PRINCE OF WALES HOSPITAL

Australian TOxicology Monitoring (ATOM) Study

Study Protocol

Australian TOxicology Monitoring (ATOM) Study

Version Number 11
16th March 2017

PRINCE OF WALES HOSPITAL

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Study Protocol

SYNOPSIS:

Protocol Title: Australian TOxicology Monitoring (ATOM) Study

Protocol version: 11

LIST OF INVESTIGATORS

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PRINCE OF WALES HOSPITAL

Australian TOxicology Monitoring (ATOM) Study

Study Protocol

Summary:

Study title: **Australian TOxicology Monitoring (ATOM) Study**

Protocol version: 11

Objectives: To study the clinical pharmacology of a number of new drugs, by modelling their concentrations and clinical effects from data collected from overdose patients.

Study Design: Prospective, Non- Blinded Observational Study

Planned sample size: up to 50 patients for each drug studied

Selection criteria: Participants will be selected by the Prince of Wales Toxicology unit, either by the Clinical Toxicologist or Toxicology Fellow. These participants will be selected depending on the drug ingested in overdose.

Study procedure: Participants will have an intravenous cannula inserted to collect blood samples. These blood samples will be analysed to measure drug levels, metabolite levels or effects of the drug on the body. ECG, clinical data and urine samples may also be collected.

Duration of the Study: 5 years

Study Protocol

1. BACKGROUND

1.1. Disease Background:

Suicide is a significant cause of mortality in patients with major psychiatric conditions such as schizophrenia, bipolar disorder and depression. The lifetime risk of completed suicide is between 10 and 15% and a very common mode of attempted and completed suicide is deliberate self-poisoning. Most commonly this involves the antidepressant and antipsychotic drugs prescribed for these conditions. The toxicity of these drugs is primarily due to their central nervous system (CNS) effects of sedation and seizures, which is treated with supportive care, and the cardiac effects of hypotension and arrhythmia. Management in overdoses is then determined by the likelihood of severe toxicity and the duration of observation that may be required.

Whilst it is assumed that blood concentration of a drug taken in overdose is the dominant determinant of toxicity, for the majority of drugs the blood level to toxicity relationship is not well understood.(1, 2) In particular, for the newer psychotropic agents there is little data on the pharmacokinetics and the likely time course of effects on a patient in overdose. Pharmacokinetics describes the time course of the change of concentration in the body of a drug and pharmacodynamics is the effect of a drug on the patient. The combination of pharmacokinetics (PK) and pharmacodynamics (PD), termed PKPD, represents the process whereby the time course of drug effects is described.

1.2. Rationale For Performing The Study:

In poisoned patients the pharmacokinetics of drugs can be quite different to that seen with therapeutic doses. There is potential for the saturation of absorption routes, of metabolic pathways and of protein binding. (3) This can lead to higher than expected blood concentrations and to a prolonged elimination phase. In a therapeutic study the dose and the timing of the dose are accurately recorded. In overdose, however, lengthy delays between the time of overdose and arrival in an emergency department are experienced, with resulting delay in observations (taking an initial blood sample). There is also the uncertainty in the information that is collected, because the overdose is impulsive and the patient may not accurately recall or retell the events. The patient may spontaneously vomit or receive some form of decontamination (usually activated charcoal), which decrease the ingested dose by an unknown amount. In summary, this means that the absorption phase of the plasma concentration-time graph is either missing or incomplete and it is usually difficult or impossible to estimate accurately the area under the curve (AUC), time to maximal plasma concentration (T_{max}) or the peak concentration (C_{max}).(4)

Defining the time course of toxicity of drugs in overdose is especially important for newly released drugs where there is relatively little clinical experience. The identification of drugs with severe toxicity at high therapeutic concentrations or a predisposition to toxicity (e.g.

ECG abnormalities that suggest a risk of sudden death) provides important information for patient management. Prolongation of the QT interval has become increasingly important for both preclinical studies of therapeutic drugs and for predicting drugs that may cause severe cardiac effects in overdose.

Newer population analysis techniques can be used to model drug concentration and clinical effects using the relatively sparse data collected in overdose patients. Such modelling requires sequential collection of drug concentrations, ECG parameters (QT interval) and other clinical effects including the occurrence of arrhythmias and seizures in drug overdose. Application of the model would then allow the development of predictors of seizures, coma and arrhythmia in drug overdose, using dose, ECG parameters and other initial clinical features.

2. STUDY OBJECTIVE

To study the clinical pharmacology of a number of new drugs, by modelling their concentrations and clinical effects from data collected from overdose patients. For the study, it is intended to employ a population analysis technique that is reliant on recording relatively sparse data obtained in drug overdose circumstances. The modelling will require the sequential collection of drug concentrations, ECG parameters (e.g. QT interval) and the tracking of associated clinical effects, including the occurrence of arrhythmias and seizures.

