person.*

To identify Novel Psychoactive Substances (sometimes called 'legal highs') that may be involved in toxicity experienced by patients presenting to acute hospitals, especially emergency departments. This will be achieved by analysis of routine data collected by UK poisons centres and NHS Toxicology laboratories and by further analysis of samples taken either during normal NHS care or, in participating hospitals, for the purposes of the research.

A11. What are the secondary research questions/objectives if applicable? *Please put this in language comprehensible to a lay person.*

Specific aims of the study are to

1. Identify trends in enquiries to the NPIS (telephone and internet) relating to NPS and characterize and monitor the epidemiology of reported exposures (Study 1)
2. Identify trends in the numbers of samples positive for NPS as identified in participating NHS laboratories (Study 2)
3. Develop sophisticated mathematical models for analyzing NPIS and toxicology laboratory data (Studies 1 and 2)

4. Develop methods of screening, analysis and quantification for new/emerging NPS in biological samples (urine, oral fluid and blood) (Studies 3 and 4)
5. Analyse samples from patients with acute toxicity relating to NPS to identify responsible agents (Studies 3 and 4)
6. Link the presence of analytically confirmed NPS exposure with the toxic effects experienced (Studies 3 and 4)

A12. What is the scientific justification for the research? *Please put this in language comprehensible to a lay person.*

The epidemiology of recreational drug use has changed substantially in recent years with rapidly increasing use of Novel Psychoactive Substances (NPS) in the UK and internationally. These compounds, sometimes erroneously referred to as 'legal highs' or ‘research chemicals’, are usually chemically similar to traditional drugs of misuse (e.g. amphetamine, MDMA [‘ecstasy’], tryptamines, ketamine, cannabinoids, cocaine or opioids) but with limited alterations made to the chemical structure so that the new compound is no longer captured by national control of drugs legislation, such as the Misuse of Drugs Act in the UK. Recent examples of NPS include cathinones (e.g. mephedrone), benzofurans (e.g. 5/6 APB or 'benzofury'), NBOMe compounds, tryptamines (e.g. alpha methyltryptamine), piperazines (e.g. benzylpiperazine), benzodiazepines (e.g. etizolam), arylcyclohexamines (e.g. methoxetamine), synthetic cannabinoid receptor agonists (SCRAs), and synthetic opioids (e.g. MT-45).

Alterations to the chemical structure of a drug of misuse to produce a NPS can result in a different toxicity profile. As NPS are not subject to any testing prior to distribution and use, some may produce severe and unexpected toxic effects. This may occur as a result of unexpectedly high potency (a low dose is required to produce desired and toxic effects), increased intrinsic toxicity (e.g. toxic effects occur at doses close to those needed to produce the desired effects) or a change in pattern of toxic effects.

NPS present particular challenges to health services because of the rapid emergence of large numbers of different compounds (e.g. 73 NPS reported in the European Union in 2012, 81 in 2013 and 37 in the first 5 months of 2014, bringing the number monitored to approximately 400) and the lack of available information on their pharmacology or toxicology as there is usually little or no research into these aspects before they are introduced onto the market.

Legal or otherwise, NPS may cause significant acute harms; the Office for National Statistics (ONS) reported 56 deaths in England and Wales in 2012 where an NPS was mentioned on the death certificate following a drug-related death, almost double the figure for 2011. ONS also reported increases in deaths related to cathinones (from 6 to 18) and to paramethoxyamph-etamine (PMA) or paramethoxymethamphetamine (PMMA, from 1 to 20) between 2011 and 2012. There is a lack of available information on indicators of morbidity, such as numbers of hospital attendances or admissions after use of NPS, although enquiries from health professionals to the UK National Poisons Information Service are common and increasing. For most NPS there is almost no available information on the longer term effects of repeated exposure in humans, although severe chronic bladder toxicity may occur after repeated exposure to methoxetamine. Traditional drugs of misuse related to some NPS have been associated with serotonergic neurotoxicity and there is emerging but inconsistent evidence from animal studies of chronic neurotoxicity after exposure to some NPS. The lack of evidence about acute harms and long term effects from NPS has been identified as an evidence gap in a 2014 Home Office report. A further difficulty is that the chemical composition of products sold may not be known or may not be as advertised to the user and may vary or involve a mixture of compounds, some of which can be illegal.

There is evidence from the UK that legal control of NPS can reduce the frequency of presentations to health services with clinical toxicity associated with that substance. This may be a direct effect of restricting supply, but could also occur because the publicity associated with legal control may better inform clinicians and users about the harms associated with use.

In the UK, legal control of drugs of misuse is determined by the Home Office after advice by the Advisory Council on Drugs of Misuse (ACMD). For control to be recommended under the 1971 Misuse of Drugs Act there must be evidence of harms associated with the drug, such as adverse societal impact or evidence of acute or chronic toxicity. From November 2011, the Misuse of Drugs Act 1971 has been amended to enable the temporary control of an NPS by invoking a temporary class drug order (TCDO). This requires that the substance is not already controlled and is subject to advice from the ACMD that the drug is likely to be misused and misuse is capable of having harmful effects. TCDOs need Parliamentary endorsement within 40 sitting days and last for up to 12 months. This is expected to provide adequate time for ACMD to provide full, independent and expert advice about the need for permanent control. Mechanisms are therefore needed for rapid collection of information on the potential harms of emerging substances to inform ACMD decisions on TCDOs and permanent control.

There is therefore a currently unmet need for a system that provides the opportunity for detailed analysis of blood, urine or other biological samples from users of recreational drugs who experience toxicity irrespective of where they present in the UK. This needs to be simple to access, well publicised to the relevant health professionals and drug user groups, have the appropriate ethical and regulatory approvals in place and be able to link biological exposure with evidence of clinical toxic effects. This needs to link with mechanisms to provide a balanced analysis of the evidence

available to NPS users, health professionals and regulatory/government organisations.

A13. Please summarise your design and methodology. *It should be clear exactly what will happen to the research participant, how many times and in what order. Please complete this section in language comprehensible to the lay person. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.*

Participants will only be involved directly in the research in Study 4, which will take place in selected participating hospitals, including their emergency departments, medical admissions units and intensive care units.

People presenting to participating hospitals with clinical features suggesting toxicity (defined further in the protocol) as a result of recreational drug use will be approached to give informed consent to provide blood, urine and/or oral fluid samples. Blood samples would usually be residual or additional blood taken during a venepuncture that is already being done for clinical purposes, so no additional venepuncture would be needed. In most cases only a single sample will be taken, as soon as possible after presentation to hospital, but in those with continuing features suggesting toxicity, further samples (up to a total of 5) may be taken to see if this is because of slow elimination of any responsible drugs (i.e. to characterise drug pharmacokinetics). Again, these samples would almost always be taken at the same time as clinically indicated blood sampling so that additional venepuncture is not needed. However, there may be an occasional need for additional venesection for the purposes of the research. This is explained in the information leaflet and would only be done with the patients verbal consent for each additional venepuncture.

We are also seeking permission to keep excess samples collected for clinical reasons from patients lacking capacity so that these can be used for the research once the patient regains capacity and provides informed consent.

Provision of these samples is the only intervention involved. Most patients will provide samples on a single occasion, but for those with ongoing toxicity sample collection may occur over 2-3 days.

A14-1. In which aspects of the research process have you actively involved, or will you involve, patients, service users, and/or their carers, or members of the public?

- [x] Design of the research
- [x] Management of the research
- [x] Undertaking the research
- [x] Analysis of results
- [x] Dissemination of findings
- [ ] None of the above

Give details of involvement, or if none please justify the absence of involvement.
We have discussed the research informally with drug users presenting to our hospital with toxicity associated with NPS. They agree that there is a need to establish what the chemicals are that are responsible for toxicity and the majority have stated that they would be content to provide blood samples should they develop suspected NPS-related toxiicty.

