**SUBSTANTIAL AMENDMENT NO 2 (SCOTLAND)**

**12TH January 2016 (Draft)**

**BACKGROUND**

The IONA study is collecting blood, urine and oral fluid samples from people presenting to UK hospitals with severe toxicity suspected to be related to use of novel psychoactive substances (sometimes called ‘legal highs’). Sample analysis is being performed to identify the substances involved and to link these with clinical features of toxicity experienced by the participant. The study currently involves 15 study sites in England and Wales and 2 sites in Scotland. Because the study can involve adults with incapacity, separate ethical approval was required in England and Wales (15/NE/0023) and Scotland (15/SS/047).

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

SUBSTANTIAL AMENDMENTS REQUESTED

1. Inclusion of patients with severe opioid toxicity

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

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

2. Changes to participant data collection sheet

We would like to make some minor changes to the data collection sheet as follows:

(a) To clarify that the patient number needed (first box in section 1) is the IONA participant number

(b) to capture admission routine observations (pulse, BP, temperature, oxygen saturations, respiratory rate) and arterial blood gas results (pH, pCO2, pO2, Base excess).

(c) To allow the researchers to indicate whether the patient has been included because of suspected severe opioid intoxication (section 1) and to report the administration of naloxone (Section 5).

A copy of the proposed revision is provided (IONA data collection Sheet V3 12th January 2017).

3. Sharing of linked anonymised samples between laboratories

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

The participant information sheet and consent form (V 3.0, 12th January 2017) and the participant information sheet and consent form (Nearest Relative/Guardian or Welfare Attorney, V 3.0, 12th January 2017) have been adjusted to explain this by inclusion of the following in each document (under ‘what will happen with any samples’)

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

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

Because there has been this change to these information sheets, the following document has been updated to refer to the updated version of the participant information sheet (V3.0, 12th Jan2017).

Consent Form (Person previously included when they did not have capacity, V3.0, 12th Jan2017)

4. Correction of errors in dates referred to in study consent forms.

Due to administrative errors, several of the documents used following the previous substantial amendment (No 1, 24th April 2016) had inconsistencies between the dates of documents and the dates referred to in the corresponding consent form as follows:   
  
(i) The consent for participants with capacity - on the consent form the date referred to for PIS given is erroneously referred to as version 2.0 25/04/2015 but the PIS is dated version 2.0 25/04/2016

(ii) On the consent form for Nearest Relative/Guardian or Welfare Attorney, the relevant information sheet erroneously referred to as v2.0, 04/04/2015, however the PIS is version 2.0 dated 25/04/2016

(iii) Similarly, in the consent form for those regaining capacity the PIS referred to is Version 2.0 25/04/2016 is given (which is correct), however the date at the top the consent form is dated 25/04/2015.

These documents are now superseded by updated documents as in the ‘list of enclosed documents’, so we do not believe that further action is required.

5. Updating of protocol

The protocol has been updated to

(a) include details of currently participating UK research sites and PIs (all previously dealt with as non-substantial amendments, pages 3-4)

(b) Include details of the proposed opioid NPS arm of the study (pages 11, 26)

(c) Detail numbers of participants intended for England and Wales following recently requested increases in recruitment detailed in a substantial amendment currently being considered by the REC in England, and to update the schedule of events accordingly (p 33-34 and 39)

(d) Include the updated data collection sheet with its explanatory notes (p 48-51).