The broad aims of the study will be to:

- measure the time course of the change of drug concentration in the body (pharmacokinetics) in overdose;
- determine the relationship between drug concentration and clinical effects (pharmacodynamics);
- Develop evidence-based clinical guidelines for the treatment of patients who have overdosed on these agents.

3. STUDY DESIGN

3.1. Design: The methodology of this study will follow that used in previous studies by Hunter Area Toxicology Service (HATS). They completed many years of clinical data collection for some new antipsychotics and antidepressants and have demonstrated the feasibility of obtaining multiple samples, patient consent, quantification of these drugs in overdose and the robustness of the datasets for population PKPD analysis. Their study included prospective collection of serial drug concentrations, ECGs and specific clinical investigations. They have completed initial studies on citalopram,(5) moclobemide,(6) nefazodone,(7) venlafaxine and quetiapine.(4)

This study is a prospective, non-blinded observational study

3.2. Number of Participants: Previous studies have developed good PKPD models by collecting approximately 300 data points from participants. For example this could mean 30 participants with 10 data points or 10 participants with 30 data points.

For each drug listed below we are aiming to recruit up to 50 patients per drug.

4. PARTCIPANT SECTION

4.1 Inclusion Criteria: Participants will be selected by the Prince of Wales Toxicology unit, either by the Clinical Toxicologist or Toxicology Fellow. These participants will be selected depending on the drug ingested in overdose.

Major drugs of interest include:

- Amisulpride, Escitalopram, Venlafaxine, Valproate and paracetamol.
- Other drugs of interest include:
  - Antidepressant such as Citalopram, Reboxetine, Mirtazapine and Bupropion.
  - Antipsychotics such as Risperidone, Quetiapine and Aripiprazole.
  - Anticonvulsants such as Carbamazepine, Phenytoin, Gabapentin and Lamotrigine.
  - And other agents such as Baclofen, Metformin and Colchicine.
  - Newly marketed drugs (if we see sufficient numbers and toxicity)

4.2 Exclusion Criteria:

- Less than 14 years of age
- In custody

5. STUDY OUTLINE

5.1. Study Design: Standard treatment in patients whom take an overdose of a medication, depends on the drug ingested. The majority of patient's whom take an overdose will have an ECG and bloods taken on arrival to the emergency department. Then depending on the drug ingested, severity of the overdose and response to treatment, the patient may require additional ECG's and blood tests. The number and timing of these investigations depends on the drug ingested and the patients' clinical condition. The Toxicologist on duty will determine how many blood samples will need to be collected.In most cases we will aim to use the cannula inserted for the patient's treatment, to collect blood samples. If this is not possible, participants will have an intravenous cannula, inserted into their hand or arm. This will be used to take the blood samples during the study to minimise discomfort.

We wish to collect and analyse excess blood that is taken as part of standard treatment. This blood would otherwise be discarded. For details of the consenting process, please refer

to section 5.4. Only after consent is received and if needed, will additional samples of blood be collected. These samples will only be used for research purposes.

Furthermore we will only collect extra blood samples once a patient has been consented. If a patient is unable to consent due to their medical condition, we will only use excess blood collect as part of their treatment. That is blood that would have otherwise been discarded. When the patient is able we will obtain consent and only after this time, if required we will collect extra samples. In most cases we will endeavor to use excess blood that is collected as standard of care. No samples will be analysed until a patient gives consent.

An electrocardiogram is recorded in all patients who present with an overdose, to detect if there is any effect on the electrical activity of the heart. We will analyse those ECG's that are collected as a part of the patient's treatment.

In some participants urine will also be collected, this again depends on the drug ingested. If urine is to be collected this will be determined by the Toxicology team. Samples will be collected at specific times for up to 24 hours. The urine samples may be used to measure the amount of a drug, metabolites or biomarkers of acute kidney injury (as relevant to the agent). .

Laboratory Assay: Serum samples will initially be frozen and stored in SEALs laboratories for later analysis. Urine samples will also be stored at SEALs for later analysis. The sample, once identified as a part of the study, will be de-identified and labelled as a study number. It is anticipated that samples may often be sent to other laboratories for analysis as many of these assays are not widely available. Any samples sent for external assay will have information that might identify the person (name, address, MRN) removed and replaced by a study number. Similarly such information will not be supplied to other external investigators. Serum samples will be analysed for drug and/or metabolite concentrations. Once the study is complete the samples will be destroyed/ discarded by the SEALs laboratory.