As an NIHR-funded study, the project is developing detailed arrangements for Patient and Public Involvement which will include discussion of research methods and dissemination of results, including to drug user groups.

4. RISKS AND ETHICAL ISSUES

RESEARCH PARTICIPANTS

A17-1. Please list the principal inclusion criteria (list the most important, max 5000 characters).

Study 1 (Use of fully anonymised aggregated NPIS data)
Enquiry involving suspected systemic NPS exposure
Originating from a UK based NHS health professional
Any age (including children).

Study 2. (Collation of fully anonymised toxicology laboratory data)
Patient with suspected NPS exposure

Sample provided as part of routine clinical care
Any age (including children)

Study 3. (Further analysis of samples already collected as part of clinical care).
Patient with suspected recreational drug exposure
Sample sent from acute NHS hospital
Presence of acute toxicity as reported in request form or sample from an acute hospital site,
Sample provided, analysed and reported as part of routine clinical care
Aged 16 years or older

Study 4. (Collection of samples for research purposes from patients attending participating emergency departments)
Patient with suspected NPS exposure,
Presence of acute toxicity (defined in protocol)
Patient consents
Aged 16 years or older

A17-2. Please list the principal exclusion criteria (list the most important, max 5000 characters).

Study 1 (Use of NPIS data)
Non UK enquiries
Enquiries made from educational public health or governmental sources
Other enquiries not involving a specific patient exposure

Study 2. (Collation of anonymised toxicology laboratory data)
Samples collected for investigation of suspected non-accidental injury
Non UK cases

Study 3. (Further analysis of samples already collected as part of clinical care)
Patients without evidence of clinical toxicity
Patients undergoing routine drug screening as part of drug treatment/rehabilitation
Children and young people <16 y
Samples collected for investigation of suspected non-accidental injury

Study 4. (Collection of samples for research purposes from patients attending participating emergency departments)
Refusal of consent
Absence of toxicity
Children and young people <16 y
Samples collected for investigation of suspected non-accidental injury

RESEARCH PROCEDURES, RISKS AND BENEFITS

A18. Give details of all non-clinical intervention(s) or procedure(s) that will be received by participants as part of the research protocol. *These include seeking consent, interviews, non-clinical observations and use of questionnaires.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days)
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Informed consent procedure (Study 4 only)	1	0	10-30 min	Appropriately trained doctor or nurse. In hospital

A19. Give details of any clinical intervention(s) or procedure(s) to be received by participants as part of the research protocol. *These include uses of medicinal products or devices, other medical treatments or assessments, mental health interventions, imaging investigations and taking samples of human biological material. Include procedures which might be received as routine clinical care outside of the research.*

Please complete the columns for each intervention/procedure as follows:

1. Total number of interventions/procedures to be received by each participant as part of the research protocol.
2. If this intervention/procedure would be routinely given to participants as part of their care outside the research, how many of the total would be routine?
3. Average time taken per intervention/procedure (minutes, hours or days).
4. Details of who will conduct the intervention/procedure, and where it will take place.

Intervention or procedure	1	2	3	4
Collection of blood sample (almost always residual of sample already taken for clniical purposes)	1-5	1-4	<5 mins (per sample)	Trained doctor. In hospital
Collection of urine and oral fluid samples	1	0	<5 mins (per sample	Trained doctor or nurse. In hospital

A21. How long do you expect each participant to be in the study in total?

Participants will only be involved directly in the research for Study 4. This involves sample collection from the patients soon after presentation for most patients, so their involvement is only to sign consent and allow provision of one set of samples at that time. Occasional patients with persisting features requiring continuing stay in hospital would have further samples taken (max 5) at intervals with their further verbal consent. If possible blood will be collected at times when venesection is done for clinical purposes. It is unlikely that sample collection would occur over more than 2-3 days.

The other 3 studies involve only use of anonymised patient data that is collected as part of routine clinical practice.

A22. What are the potential risks and burdens for research participants and how will you minimise them?

For all studies, describe any potential adverse effects, pain, discomfort, distress, intrusion, inconvenience or changes to lifestyle. Only describe risks or burdens that could occur as a result of participation in the research. Say what steps would be taken to minimise risks and burdens as far as possible.

The risk of physical harm is very small because the study only involves collection of blood or (non-interventional) collection of urine and/or oral fluid. Most blood will be taken at the same time as blood sampling for clinical indications, so there is no additional venepuncture. If there is additional venepuncture, there is some discomfort but the risks are minimal.

A24. What is the potential for benefit to research participants?

The study may identify NPS and this will be of interest to some participants. Occasionally the identification of a NPS as a cause of toxicity may prevent the need for other investigations, but this will be unusual, in part because in most cases research assay results will not be available while the patient is still in hospital. Thus for most participants the study will not have direct health benefits

RECRUITMENT AND INFORMED CONSENT

In this section we ask you to describe the recruitment procedures for the study. Please give separate details for different study groups where appropriate.

A27-1. How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?*For example, identification may involve a disease register, computerised search of GP records, or review of medical records. Indicate whether this will be done by the direct healthcare team or by researchers acting under arrangements with the responsible care organisation(s).*

For studies 1 and 2, patient data that meets the entry criteria for the study will be collated and appropriately anonymised by the clinical teams who collect and hold these data as part of their routine activities. For study 1 this is the National Poisons Information Service and for study 2 these are NHS Toxicology laboratories. These data are provided to the research team in fully anonymised format.

Study 3 will use residuals of blood samples from patients with toxicity related to possible recreational drug use. These will have been sent for clinical reasons to a participating NHS laboratory for drug screening. Samples sent to Newcastle University will be identified only by a code number, with the link to the patient's identity maintained in the clinical site responsible for holding that data

For study 4, potential participants will be approached directly and asked about their interest in the study by the clinicians managing them. If they express interest, one of the research team within that department will seek informed consent using the participant information sheets and consent forms provided with this application.

A27-2. Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?

○ Yes ◉ No

Please give details below:
There is no need to interrogate hospital databases to identify participants.

A28. Will any participants be recruited by publicity through posters, leaflets, adverts or websites?

○ Yes ◉ No

A29. How and by whom will potential participants first be approached?

Direct approach to potential participants is only proposed for Study 4. Following capacity assessment by the responsible clinical team, suitable patients with capacity will be asked by their treating clinicians if they are willing to discuss the study further. Those that are will be seen by a local member of the research team who will seek informed consent.

The capacity status of those who initially do not have capacity will be monitored by the local clinical team who will discuss possible involvement in the study once capacity to make a decision on this issue has been regained. At that point the potential participant will be asked if they are willing to be approached by the research team. Those that are will be seen by a local member of the research team who will seek informed consent.

A30-1. Will you obtain informed consent from or on behalf of research participants?

◉ Yes ○ No

If you will be obtaining consent from adult participants, please give details of who will take consent and how it will be done, with details of any steps to provide information (a written information sheet, videos, or interactive material). Arrangements for adults unable to consent for themselves should be described separately in Part B Section 6, and for children in Part B Section 7.

If you plan to seek informed consent from vulnerable groups, say how you will ensure that consent is voluntary and fully informed.

All patients with capacity taking part in study 4 will provide informed consent. The study will be introduced to potential participants considered to have capacity by members of the clinical team looking after them. If the potential participant is interested in discussing the study further they will be seen by a member of the research team in that site. The study will be explained and the participant information sheet provided. The potential participant will be given the time that they need to consider participation. If they are willing they will be asked to sign a consent form. Copies of the PIS and consent form are provided with this application.

As explained in other sections, delayed consent will be sought from those who present initailly without capacity due to drug or alcohol intoxication. The process described above will be followed once the potential participant is considered by the clinical team to have capacity.

If you are not obtaining consent, please explain why not.

Patient consent is not being sought for use of anonymised data for studies 1-3. Current guidance from the MRC indicates that that use of fully anonymised data (Studies 1 and 2) and linked anonymised samples and data can be used without consent (Study 3). This approach, however, requires careful justification and this is provided in part B: Section 4 - question 5.

Please enclose a copy of the information sheet(s) and consent form(s).

A30-2. Will you record informed consent (or advice from consultees) in writing?

(●) Yes ( ) No

A31. How long will you allow potential participants to decide whether or not to take part?

If participants are willing to give informed consent immediately they will be able to do so and can provide samples without further delay. If they want more time to consider and discuss participation with others this will be accommodated. Samples taken for clinical reasons would be retained pending their decision using the same process as for patients presenting without capacity. These arrangements are considered ethically appropriate for a non-interventional study where for most of those involved participation takes only a short time.

A33-1. What arrangements have been made for persons who might not adequately understand verbal explanations or written information given in English, or who have special communication needs?*(e.g. translation, use of interpreters)*

Translation of participant information will be offered to those who request this via usual NHS translation services.

A33-2. What arrangements will you make to comply with the principles of the Welsh Language Act in the provision of information to participants in Wales?

Translation of participant information will be offered to those who request this via usual NHS translation services.

A35. What steps would you take if a participant, who has given informed consent, loses capacity to consent during the study? *Tick one option only.*

( ) The participant and all identifiable data or tissue collected would be withdrawn from the study. Data or tissue which is not identifiable to the research team may be retained.

( ) The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant.

(●) The participant would continue to be included in the study.

( ) Not applicable – informed consent will not be sought from any participants in this research.

( ) Not applicable – it is not practicable for the research team to monitor capacity and continued capacity will be assumed.

Further details:

Should a patient lose capacity after giving informed consent then we would continue to collect and analyse their samples. The risks to the patient from this are minor, consent has already been provided and the eventuality is explained in the participant information sheet. Furthermore, it is especially important that drug toxicity that results in such a deterioration in capacity is documented accurately, including identification of responsible drugs.

Please complete Part B, Section 6, giving further information about arrangements for including adults unable to consent for themselves.

CONFIDENTIALITY

In this section, personal data means any data relating to a participant who could potentially be identified. It includes pseudonymised data capable of being linked to a participant through a unique code number.

Storage and use of personal data during the study

A36. Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)?*(Tick as appropriate)*

- [ ] Access to medical records by those outside the direct healthcare team
- [x] Electronic transfer by magnetic or optical media, email or computer networks
- [x] Sharing of personal data with other organisations
- [ ] Export of personal data outside the EEA
- [ ] Use of personal addresses, postcodes, faxes, emails or telephone numbers
- [ ] Publication of direct quotations from respondents
- [ ] Publication of data that might allow identification of individuals
- [ ] Use of audio/visual recording devices
- [x] Storage of personal data on any of the following:
  - [ ] Manual files including X−rays
  - [x] NHS computers
  - [ ] Home or other personal computers
  - [x] University computers
  - [ ] Private company computers
  - [ ] Laptop computers

Further details:
To minimise risks of breaches of confidentiality, all patient identifiers will be held on computers within the host NHS Trust according to their data protection policies. Only fully anonymised data (Studies 1 and 2) or linked anonymised data (Studies 3 and 4) will be provided to the Newcastle University HPRU research team or (for study 4 in Scotland) the SPA Forensic Sciences lab.

A38. How will you ensure the confidentiality of personal data?*Please provide a general statement of the policy and procedures for ensuring confidentiality, e.g. anonymisation or pseudonymisation of data.*

All staff involved in the research will follow the NHS Code of Confidentiality. All staff able to access identifiable patient data have NHS contracts and are subject to the host NHS Foundation Trust's information governance policies.

A40. Who will have access to participants' personal data during the study? *Where access is by individuals outside the direct care team, please justify and say whether consent will be sought.*

Access to identifiable personal data provided by research participants will only be available to members of the immediate clinical team. Only linked anonymised (link held in NHS Trust providing the data) or fully anonymised data will be available to the research teams in Newcastle University and the Scottish Police Authority Forensic Services (Edinburgh.

Storage and use of data after the end of the study

A43. How long will personal data be stored or accessed after the study has ended?

- ○ Less than 3 months
- ○ 3 – 6 months
- ◉ 6 – 12 months
- ○ 12 months – 3 years
- ○ Over 3 years

INCENTIVES AND PAYMENTS

A46. Will research participants receive any payments, reimbursement of expenses or any other benefits or incentives for taking part in this research?

○ Yes ◉ No

A47. Will individual researchers receive any personal payment over and above normal salary, or any other benefits or incentives, for taking part in this research?

○ Yes ◉ No

A48. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

○ Yes ◉ No

NOTIFICATION OF OTHER PROFESSIONALS

A49-1. Will you inform the participants' General Practitioners (and/or any other health or care professional responsible for their care) that they are taking part in the study?

○ Yes ◉ No

If Yes, please enclose a copy of the information sheet/letter for the GP/health professional with a version number and date.

PUBLICATION AND DISSEMINATION

A50. Will the research be registered on a public database?

◉ Yes ○ No

Please give details, or justify if not registering the research.
The research will be described on NIHR HPRU website and results will be made publically available via that route. The study has been adopted onto the NIHR portfolio and details will shortly be available on the NIHR portfolio website.

Registration of research studies is encouraged wherever possible.
You may be able to register your study through your NHS organisation or a register run by a medical research charity, or publish your protocol through an open access publisher. If you are aware of a suitable register or other method of publication, please give details. If not, you may indicate that no suitable register exists. Please ensure that you have entered registry reference number(s) in question A5-1.

A51. How do you intend to report and disseminate the results of the study? *Tick as appropriate:*

- ☑ Peer reviewed scientific journals
- ☐ Internal report
- ☑ Conference presentation
- ☑ Publication on website
- ☐ Other publication
- ☑ Submission to regulatory authorities

☐ Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators

☐ No plans to report or disseminate the results

☑ Other (please specify)

Reports (aggregated anonymised data) will also be provided to government organisations responsible for monitoring drug misuse, such as the ACMD and Drugs Early Warning System. Data will inform 'the Talk to Frank' recreational drug information website and medical management of cases via the NPIS website TOXBASE.

A53. Will you inform participants of the results?

◉ Yes ○ No

Please give details of how you will inform participants or justify if not doing so.
Results of the study will be available in via the NIHR HPRU website. Participants will will be told about and will have access to this website.

5. Scientific and Statistical Review

A54. How has the scientific quality of the research been assessed? *Tick as appropriate:*

☑ Independent external review

☐ Review within a company

☑ Review within a multi−centre research group

☐ Review within the Chief Investigator's institution or host organisation

☐ Review within the research team

☐ Review by educational supervisor

☐ Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:
Peer review as part of the NIHR HPRU funding process, as well as detailed review by the research team (for details of membership see protocol).

For all studies except non-doctoral student research, please enclose a copy of any available scientific critique reports, together with any related correspondence.

For non-doctoral student research, please enclose a copy of the assessment from your educational supervisor/ institution.

A56. How have the statistical aspects of the research been reviewed? *Tick as appropriate:*

☐ Review by independent statistician commissioned by funder or sponsor

☐ Other review by independent statistician

☐ Review by company statistician

☐ Review by a statistician within the Chief Investigator's institution

☑ Review by a statistician within the research team or multi−centre group

☐ Review by educational supervisor

☐ Other review by individual with relevant statistical expertise

☑ No review necessary as only frequencies and associations will be assessed – details of statistical input not required

In all cases please give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

	Title	Forename/Initials	Surname
	Prof	Stephen	Rushton
Department	Professor of Biological Modelling, School of Biology		
Institution	Newcastle University		
Work Address			
	Newcastle		
Post Code	NE2 4HH		
Telephone	01912083046		
Fax			
Mobile			
E-mail	stephen.rushton@ncl.ac.uk		

Please enclose a copy of any available comments or reports from a statistician.