Data Collection and Monitoring Form: Each participant will have a data collection form completed to monitor progress through the study. This will contain information on their age, weight, sex , drug ingested, time drug ingested, background history, usual medications, unique study ID number, what samples were collected , time samples collected and ECGs(as required). This clinical data collected, is information collected on all toxicology patients as a part of their clinical assessment.(see attached form – which is the toxicology admission form) The clinical, ECG and drug/ metabolite concentration data will be entered onto a database. This database will be password protected. Only members of the toxicology unit will have access to this database. When the data is being analysed the participant will be de-identified and given a study number. Each participant will be given a study code; this code will be used on all forms of data (clinical data and blood and urine samples) collected on the participants. This master

code will be stored in an excel document that is password protected and only available to the investigators.

5.2. Study Procedure Risks: The only risk of being involved in the study is the additional need for an intravenous cannula. Not all patients will require an extra cannula, in most we will use the cannula inserted as a part of their management. But in some that cannula may be in use for fluids or medications, hence in these patients we will insert a second cannula to collect samples. This is more comfortable for the patient as it allows us to collect blood samples without having to venipuncture the patient on multiple occasions. This cannula will be inserted by experienced health care staff. There are minimal risks from taking blood, but they include a small risk of bruising at the site, dizziness and fainting, and the small chance of an infection developing from the presence of the cannula. The standard precautions of using a sterile technique to collect blood and insert the cannula will significantly reduce the risk of this and will be adhered during the study. There is no risk from additional electrocardiograms which will be recorded by trained technicians or nursing staff. There is no risk from urine collection, which will be collected by nursing staff.

5.3. Recruitment and Screening: Participants will be selected by the Prince of Wales Toxicology unit, either by the Clinical Toxicologist or Toxicology Fellow. These participants will be selected depending on the drug ingested in overdose.

Patients who present to Prince of Wales Emergency Department after an overdose are discussed with the clinical toxicologist on duty, the fellow or registrar. The toxicology registrar discusses all their cases with either the Toxicologist on call or the Fellow. If a patient has ingested a drug of interest, the toxicologist or fellow will ask if the patient can be recruited into the study. During business hours the patient will be seen by a member of the toxicology unit and the study explained. Or if after hours consented by the emergency department and the following day reviewed by the toxicology team and the consent verified.

Furthermore the Prince of Wales Hospital, Toxicology service consults and reviews children at the Sydney Children's Hospital Randwick. And we offer phone advice for those patients who present following an overdose at St George, Sutherland and Wollongong Hospital. If we are consulted about a patient with an overdose of a drug of interest we will ask the treating doctor if they can enrol them into the study. We will only recruit patients we are asked to consult on.

This study is a multi-centre study with various other participating sites throughout NSW. Patients at these sites are recruited by the treating toxicology team, for example at Westmead and Royal Prince Alfred Hospital. NSW Poison's Information Centre (Children's Hospital Westmead) gives phone medical toxicology advice to hospitals throughout NSW and Australia. If we are consulted about a patient with an overdose of a drug of interest (as outlined in the protocol appendix) we will ask the treating doctor if they can enrol them into the study.

We will only recruit patients we are asked to consult on within NSW, from calls to the NSW Poison's Information Centre.

5.4. Informed Consent Process: Participants will be explained the study by the toxicology team or the treating doctor. They will be given a copy of the consent/ patient information sheet. They may ask the consenting doctor or can call the number on the patient information sheet and ask the principal investigator any questions regarding the study. Patients will not be coerced to participate in the study.

With consents obtained via recruitment through the NSW PIC, an investigator will be made available by phone to have a three- way conversation with the treating doctor on site, participant and the researcher. The treating doctor will be asked to obtain the consent, via a three- way conversation (preferred option). However this may not always be feasible, a second option will be for the participant to speak with the principal investigator by phone, if required to answer any questions.

If a patient is unable to give consent as they are unconscious or too unwell, consent will be obtained from their next of kin initially. In this situation, blood will not be collected at time points outside of the patient's standard management. When the patient has improved, a member of the treating toxicology team or the treating doctor will talk with them about the study and ask if they consent to participate. Blood samples will be stored but not be used until consent from the patient is obtained. If extra blood samples are needed, these will only be collected with the patient's consent. If consent is declined the blood samples will be destroyed.

In the rare event that a patient is deceased before we can obtain consent for samples taken, we will obtain consent from the next of kin. Samples will be stored but not analysed until consent is obtained. If we cannot obtain consent from a guardian or next of kin the samples will be destroyed.

6. STORAGE AND ARCHIEVING OF DOCUMENTS

All study documents will be stored in a computer that is password protected. Paper documents such as the consent forms will be stored in a locked filing cabinet in a locked office. The results will be stored at Prince of Wales Hospital in the Department of Clinical Toxicology offices. Results will be stored for a minimum of 7 years.