A57. What is the primary outcome measure for the study?

There is no primary outcome measure for this study which is not a comparative clinical trial.

Descriptive statistics will be used for studies 1 and 2 and will characterize the epidemiology of poisons service enquiries about NPS and of positive toxicology screening samples handled in NHS Toxicology laboratories.

For studies 3 and 4, formal statistical analysis is unlikely to be required. Useful data linking particular features of toxicity with analytical confirmation of exposure is valuable even if this is achieved in a single patient.

No hypothesis testing, e.g. comparing toxicity between agents, is envisaged for data collected in any of the studies and as such formal power calculations are not needed.

A58. What are the secondary outcome measures?*(if any)*

n/a

A59. What is the sample size for the research? *How many participants/samples/data records do you plan to study in total? If there is more than one group, please give further details below.*

Total UK sample size:	800
Total international sample size (including UK):	800
Total in European Economic Area:	800

Further details:
Please note that the numbers quoted above refer to studies 3 and 4 only as these are the 2 studies that are not using routinely collected and fully anonymised clinical data. The figures below give further information across all studies. All figures quoted are totals from all contributing research sites over the 4 year duration of data collection. They include people with less severe toxicity being studied in Scotland (n=400)

Study 1. n = 1600 (estimated). NPIS currently collects data on approximately 400 NPS presentations annually.

Study 2. n=4000 (estimated). NHS specialist toxicology labs estimate that they each collect about 5 samples weekly for extended screening from patients with acute toxicity from suspected exposure to a NPS

Study 3. n=200. Approximately 1 sample of interest will be per week will be provided per week to Newcastle over the 4 years of the study

Study 4. n=600. It is intended that 50 consenting patients presenting with suspected severe NPS toxicity to participating emergency departments will be studied annually. In addition, a further 100 patients annually with less severe toxicity will be studied in Scotland annually.

For studies 2-4, these figures are estimates. Further information will be provided to the REC if recruitment is higher or lower than these estimates.

A60. How was the sample size decided upon? *If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.*

This study will use all the available data that can be collected and analysed within the resources allocated to the research.

Statistical comparisons are not essential for the study and as such power calculations are not required. Identification of a previously undocumented NPS causing clinical toxicity in a single patient would be valuable.

A61. Will participants be allocated to groups at random?

○ Yes ◉ No

A62. Please describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

NPIS telephone and TOXBASE enquiries as well as positive laboratory results will be used as indices of NPS use. Temporal trends in these data will be analysed using time series analyses undertaken at short sample periods, which will be used to alert the HPRU to trends in use. Bayesian disease mapping techniques will be used to analyse spatial and temporal trends in records for NPS. Area-based autoregressive modeling (CAR models) will identify spatial variation in NPS use across the study area, whilst also highlighting potential risk factors (socio-economic status, age distribution etc). State-space time series analysis will be used to investigate the impact of drug control policies and the interplay between telephone and web enquiries.

6. MANAGEMENT OF THE RESEARCH

A63. Other key investigators/collaborators. *Please include all grant co−applicants, protocol co−authors and other key members of the Chief Investigator's team, including non-doctoral student researchers.*

	Title	Forename/Initials	Surname
	Dr	Michael	Dunn
Post Qualifications			
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	Title	Forename/Initials	Surname
	Dr	Christopher M	Morris
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Title	Forename/Initials	Surname
Prof	Peter G	Blain

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Dr	Alasdair	Blain

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	Title	Forename/Initials	Surname
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	Dr	Jonathan	Berg
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	Title	Forename/Initials	Surname
	Dr	Alun	Hutchins
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Title	Forename/Initials	Surname
Prof	Michael	Eddleston

Post	Director, National Poisons Information Service (Edinburgh) and Professor of Clinical Toxicology
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Title	Forename/Initials	Surname
Prof	Allister	Vale

Post	Director, West Midlands Poisons Unit and NPIS (Birmingham Unit)
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Title	Forename/Initials	Surname

	Dr John Thompson
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Title	Forename/Initials	Surname
Dr	Paul	Dargan

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Fax	020 7188 4292
Mobile	07500 915555
Work Email	paul.dargan@gstt.nhs.uk

Title	Forename/Initials	Surname
Dr	David	Wood

Post	Consultant Physician and Clinical Toxicologist; Clinical/Service Lead for Medicine
Qualifications	BSc (Hons) 1st Class; MB ChB (Hons), MD, FRCP, FACMT, FBPharmacolS
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Title	Forename/Initials	Surname
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Title	Forename/Initials	Surname
Dr	Jonathan	Wraight

Post	Consultant in Emerg Medicine & Toxicology
Qualifications	MB FACEM
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Title	Forename/Initials	Surname
Dr	Simon	Hill

Post	Consultant/Senior Lecturer - Clinical Toxicology
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Employer	Newcastle Hospitals NHS Foundation Trust
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Title	Forename/Initials	Surname
Ms	Jane	Officer

Post	Lead Scientist Toxicology/Drugs
Qualifications	BSc (Hons) MSc
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Telephone	01316661212
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Mobile	
Work Email	jane.officer@spa.pnn.police.uk

A64. Details of research sponsor(s)

A64-1. Sponsor

Lead Sponsor

Status:
- (●) NHS or HSC care organisation
- ( ) Academic
- ( ) Pharmaceutical industry
- ( ) Medical device industry
- ( ) Local Authority
- ( ) Other social care provider (including voluntary sector or private organisation)
- ( ) Other

Commercial status: Non-Commercial

If Other, please specify:

Contact person

Name of organisation	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Given name	Sean
Family name	Scott
Address	Newcastle Joint Research Office, Level 6, Royal Victoria Infirmary
Town/city	Newcastle
Post code	NE1 4LP
Country	UNITED KINGDOM
Telephone	0191 282 5490
Fax	
E-mail	Sean.Scott@nuth.nhs.uk

Is the sponsor based outside the UK?

( ) Yes (●) No

Under the Research Governance Framework for Health and Social Care, a sponsor outside the UK must appoint a legal representative established in the UK. Please consult the guidance notes.

A65. Has external funding for the research been secured?

- [x] Funding secured from one or more funders
- [ ] External funding application to one or more funders in progress
- [ ] No application for external funding will be made

What type of research project is this?

- ( ) Standalone project
- (●) Project that is part of a programme grant
- ( ) Project that is part of a Centre grant
- ( ) Project that is part of a fellowship/ personal award/ research training award
- ( ) Other

Other – please state:

Please give details of funding applications.

Organisation	National Institute for Health Research
Address	Central Commissioning Facility Grange House, 15 Church Street Twickenham
Post Code	TW1 3NL
Telephone	020 8843 8000
Fax	020 8843 8001
Mobile	
Email	info@nihr-ccf.org.uk

Funding Application Status: (●) Secured ( ) In progress

Amount: £3,352,468

Duration
Years: 5
Months: 0

If applicable, please specify the programme/ funding stream:

What is the funding stream/ programme for this research project?
NIHR - Health Protection Research Units

A67. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK or another country?

( ) Yes (●) No

Please provide a copy of the unfavourable opinion letter(s). You should explain in your answer to question A6-2 how the reasons for the unfavourable opinion have been addressed in this application.

A68-1. Give details of the lead NHS R&D contact for this research:

Title	Forename/Initials	Surname
Mr	Michael	White

Organisation	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Address	Joint Research Office, Level 6, Leazes Wing, Royal Victoria Infirmary Queen Victoria Road, Newcastle upon Tyne
Post Code	NE1 4LP
Work Email	Michael.White@nuth.nhs.uk
Telephone	0191 2825959
Fax	0191 2824524
Mobile	

Details can be obtained from the NHS R&D Forum website: http://www.rdforum.nhs.uk

A68-2. Select Comprehensive Local Research Network for this NHS organisation:

To support communication between the REC and R&D contacts for this study, please select the Comprehensive Local Research Network (CLRN) for this NHS organisation. This CLRN will be the Lead CLRN for your study.