7. REFERENCES

1. Dawson AH, Whyte IM. Therapeutic drug monitoring in drug overdose. Br J Clin Pharmacol 1999; 48 :278-283.

2. Bailey B, Buckley NA, Amre DK. A meta-analysis of prognostic indicators to predict seizures, arrhythmias or death after tricyclic antidepressant overdose. J Toxicol Clin Toxicol 2004; 42(6):877-888.
3. Watson WA, Rose SR. Pharmacokinetics and toxicokinetics. Clinical Toxicology. WB Saunders, 2001: 73-79.
4. Balit CR, Isbister GK, Hackett LP, Whyte IM. Quetiapine poisoning: A case series. Ann Emerg Med 2003; 42(6):751-758.
5. Duffull SB, Isbister GK, Dawson AH, Hackett LP, Whyte IM. Estimating population pharmacokinetic parameters when dose and dose-time are not known accurately. Journal of Toxicology: Clinical Toxicology 2003; 41(5):652-653.
6. Isbister GK, Hackett LP, Dawson AH, Whyte IM, Smith AJ. Moclobemide poisoning: toxicokinetics and occurrence of serotonin toxicity. Br J Clin Pharmacol 2003; 56(4):441-450.
7. Isbister GK, Hackett LP. Nefazodone poisoning: toxicokinetics and toxicodynamics using continuous data collection. J Toxicol Clin Toxicol 2003; 41(2):167-173.

Appendix:

1/ Appendix 1: Australian Paracetamol Project: APP: "ATOM: APP Protocol: Master Version 1: 10th July 2013": page 11-14

2/ Appendix 2: Digoxin Overdose & Response to Antibodies (DORA): "ATOM: DORA Protocol Master Version 1: 1st July 2013": page 15 – 19

3/ Appendix 3: Dihydropyridine Toxicity Project (DTP): "ATOM: DTP Protocol Master Version 2: 30th May 2014": page 20 – 23

4/ Appendix 4: Anticoagulation Project Time & Treatment (aPTT): "ATOM: aPTT Protocol Master Version 1: 11th June 2014": page 24 – 28

5/ Appendix 5: Dialysis of Toxins Study (DOTS): "ATOM: DOTS Protocol: Master Version 1: June 2014: page 29- 35

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Appendix 1: Australian Paracetamol Project: APP: "ATOM: APP Protocol: Master Version 1: 10th July 2013": page 11-14

Australian TOxicology Monitoring(ATOM) Study

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Australian Paracetamol Project (APP)

Procedure

AIMS: To investigate the pharmacokinetics and dynamics of paracetamol in overdose. In particular large paracetamol overdoses, sustained release preparation and those with established hepatotoxicity.

INCLUSION:

1/ Ingestion of **> 35g** of paracetamol

2/ Paracetamol level **> 2000umol/L (300mg/L) at anytime**

3/ Ingestion of **> 10g of sustained release paracetamol**

4/ Any patients with deranged LFT: AST > 500IU/L, ALT > 500IU/L (that is 10X the upper limit of normal)

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves using serum already collected and obtaining new serum samples, while the patient is in hospital. Patients' should be informed that extra blood samples will be taken. At the most we will collect 4 extra blood samples per 24 hours. The majority of these samples will be taken with the patients routine bloods. Hence there are minimal risks from this study, only that of collecting an extra blood sample. The patient will be de-identified. Samples are tested for drug and metabolite levels, these include, paracetamol and its' metabolites and N- acetyl cysteine (NAC) levels. Once the study is completed the samples are destroyed. As a part of this study we will also be accessing the patient's medical records. This study will allow us to better understand paracetamol in overdose.

METHOD:

STEP 1 - Obtain **consent** from the patient. Please ask them to sign **page 4** of the **"Subject Information and Consent form"** and then please fax this page to: **(02) 80160860.**

STEP 2 - Complete the patient data form and please fax the completed form to **(02) 80160860**

STEP 3 - Research samples are to be collected in a **serum tube**. **Note** on all request forms **"Australian Paracetamol Project"** – research sample. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

BLOOD SAMPLE TIMING

Research samples to be collected are 5mL serum samples (SST)

SAMPLING TIMES: Please collect a serum tube for research purposes at these times:

a/ **4 hour level**

b/ **8-12 hour** paracetamol level + collect an extra research tube. This paracetamol level is required in the management of sustained release paracetamol overdose and is useful in guiding management in large paracetamol overdoses.

c/ **1-2 hours prior to completion of the third bag** of IV NAC, the patient should have repeat **LFT's, INR, paracetamol level + extra serum tube for research.** These investigations are required, to determine the need for ongoing treatment with IV NAC treatment.

d/ If the patient requires ongoing NAC please repeat **LFTs and INR every 12 hours** and collect an **extra serum sample tube** for research purposes.

If you have any questions please call Dr Angela Chiew on 0412575580 or 1800 676 944

Please fax all forms to (02) 80160860

ATOM: APP Protocol: Master Version 1: 10th July 2013 Page 1 of 4

Australian TOxicology Monitoring (ATOM) Study

Australian Paracetamol Project

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PATIENT DATA SHEET

PATIENT STICKER:	**DATE AND TIME PRESENTED TO ED:**
	CONSENT OBTAINED: YES NO
WEIGHT (KG): **HEIGHT (CM):**	**ETOH INTAKE: standard drinks / day**
PAST MEDICAL HISTORY:	**ANY VOMITING POST PARACETAMOL INGESTION:** **YES / NO**
DOSE OF PARACETAMOL TAKEN: Patient certain of dose ingested: YES / NO	**TIME OF INGESTION:** Patient certain of time of ingestion: YES / NO
SLOW RELEASE PREPARATION: **YES / NO**	**CHARCOAL GIVEN: YES NO** **TIME AND DOSE:**

CO INGESTIONS :DRUGS OR ETOH	AMOUNT	TIME INGESTED

Time and date NAC commenced:

Rate of first/ loading dose of NAC: **(loading dose given (mg) AND over how many minutes)**

Please fax completed form to (02) 80160860

If you have any questions please call Dr Angela Chiew on 0412575580 or 1800676944

Study Protocol

Australian TOxicology Monitoring (ATOM) Study

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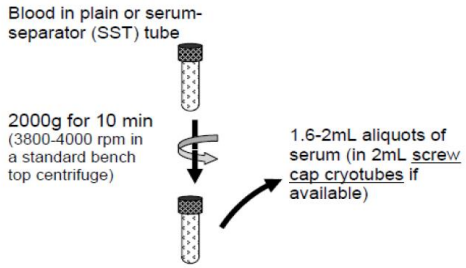
Australian Paracetamol Project

Laboratory Protocol

Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum



Label each tube with **sample type** ("**Ser**"), **patient ID**, **date & time of collection**.

Keep samples from each collection time separate in a single specimen bag, along with a copy of the corresponding request form.

Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient and doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are **not discarded** without first discussing with a study coordinator (contact details at the bottom of this page).

3. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and coagulation). Please either fax to **(02) 80160860**

OR :

Post to: Dr Angela Chiew
Prince of Wales Hospital
Emergency Department
Barker Street, Randwick NSW 2031

If you have any questions please call Dr Angela Chiew (principal investigator) on **0412575580**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160860

Australian TOxicology Monitoring (ATOM) Study

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Australian Paracetamol Project

Laboratory Protocol

4. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:

"Australian Paracetamol Project: Study Hold for Dr Isbister"

These samples are to be sent to:

NSW:

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service, John Hunter Hospital,
Lookout Road, New Lambton Heights,
NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:

The Australian Paracetamol Project (APP) aims to investigate the pharmacokinetics and dynamics of paracetamol in overdose. In particular large paracetamol overdoses, sustained release preparation and those with established hepatotoxicity. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call Dr Angela Chiew (principal investigator) on **0412575580**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160860

Appendix 2: Digoxin Overdose & Response to Antibodies: DORA: "ATOM: DORA Protocol Master Version 1: 1st July 2013": page 15– 19

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Australian TOxicology Monitoring (ATOM) Study
Digoxin Overdose & Response to Antibodies (DORA)
Procedure

AIMS: to investigate the effects and pharmacokinetics of digoxin and digoxin Fab in acute and chronic toxicity in order to improve the dosing and indications for digifab.

INCLUSION:

1/ Any patient presenting with an acute digoxin poisoning.
2/ Any patients presenting with suspected chronic digoxin poisoning.

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves a structured audit of the outcomes of standard management - doing ECGs, clinical observation (pulse, BP), taking blood samples and documenting common clinical symptoms. These should be done on admission, 1, 4 hours later and when clinically indicated until discharge. Care should be taken not to take blood out of the cannula used to administer antibodies (an additional cannula may need to be inserted).

METHOD:

STEP 1 - Obtain **consent** from the patient. Please ask them to sign **page 4** of the **"Subject Information and Consent form"** and then please fax this page to: **(02) 80160868** (or email to **betty.chan@sesiahs.health.nsw.gov.au)**
STEP 2 - For this study extra blood samples will be required to be collected. Consider inserting an extra cannula to collect blood samples to avoid repeated venipuncture.
STEP 3 – Perform ECG at the time when blood samples are taken.
STEP 4 - Complete the patient data form and please fax the completed form to **(02) 80160868** (or email to above address).
STEP 5 – Research samples are to be collected in a **serum tube**. **Note** on all request forms **"DORA study"** – research samples. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

ECG AND BLOOD SAMPLE TIMES:
Research samples to be collected are 5mL serum samples (SST)

Please collect a serum tube for research purposes at these times: (Please note that potassium levels should be checked after the administration of digoxin Fab at 1 and 4 hrs.)

a) 1 hour following admission or 1 hour after infusion of digoxin Fab
b) 4 hour following admission or 4 hours after infusion of digoxin Fab.
c) Anytime when blood or ECG is taken for clinical monitoring.