Northumberland Tyne and Wear

For information about support and advice available through the Lead CLRN and the CLRNs for participating sites see http://www.crncc.nihr.ac.uk/about_us/processes/csp. A map showing the CLRNs is available at http://www.crncc.nihr.ac.uk/about_us/ccrn.

A69-1. How long do you expect the study to last in the UK?

Planned start date: 01/04/2015

Planned end date: 01/04/2019

Total duration:

Years: 4 Months: 0 Days: 0

A70. Definition of the end of trial, and justification in the case where it is not the last visit of the last subject undergoing the trial (1)

The study does not involve any additional patient visits.The study will end on 1st April 2019. If there are patients with serious toxicity undergoing blood sampling that will continue as per protocol (maximum duration 3 days).

A71-2. Where will the research take place? *(Tick as appropriate)*

- [x] England
- [x] Scotland
- [x] Wales
- [ ] Northern Ireland
- [ ] Other countries in European Economic Area

Total UK sites in study 25 (est)

Does this trial involve countries outside the EU?

○ Yes ◉ No

A72. What host organisations (NHS or other) in the UK will be responsible for the research sites? *Please indicate the type of organisation by ticking the box and give approximate numbers of planned research sites:*

[x] NHS organisations in England	19
[x] NHS organisations in Wales	2
[x] NHS organisations in Scotland	4
[ ] HSC organisations in Northern Ireland	
[ ] GP practices in England	
[ ] GP practices in Wales	
[ ] GP practices in Scotland	
[ ] GP practices in Northern Ireland	
[ ] Social care organisations	
[ ] Phase 1 trial units	
[ ] Prison establishments	
[ ] Probation areas	
[ ] Independent hospitals	

- ☐ Educational establishments
- ☐ Independent research units
- ☐ Other (give details)

Total UK sites in study: 25

A76. Insurance/ indemnity to meet potential legal liabilities

***Note:** in this question to NHS indemnity schemes include equivalent schemes provided by Health and Social Care (HSC) in Northern Ireland*

A76-1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research? *Please tick box(es) as applicable.*

Note: Where a NHS organisation has agreed to act as sponsor or co-sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, please describe the arrangements and provide evidence.

- ☑ NHS indemnity scheme will apply (NHS sponsors only)
- ☐ Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A76-2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research? *Please tick box(es) as applicable.*

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), please describe the arrangements and provide evidence.

- ☑ NHS indemnity scheme will apply (protocol authors with NHS contracts only)
- ☐ Other insurance or indemnity arrangements will apply (give details below)

Please enclose a copy of relevant documents.

A76-3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research?

Note: Where the participants are NHS patients, indemnity is provided through the NHS schemes or through professional indemnity. Indicate if this applies to the whole study (there is no need to provide documentary evidence). Where non-NHS sites are to be included in the research, including private practices, please describe the arrangements which will be made at these sites and provide evidence.

- ☑ NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)
- ☐ Research includes non-NHS sites (give details of insurance/ indemnity arrangements for these sites below)

Please enclose a copy of relevant documents.

Part B: Section 4 – Use of residual or existing stored human tissue(or other human biological materials)

1. What types of human tissue or other biological material will be included in the study?

Whole blood, plasma, urine, oral fluid. These are residuals of samples either (a) sent for clinical reasons to participating NHS Toxicology labs (Study 3) or (b) kept in the NHS labs of participating research sites pending recovery of capacity and participant consent (Study 4).

2. Will the samples be released to the researcher:

In fully anonymised form? *(link to stored tissue and data is broken)*
○ Yes ◉ No

In linked anonymised form? *(linked to stored tissue but donor not identifiable to researchers)*
◉ Yes ○ No

In a form in which the donor could be identifiable to researchers?
○ Yes ◉ No

3. Has consent been obtained previously to use the samples for research

○ Consent has been given for all samples
◉ Consent has been given for some of the samples
○ No consent has been given

4. Please outline what consents are already in place, distinguishing between different groups of samples where appropriate.

For Study 4 only, consent from participants with (or regaining) capacity will be obtained before samples that have been retained in local NHS laboratories for clinical reasons are passed on to the research team for further analysis. For participants without capacity samples will be transferred to the research team only after appropriate declarations from personal or nominated consultees (England and Wales) or consent from persons with relevant powers (Scotland) have been obtained.

5. Is it proposed to seek further consent to use the samples in this research?

○ Yes ◉ No

If No, please justify:

In Study 3, samples sent to NHS toxicology labs as part of usual clinical care will be used in the study without patient consent. These samples will be provided in linked anonymised format, with the link retained only in the NHS laboratory providing the sample.

It is not feasible/possible for patient consent to be obtained, as the patients in most cases would be located in other NHS Trusts or will already have been discharged home.

We suggest that this is consistent with current MRC guidance and the Human Tissue Act 2004, as the samples are not identifiable to the research team. We suggest that the approach of using linked anonymised samples is ethically justificable because:

(a) The study involves the study of biological samples that have already been provided for similar clinical purposes (identification of recreational drugs, including traditional illegal drugs)
(b) More detailed analysis of samples may reveal NPS associated with toxicity and this has potentially important benefits for recreational drug users in general
c) Identification of NPS can be fed back to the Toxicology lab and subsequently to the clinical team managing the

patient. Although this will only be of clinical value in a small number of patients with prolonged features, this may occasionally prevent other investigations being performed.
(d) Results will be of interest to the drug user and the clinicians involved in management.
(e) Samples are suitably anonymised so cannot be identified except by the toxicology laboratory supplying the sample. The HPRU research team and SPA Forensic Sciences laboratory will not be able to identify the individual, although the linked-anonymised design allows the local NHS laboratory to contact the responsible clinical team to clarify clinical information or to feed back results of clinical relevance as needed.

6. Will any tissues or cells be used for human application or to carry out testing for human application in this research?

○ Yes ◉ No

8. What types of test or analysis will be carried out on the samples?

Samples will be analysed for the presence of new or emerging NPS only. No genetic or other studies will be performed.

9. Will the research involve the analysis or use of human DNA in the samples?

○ Yes ◉ No

10. Is it possible that the research could produce findings of clinical significance for donors or their relatives?

◉ Yes ○ No

11. If so, will arrangements be made to notify the individuals concerned?

◉ Yes
○ No
○ Not applicable

If No, please justify. If Yes, say what arrangements will be made and give details of the support or counselling service.

Imnportant results will be notified to the toxicology laboratory providing the sample and via that lab to the clinical team that sent the sample originally. Due to the complexity of discovery analysis performed in in the Newcastle University HPRU and SPA Forensic Sciences Lab, we cannot guarantee that this will occur in a clinically relevant time (i.e. while the patient is still in hospital) but we will provide results as soon as possible.

12. Who is the holder of the samples?

Please tick either/both boxes as applicable.

☑ NHS pathology department(s) / diagnostic archive(s)
Specific details of each department/archive are not required

☐ Other research tissue bank(s) or sample collection(s)
Please provide further details of each bank/collection below

13. Will any of the samples be imported from outside the UK?

○ Yes ◉ No

14. Please give details of where the samples will be stored, who will have access and the custodial arrangements.

Samples are labelled with a unique number and stored in a freezer within the Newcastle University HPRU or SPA Forensic Sciences Lab A log will be kept of the type of sample received (blood/plasma/serum/urine/oral fluid), its unique number and volume. Only authorised staff will have access to the sample and use will be recorded in the log.

15. What will happen to the samples at the end of the research? *Please tick all that apply and give further details.*

- ☐ Return to current holder of the samples
- ☐ Transfer to another tissue bank

(If the bank is in England, Wales or Northern Ireland a licence from the Human Tissue Authority will be required to store relevant material for possible further research.)