ATOM: DORA Protocol Master Version 1 : 1st July 2013 Page 1 of 5

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AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY

Patient Data Sheet #1 – Digoxin Poisoning

Digoxin Overdose & Response to Antibodies (DORA) study

PATIENT STICKER:	DATE AND TIME PRESENTED TO ED: CONSENT OBTAINED: YES NO	
WEIGHT (KG): HEIGHT (CM):	Please circle: ACUTE / CHRONIC DIGOXIN POISONING	
CURRENT MEDICATIONS:	PAST MEDICAL HISTORY:	
DOSE OF DIGOXIN TAKEN: TIME OF INGESTION:	DOSE OF DIGOXIN TAKEN DAILY: TIME OF LAST DOSE DIGOXIN INGESTION:	
SYMPTOMS ON PRESENTATION: (PLEASE CIRCLE) CVS: Arrhythmias – Atrial fibrillation / Bradycardia /Junctional bradycardia / Complete heart block / Ventricular ectopics / Atrial tachycardia / Ventricular tachycardia / Ventricular fibrillation. GIT: Nausea / Vomiting / Abdominal pain CNS: Confusion / Visual disturbances Others:		
CO INGESTION :DRUG	AMOUNT	TIME INGESTED
Initial Digoxin level: Time taken:	Initial K: Cr: Time taken:	
CHARCOAL GIVEN: YES NO TIME AND DOSE:	Time & date Digoxin Fab commenced: Dose Digoxin Fab:	

Study Protocol

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AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY

Patient Data Sheet #2 – Digoxin Poisoning

Digoxin Overdose & Response to Antibodies (DORA) study

Time (indicative times given but write actual times)	Blood Sample/ ECG (tick)	HR	BP	Level of Coma (Awake or GCS)	CNS or Abdominal symptoms	Other Comments (Record other treatments given and whether patient has responded)
Baseline *						
0.5 hr						
1hr*						
2hr						
4hr*						
Blood taken						

* do ECG & take blood for EUC, digoxin level plus one gold top tube for research purpose. Please take one extra gold top tube whenever blood is taken from patient for clinical monitoring purpose. (**Note** – Digoxin levels may be misleading after digifab, as they measure digoxin bound to DigiFab as well as 'free' digoxin)

Response to Digoxin Fab: (please circle & provide information)

Time taken for digoxin Fab to work (from the end of infusion): _____ HR _____ BP _____

(1) Resolution of ventricular arrhythmias: _____

(2) Improvement of BP: _____

(3) Resolution of bradycardia (HR<50): _____

(4) Improvement of _____: _____

Thanks very much!

If you would like to receive a copy of the results of this study or the results of the assays for free digoxin levels on your patient put your email address here _____

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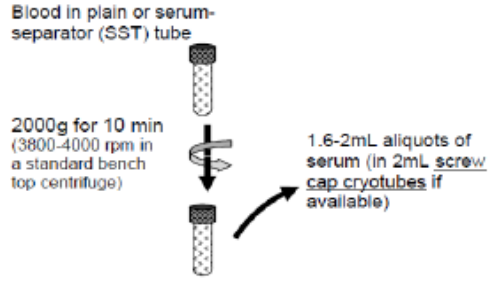
Australian TOxicology Monitoring (ATOM) Study

Digoxin Overdose and Response to Antibody (DORA) Study

Laboratory Protocol

Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum



Label each tube with sample type ("Ser"), patient ID, date & time of collection.

Keep samples from each collection time separate in a single specimen bag, along with a copy of the corresponding request form.

Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient and doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are **not discarded** without first discussing with a study coordinator (contact details at the bottom of this page).

3. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and coagulation).
Please either fax to **(02) 80160868**

OR:

Post to: Dr Betty Chan
Prince of Wales Hospital
Emergency Department
Barker Street, Randwick NSW 2031

If you have any questions please call Dr Betty Chan (principal investigator) on **0439601068**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160868

Insert hospital letterhead here

Australian TOxicology Monitoring (ATOM) Study

Digoxin Overdose and Response to Antibody (DORA) Study

Laboratory Protocol

4. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:

"Digoxin Overdose and Response to Antibody (DORA): Study Hold for Dr Isbister"

These samples are to be sent to:

NSW:

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service, John Hunter Hospital,
Lookout Road, New Lambton Heights,
NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:

The Digoxin Overdoes and Response to Antibody (DORA) study aims to investigate the pharmacokinetics and dynamics of digoxin and response to digoxin Fab in acute overdoses and chronic poisonings. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call Dr Betty Chan (principal investigator) on **0439601068**. IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160868

Appendix 3: Dihydropyridine Toxicity Project: "ATOM: DTP Protocol Master Version 2: 30th May 2014": page 20-23

INSERT HOSPITAL LOGO

Australian TOxicology Monitoring (ATOM) Study
Dihydropyridine Toxicity Project (DTP)

AIMS: to investigate the toxic effects and pharmacokinetics of amlodipine or lercarnidipine in single and combination overdoses with other anti-hypertensive agents.

INCLUSION:
1. Any patient presenting with a dihydropyridine poisoning (for example amlodipine, lercarnidipine or felodipine)
2. Any patient presenting with a combination product of dihydropyridine poisoning (e.g.: with angiotensive converting enzyme inhibitor, angiotensin receptor blocker, diuretics or statin).

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves a structured audit of the outcomes of standard management – ECGs, clinical observation (pulse, BP), taking blood samples and documenting common clinical symptoms. These should be done on admission, 4 hours later and when clinically indicated until discharge.

METHOD:
STEP 1 - Obtain consent from the patient. Please ask them to sign page 4 of the "Subject Information and Consent form" and then please fax this page to: (02) 80160868 (or email to betty.chan@sesiahs.health.nsw.gov.au)
STEP 2 - For this study extra blood samples will be required to be collected with routine blood tests.
STEP 3 – Perform ECG at the time when blood samples are taken.
STEP 4 - Complete the patient data form and please fax the completed form to (02) 80160868 (or email to above address).
STEP 5 – Research samples are to be collected in a serum tube. Note on all request forms "DTP study": research samples. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

ECG AND BLOOD SAMPLE TIMES:

Research samples to be collected are 5mL serum samples (SST)

ECG should be done on admission and when clinically indicated.

Please collect a serum tube for research purposes:
1) On admission,
2) 4 – 6 hours post admission bloods
3) As indicated for clinical monitoring.

ATOM: DTP Protocol Master Version 3: 18th July 2015 Page 1 of 4

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY

Patient Data Sheet #1 – Dihydropyridine Toxicity Project (DTP)

INSERT HOSPITAL

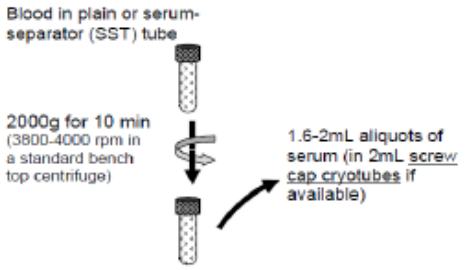
PATIENT STICKER:	DATE AND TIME PRESENTED TO ED: CONSENT OBTAINED: YES NO	
WEIGHT (KG): HEIGHT (CM):	DATE & TIME OF INGESTION: CERTAIN OF TIME OF INGESTION: Y / N INTENTIONAL / ACCIDENTAL INGESTION (circle)	
DIHYDROPYRIDINE TAB STRENGTH: DOSE OF DIHYDROPYRIDINE TAKEN: CERTAIN OF DOSE INGESTED: Y / N	DIHYDROPYRIDINE PRODUCT BRAND NAME :	
CO-INGESTED DRUGS:	AMOUNT	TIME INGESTED
CURRENT MEDICATIONS:	PAST MEDICAL HISTORY:	
Initial HR: BP: Time taken:	CHARCOAL GIVEN: YES NO TIME AND DOSE:	
SYMPTOMS ON PRESENTATION: (PLEASE CIRCLE) CVS: Arrhythmias – Atrial fibrillation / Bradycardia /Junctional bradycardia / Complete heart block / Ventricular ectopics / Atrial tachycardia / Ventricular tachycardia / Ventricular fibrillation / Hypotension. Others:		

Insert Hospital logo

Australian TOxicology Monitoring (ATOM) Study
Dihydropyridine Toxicity Project (DTP)

Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum



Label each tube with **sample type** ("**Ser**"), **patient ID**, **date & time of collection**.

Keep samples from each collection time separate in a single specimen bag, along with a copy of the corresponding request form.

Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient and doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are **not discarded** without first discussing with a study coordinator (contact details at the bottom of this page).

3. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and coagulation). Please either fax to **(02) 80160868**

OR:

Post to: Dr Betty Chan
Prince of Wales Hospital
Emergency Department
Barker Street, Randwick NSW 2031

If you have any questions please call Dr Betty Chan (principal investigator) on **0413286663** or **0439601068**.
IF THIS FAILS please call the ASP study line on 1800676944.