- ☐ Storage by research team pending ethical approval for use in another project

(Unless the researcher's institution holds a storage licence from the Human Tissue Authority, or the tissue is stored in Scotland, or it is not relevant material, a further application for ethical review should be submitted before the end of this project.)

- ☐ Storage by research team as part of a new research tissue bank

(The institution will require a storage licence for research from the Human Tissue Authority if the bank will be storing relevant material in England, Wales or Northern Ireland. A separate application for ethical review of the tissue bank may also be submitted.)

- ☐ Storage by research team of biological material which is not “relevant material” for the purposes of the Human Tissue Act
- ☑ Disposal in accordance with the Human Tissue Authority Code of Practice
- ☐ Other
- ☐ Not yet known

Please give further details of the proposed arrangements:

Samples will be destroyed once analysis for NPS is complete and in all cases within 1 year of the end of the research study.

Part B: Section 5 – Use of newly obtained human tissue(or other human biological materials) for research purposes

1. What types of human tissue or other biological material will be included in the study?

Whole blood, plasma, urine, oral fluid

2. Who will collect the samples?

Appropriately qualified and trained clinical staff in research sites (Study 4)

3. Who will the samples be removed from?

- [x] Living donors
- [ ] The deceased

4. Will informed consent be obtained from living donors for use of the samples? *Please tick as appropriate*

In this research?

○ Yes ◉ No

In future research?

○ Yes ○ No ◉ Not applicable

If answering No in either case, please justify:

In most cases samples will be provided with full consent. As explained elsewhere, for a small number patients with delayed or no recovery of capacity, we are proposing that sample use for research will be authorised by means of appropriate declarations from personal or nominated consultees (England and Wales) or consent from persons with relevant powers (Scotland).

6. Will any tissues or cells be used for human application or to carry out testing for human application in this research?

○ Yes ◉ No

8. Will the samples be stored: *[Tick as appropriate]*

In fully anonymised form? *(link to donor broken)*

○ Yes ◉ No

In linked anonymised form? *(linked to stored tissue but donor not identifiable to researchers)*

◉ Yes ○ No

If Yes, say who will have access to the code and personal information about the donor.

For the duration of the current project blood samples will be held in linked anonymised format. The personal information and the code linking the sample with the participant's identity will be held within the NHS trust providing the sample

In a form in which the donor could be identifiable to researchers?

○ Yes ◉ No

9. What types of test or analysis will be carried out on the samples?

Analysis for Novel Psychoactive Substances (NPS) only.

10. Will the research involve the analysis or use of human DNA in the samples?

○ Yes ◉ No

11. Is it possible that the research could produce findings of clinical significance for donors or their relatives?

◉ Yes ○ No

12. If so, will arrangements be made to notify the individuals concerned?

◉ Yes ○ No ○ Not applicable

If No, please justify. If Yes, say what arrangements will be made and give details of the support or counselling service.

Positive results will be returned to the research sites who will notify the clinical teams who will be able to identify and inform the participants. Note, however, that discovery analysis for NPS is complex and positive results may not be available until after participants have been discharged from hospital.

13. Give details of where the samples will be stored, who will have access and the custodial arrangements.

Samples are labelled with a unique number and stored in a freezer within the Newcastle University HPRU or the Scottish Police Authority Forensic Services (Edinburgh). A log will be kept of the type of sample received (blood/plasma/serum/urine/oral fluid), its unique number and volume. Only authorised staff of the HPRU or the SPAFL will have access to the sample and use will be recorded in the log. Samples may be shared with other researchers within the research team as listed in the ethical application for confirmatory analysis or quality control purposes. Only the clinical team at the research site providing the samples will be able to link the unique number to the participant's identity. The link to the patients identity in all data sets and all samples held in the HPRU will be destroyed within 1 year of conclusion of the research.

14. What will happen to the samples at the end of the research? *Please tick all that apply and give further details.*

☐ Transfer to research tissue bank

(If the bank is in England, Wales or Northern Ireland the institution will require a licence from the Human Tissue Authority to store relevant material for possible further research.)

☐ Storage by research team pending ethical approval for use in another project

(Unless the researcher's institution holds a storage licence from the Human Tissue Authority, or the tissue is stored in Scotland, or it is not relevant material, a further application for ethical review should be submitted before the end of this project.)

☐ Storage by research team as part of a new research tissue bank

(The institution will require a licence from the Human Tissue Authority if the bank will be storing relevant material in England, Wales or Northern Ireland. A separate application for ethical review of the tissue bank may also be submitted.)

☐ Storage by research team of biological material which is not "relevant material" for the purposes of the Human Tissue Act

☑ Disposal in accordance with the Human Tissue Authority's Code of Practice

☐ Other

☐ Not yet known

Please give further details of the proposed arrangements:

All biological samples used will be destroyed within one year of the end of the study.

B. All research other than CTIMPs

In this sub-section, an adult means a person aged 16 or over.

B1. What impairing condition(s) will the participants have?

The study must be connected to this condition or its treatment.

Some potential participants will be intoxicated when they present to hospital, as a result of suspected recreational drug use with or without alcohol, and this may impair their capacity. Consent will also be impossible to obtain in patients who are critically ill requiring intubation and ventilation. In view of the time critical nature of sampling, we would like to be able to collect samples under these circumstances so that these can be stored locally, pending delayed consent. For blood sampling this would involve collection of a small amount (10 ml) additional blood at times when venepuncture was already being done for clinical reasons. Note that clinical features will not be recorded until consent has been obtained. Once potential participants have regained capacity they will be approached for informed consent to participate in the study. If they agree, the samples collected while they had impaired capacity will be used for the research, with their knowledge and permission. At this stage clinical details will also be recorded. If they decline to consent, samples collected/stored will not be used and will be destroyed according to local NHS policies. Please note that what we are suggesting is an extension of normal NHS laboratory practice to retain residuals of patient samples for a few days after collection in case further clinical analysis is subsequently requested. This model of delayed consent has been used previously for investigating the toxic effects of recreational drugs (e.g. REC 11/LO/0976).

We are also proposing that for patients where capacity is not restored within at least 12 h, agreement for participation can be sought from a personal or nominated consultee (England and Wales) or consent from a person with relevant powers (Scotland).

B2. Justify the inclusion of adults unable to consent for themselves. It should be clear why the research could not be carried out as effectively if confined to adults capable of giving consent.

Impaired capacity is common in patients presenting to hospital with toxicity arising from recreational drug use, including use of NPS and is more common in those with severe toxicity. Identification of NPS responsible for such episodes of severe toxicity is of particular importance. Furthermore, if responsible NPS are to be identified it is important that sampling takes place as soon as possible after presentation to hospital, when NPS concentrations in biological fluids are likely to be highest but when patients are also most likely to have impairment of capacity as a result.

While sampling could be delayed until informed consent is obtained, NPS will be more difficult and in some cases impossible to detect if there is a long delay. Drug concentrations associated with severe toxicity will be more difficult to identify and there would be less opportunity for the pharmacokinetics (i.e. handling by the body) of the NPS to be characterised.

Collection of samples from participants with toxicity associated with delayed or no recovery of capacity is important as this is a group with the most severe poisoning. Excluding access to the research for this group would bias data collection towards less severe poisoning and potentially delay the identification of NPS associated with severe poisoning.

B3. Who in the research team will decide whether or not the participants have the capacity to give consent? What training/experience will they have to enable them to reach this decision?

Capacity will be assessed by an appropriately trained clinician responsible for the care of the potential participant. Such capacity assessment is a common and routine component of the care of patients with intoxication arising from recreational drug toxicity.

B4. Does the research have the potential to benefit participants who are unable to consent for themselves?

(●) Yes ( ) No

If Yes, please indicate the nature of this benefit. You may refer back to your answer to Question A24.

The research may identify an NPS as cause of the clinical presentation and this may obviate the need for other investigations. It should be noted, however, that it will be uncommon for this to occur quickly enough for this to be of clinical value and in most cases the participant will not benefit directly.

B5. Will the research contribute to knowledge of the causes or the treatment or care of persons with the same impairing condition (or a similar condition)?

◉ Yes ○ No

If Yes, please explain how the research will achieve this:

Identification of emerging NPS and the clinical features associated with intoxication is helpful in managing subsequent patients. Information available from this study can be passed onto clinicians throughout the UK by the updating of NPIS/TOXBASE information, which is available to all UK registered health professionals. This can be achieved rapidly as members of the TOXBASE editorial team are included in this research.

B6. Will the research involve any foreseeable risk or burden for these participants, or interfere in any way with their freedom of action or privacy?

○ Yes ◉ No

Questions B7 and B8 apply to any participants recruited in England and Wales.

B7. What arrangements will be made to identify and consult persons able to advise on the presumed wishes and feelings of participants unable to consent for themselves and on their inclusion in the research?

For research sites in England and Wales participating in Study 4, it is proposed that if after at least 12 hours capacity has not been regained, support for inclusion of the potential participant will be sought from a consultee, consistent with Department of Health Guidance and Section 32(3) of the Mental Capacity Act 2005. This would be a personal consultee if available, i.e. a person who knows the person lacking capacity well, but is not acting in a professional or paid capacity, such as a family member, non-paid carer or friend. If an appropriate personal consultee cannot be identified after reasonable steps have been taken, a nominated consultee will be approached. Arrangements for nominated consultees will be made locally in research sites, in accordance with DH guidance. Advice from the consultee on inclusion of the potential participant in the research will be sought using the Participant Information Sheet and recorded using a Consultee Declaration Form.
Note that consent from the partiicpant for further involvement in the research will be sought when/if capacity has been regained. They will be able to consent to partiicpation, refuse consent for further participation and for use of data/samples collected so far or refuse consent for further participation but consent to use of data/samples collected so far.Consent for inclusion of the potential participant in the research will be sought using the Participant Information Sheet and recorded using a consent form for persons with nominated powers.

Note that consent from the partiicpant for further involvement in the research will be sought when/if capacity has been regained. They will be able to consent to partiicpation, refuse consent for further participation and for use of data/samples collected so far or refuse consent for further participation but consent to use of data/samples collected so far.

Please enclose a copy of the written information to be provided to consultees. This should describe their role under section 32 of the Mental Capacity Act and provide information about the research similar to that which might be given to participants able to consent for themselves.

B8. Is it possible that a participant requiring urgent treatment might need to be recruited into research before it is possible to identify and consult a person under B7?

○ Yes ◉ No

If Yes, say whether arrangements will be made instead to seek agreement from a registered medical practitioner and outline these arrangements. Or, if this is also not feasible, outline how decisions will be made on the inclusion of participants and what arrangements will be made to seek consent from the participant (if capacity has been recovered) or advice from a consultee as soon as practicable thereafter.

This research does not involve any urgent treatment. Samples may be stored pending consultation as described above.

Question B7-1 applies to any participants recruited in Scotland.

B7-1. What arrangements will be made to identify and seek consent from a guardian or welfare attorney or, if there is no such person, from the participant's nearest relative?

For research sites in Scotland, arrangements will be consistent with the Adults with Incapacity (Scotland) Act 2008. It is proposed that if after at least 12 hours capacity has not been regained, consent for inclusion of the potential participant will be sought from a 'person with relevant powers' (i.e. their guardian or welfare attorney or their closest family member if these have not been appointed). This will be sought using an adapted Participant Information Sheet and recorded using a specific Consent Form (Person with relevant powers).

Please enclose a copy of the written information to be provided and the consent form to be used. The information sheet should provide information about the research similar to that which might be given to participants able to consent for themselves.

B9. What arrangements will be made to continue to consult such persons during the course of the research where necessary?

Consenting persons with relevant powers will be kept updated on study progress and will be able to withdraw the participant from the research at any time should they feel that appropriate.
Note that consent from the participant for further involvement in the research will be sought when/if capacity has been regained. They will be able to consent to participation, refuse consent for further participation and for use of data/samples collected so far or refuse consent for further participation but consent to use of data/samples collected so far.

B10. What steps will you take, if appropriate, to provide participants who are unable to consent for themselves with information about the research, and to consider their wishes and feelings?

Irrespective of the advice of consultees (England and Wales) or consent provided by people with relevant powers (Scotland), potential participants without capacity will be informed about the research in as clear and appropriate a way as possible and those that express objections to participation will be not be included.

B11. Is it possible that the capacity of participants could fluctuate during the research? How would this be handled?

Yes. In the great majority of cases this is a recovery of capacity as intoxication reduces. Arrangements for those recovering capacity are described above. For those who give consent and subsequently lose capacity (e.g. a patient who deteriorates and requires intubation), we plan to continue sample collection and analysis which we suggest is justified as the patient has already given consent for that.

B12-1. What will be the criteria for withdrawal of participants?

Patients who recover capacity and decline consent at that point will be withdrawn from the research as described in Sections B7 and B9.

B13. Describe what steps will be taken to ensure that nothing is done to which participants appear to object (unless it is to protect them from harm or minimise pain or discomfort).

There are no invasive activities planned in advance of consent in this study, other than the collection of additional samples. In advance of consent, additional blood for research will only be collected as part of a venesection already being done for clinical purposes. For participants without capacity, research procedures will not be performed if they indicate that they are unwilling or otherwise display distress.

B14. Describe what steps will be taken to ensure that nothing is done which is contrary to any advance decision or statement by the participant?

Advance decisions will be respected, although these are unlikely to be relevant to the provision of biological samples for research under these circumstances.

PART B: Section 7 - Children

1. Please specify the potential age range of children under 16 who will be included and give reasons for carrying out the research in this age group.

Children under 16 years are only involved in the research using fully anonymised data (studies 1 and 2). This will provide some data on the frequency of use of NPS in children and young people (under 16 years of age).

2. Indicate whether any children under 16 will be recruited as controls and give further details.

n/a

3-2. Please describe the arrangements for seeking informed consent from a person with parental responsibility and/or from children able to give consent for themselves.

As fully anonoymised an aggregated data is being provided, informed consent from people with parental responsibility is not being sought.

4. If you intend to provide children under 16 with information about the research and seek their consent or agreement, please outline how this process will vary according to their age and level of understanding.

n/a

Copies of written information sheet(s) for parents and children, consent/assent form(s) and any other explanatory material should be enclosed with the application.

PART C: Overview of research sites

Please enter details of the host organisations (Local Authority, NHS or other) in the UK that will be responsible for the research sites. *For NHS sites, the host organisation is the Trust or Health Board. Where the research site is a primary care site, e.g. GP practice, please insert the host organisation (PCT or Health Board) in the Institution row and insert the research site (e.g. GP practice) in the Department row.*

Investigator identifier	Research site		Investigator Name	
IN3 ☐	○ NHS site ◉ Non-NHS site		Forename Middle name Family name Email Qualification (MD...) Country	Simon Hugh Thomas simon.thomas@ncl.ac.uk BSc, MBBS, MD, FRCP, FRCP(Edin), UNITED KINGDOM
	Institution name Department name Street address Town/city Post Code Country	Newcastle University NIHR Health Protection Unit Wolfson Building Newcastle NE2 4HH UNITED KINGDOM		
IN4 ☐	◉ NHS site ○ Non-NHS site Country: Scotland		Forename Middle name Family name Email Qualification (MD...) Country	Michael Eddleston m.eddleston@ed.ac.uk ScD, FRCP(Edin), FEAPCCT UNITED KINGDOM
	Institution name Department name Street address Town/city Post Code	Royal Infirmary of Edinburgh Emergency Department Little France Crescent Edinburgh EH16 4TJ		
IN5 ☐	◉ NHS site ○ Non-NHS site Country: England		Forename Middle name Family name Email Qualification (MD...) Country	Jonathan Berg johnathanberg@nhs.net UNITED KINGDOM
	Organisation name Address	SANDWELL AND WEST BIRMINGHAM HOSPITALS NHS TRUST CITY HOSPITAL DUDLEY ROAD BIRMINGHAM WEST MIDLANDS		

Post Code	B18 7QH

IN6 ☐

◉ NHS site
○ Non-NHS site

Country: Wales

Institution name	University Hospital Llandough
Department name	Cardiff Toxicology Laboratories
Street address	
Town/city	Penarth, Vale of Glamorgan,
Post Code	CF64 2XX

Forename	Alun
Middle name	
Family name	Hutchings
Email	HutchingsAD@cardiff.ac.uk
Qualification (MD...)	
Country	UNITED KINGDOM

IN7 ☐

◉ NHS site
○ Non-NHS site

Country: England

Organisation name	SANDWELL AND WEST BIRMINGHAM HOSPITALS NHS TRUST
Address	CITY HOSPITAL DUDLEY ROAD BIRMINGHAM WEST MIDLANDS
Post Code	B18 7QH

Forename	Allister
Middle name	
Family name	Vale
Email	allistervale@npis.org
Qualification (MD...)	MD FRCP FRCPE FRCPG FFOM FAACT FBTS FBPharmacolS FEAPPCT Hon FRCPSG
Country	UNITED KINGDOM

IN8 ☐

◉ NHS site
○ Non-NHS site

Country: England

Organisation name	GUY'S AND ST THOMAS' NHS FOUNDATION TRUST
Address	TRUST OFFICES GUY'S HOSPITAL GREAT MAZE POND LONDON GREATER LONDON

Forename	David
Middle name	
Family name	Wood
Email	David.Wood@gstt.nhs.uk
Qualification (MD...)	BSc (Hons) 1st Class; MB ChB (Hons), MD, FRCP, FACMT, FBPharmacolS
Country	UNITED KINGDOM

Post Code SE1 9RT

IN9 ☐

◯ NHS site
◉ Non-NHS site

Forename	John
Middle name	P
Family name	Thompson
Email	thompsonjp@cardiff.ac.uk
Qualification (MD...)	MB ChB BMedSc FRCP FBTS FEAPCCT
Country	UNITED KINGDOM

Institution name	University Hospital Llandough
Department name	Emergency Department
Street address	
Town/city	Penarth, Vale of Glamorgan,
Post Code	CF64 2XX
Country	UNITED KINGDOM

IN10 ☐

◉ NHS site
◯ Non-NHS site

Country: England

Forename	Nigel
Middle name	
Family name	Brown
Email	nigel-william.Brown@northumbria-healthcare.nhs.uk
Qualification (MD...)	PhD, FIBMS, FRCPath, MRSC
Country	UNITED KINGDOM

Organisation name	NORTHUMBRIA HEALTHCARE NHS FOUNDATION TRUST
Address	RAKE LANE NORTH SHIELDS TYNE AND WEAR
Post Code	NE29 8NH

IN11 ☐

◉ NHS site
◯ Non-NHS site

Country: England

Forename	Simon
Middle name	Leslie
Family name	Hill
Email	simon.hill@nuth.nhs.uk
Qualification (MD...)	MBBS, MRCP
Country	UNITED KINGDOM

Organisation name	THE NEWCASTLE UPON TYNE HOSPITALS NHS FOUNDATION TRUST
Address	FREEMAN HOSPITAL FREEMAN ROAD HIGH HEATON NEWCASTLE-UPON-TYNE TYNE AND WEAR
Post Code	NE7 7DN

IN12 ☐

○ NHS site
◉ Non-NHS site

Institution name	Scottish Police Authority
Department name	Forensic Services (Edinburgh)
Street address	11 Howdenhall Road
Town/city	Edinburgh
Post Code	EH16 6TL
Country	UNITED KINGDOM

Forename	Jane
Middle name	Alexandra
Family name	Officer
Email	jane.officer@spa.pnn.police.uk
Qualification (MD...)	
Country	UNITED KINGDOM

PART D: Declarations

D1. Declaration by Chief Investigator

1. The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.

2. I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.

3. If the research is approved I undertake to adhere to the study protocol, the terms of the full application as approved and any conditions set out by review bodies in giving approval.

4. I undertake to notify review bodies of substantial amendments to the protocol or the terms of the approved application, and to seek a favourable opinion from the main REC before implementing the amendment.

5. I undertake to submit annual progress reports setting out the progress of the research, as required by review bodies.

6. I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer. I understand that I am not permitted to disclose identifiable data to third parties unless the disclosure has the consent of the data subject or, in the case of patient data in England and Wales, the disclosure is covered by the terms of an approval under Section 251 of the NHS Act 2006.

7. I understand that research records/data may be subject to inspection by review bodies for audit purposes if required.

8. I understand that any personal data in this application will be held by review bodies and their operational managers and that this will be managed according to the principles established in the Data Protection Act 1998.

9. I understand that the information contained in this application, any supporting documentation and all correspondence with review bodies or their operational managers relating to the application:

    - Will be held by the REC (where applicable) until at least 3 years after the end of the study; and by NHS R&D offices (where the research requires NHS management permission) in accordance with the NHS Code of Practice on Records Management.
    - May be disclosed to the operational managers of review bodies, or the appointing authority for the REC (where applicable), in order to check that the application has been processed correctly or to investigate any complaint.
    - May be seen by auditors appointed to undertake accreditation of RECs (where applicable).
    - Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.
    - May be sent by email to REC members.

10. I understand that information relating to this research, including the contact details on this application, may be held on national research information systems, and that this will be managed according to the principles established in the Data Protection Act 1998.

11. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named below. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

Contact point for publication*(Not applicable for R&D Forms)*

NRES would like to include a contact point with the published summary of the study for those wishing to seek further information. We would be grateful if you would indicate one of the contact points below.

- (•) Chief Investigator
- ( ) Sponsor

- ◯ Study co-ordinator
- ◯ Student
- ◯ Other – please give details
- ◯ None

Access to application for training purposes *(Not applicable for R&D Forms)*

Optional – please tick as appropriate:

☑ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

This section was signed electronically by Simon Thomas on 03/03/2015 15:23.

Job Title/Post:	Consultant
Organisation:	Newcastle Hospitals NHS Foundation Trust
Email:	simon.thomas@ncl.ac.uk

D2. Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co−sponsors by a representative of the lead sponsor named at A64-1.

I confirm that:

1. This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.

2. An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.

3. Any necessary indemnity or insurance arrangements, as described in question A76, will be in place before this research starts. Insurance or indemnity policies will be renewed for the duration of the study where necessary.

4. Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.

5. Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.

6. The duties of sponsors set out in the Research Governance Framework for Health and Social Care will be undertaken in relation to this research.

7. Where the research is reviewed by a REC within the UK Health Departments Research Ethics Service, I understand that the summary of this study will be published on the website of the National Research Ethics Service (NRES), together with the contact point for enquiries named in this application. Publication will take place no earlier than 3 months after issue of the ethics committee's final opinion or the withdrawal of the application.

8. Specifically, for submissions to the Research Ethics Committees (RECs) I declare that any and all clinical trials approved by the HRA since 30th September 2013 (as defined on IRAS categories as clinical trials of medicines, devices, combination of medicines and devices or other clinical trials) have been registered on a publically accessible register in compliance with the HRA registration requirements for the UK, or that any deferral granted by the HRA still applies.

This section was signed electronically by Mr Sean Scott on 04/03/2015 15:41.

Job Title/Post:	RM&G Manager
Organisation:	The Newcastle upon Tyne Hospitals NHS Foundation Trust
Email:	sean.scott@nuth.nhs.uk