Insert hospital logo	Australian TOxicology Monitoring (ATOM) Study Dihydropyridine Toxicity Project (DTP)

4. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:
"Dihydropyridine Toxicity Project (DTP): Study Hold for Dr Isbister"

These samples are to be sent to:
NSW:

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service, John Hunter Hospital,
Lookout Road, New Lambton Heights, NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:

Dihydropyridine is now one of the commonest prescribed anti-hypertensive agents in Australia. The Dihydropyridine Toxicity Project (DTP) aims to investigate the pharmacokinetics and dynamics of amlodipine and lercanidipine in single and combination products with or without other anti-hypertensive co-ingestion. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call Dr Betty Chan (principal investigator) on **0413286663** or **0439601068**. IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160868

Appendix 4: Anticoagulation Project Time & Treatment: "ATOM: aPTT Protocol Master Version 1: 11th June 2014": page 24 – 28

ATOM STUDY: Australian Toxicology Monitoring

Insert Hospital Logo

Anticoagulation Project Time & Treatment (aPTT)

PROCEDURE

AIM: To investigate the pharmacokinetics and dynamics of warfarin, super-warfarins and newer anticoagulant agents in overdose.

INCLUSION:

1/ Any intentional ingestion of warfarin, dabigatran, bivalirudin, rivaroxaban, apixaban, brodifacoum, other long-acting super warfarins and any heparin overdoses.

EXCLUSION:

Age < 14 years

WHAT IS INVOLVED:

This study involves using serum already collected and obtaining new serum samples, while the patient is in hospital. Patients' should be informed that extra blood samples will be taken. At the most we will collect 4 extra blood samples per 24 hours. The majority of these samples will be taken with the patients routine bloods. Hence there are minimal risks from this study, only that of collecting an extra blood sample. The patient will be de-identified. Samples are tested for drug and clotting factor levels, these include, warfarin (or appropriate ingested drug) and aPTT, PT and factor II, VII, IX and X levels. Once the study is completed the samples are destroyed. As a part of this study we will also be accessing the patient's medical records. This study will allow us to better understand anticoagulants in overdose.

METHOD:

STEP 1 - Obtain **consent** from the patient. Please ask them to sign **page 4** of the **"Subject Information and Consent form"** and then please fax this page to: **(02) 49110501.**

STEP 2 - Complete the patient data form and please fax the completed form to **(02) 49110501**

STEP 3 - Research samples are to be collected in a **serum tube**.
Note on all request forms **"Anticoagulation Project"** – research sample.
Please send the "Laboratory Protocol" to your pathology laboratory with the first serum sample collected.

BLOOD SAMPLE TIMING

Research samples to be collected are 5mL serum samples (SST) and a coagulation/citrate tube correctly filled

SAMPLING TIMES:

Please collect a **serum tube** for research purposes at these times:

a/ **Presentation**; along with coagulation studies (INR/PT, aPTT)

b/ **6-8 hourly;** Along with coagulation studies (and as required to guide treatment)

ANTIDOTE TREATMENT

Please document any treatment given (e.g. Vitamin K, FFP, prothrombin X) and the **time given** on the datasheet attached.

If you have any questions please call Dr Ingrid Berling on 0403026477 or 1800 676 944

Please fax all forms to (02) 49110501.

ATOM: aPTT Protocol: Master Version 1: 11th June 2014 Page 1 of 5

Study Protocol

ATOM Study: Australian Toxicology Monitoring

Anticoagulation Project Time & Treatment

Insert hospital letterhead here

PATIENT DATA SHEET

PATIENT Sticker/Details:	**Presentation to ED** **DATE:** **TIME:**
	CONSENT OBTAINED: YES / NO
INGESTION details **DATE:** **TIME:**	**Weight (KG):** **Height (CM):**
Study medication ingested (circle): WARFARIN / DABIGATRAN / BIVALIRUDIN / RIVAROXABAN / APIXABAN / BRODIFACOUM OTHER: **DOSE ingested:**	**Usual medication:** YES / NO **Reason for anticoagulation:** DVT / PE / AF / VALVE / OTHER **INTENTION / ACCIDENTAL ingestion (circle)**
CO INGESTIONS : Drugs or EtOH	**CHARCOAL GIVEN:** YES / NO **TIME and DOSE (eg 50g):**

TREATMENT(S) GIVEN:

Vitamin K:

IV / PO:	Dose (mg):	Date:	Time:

FFP (amount/time): _____ **Other:**

Prothrombin X (amount/time):_____

LMWH/Heparin (amount/time):_____

Please fax completed form to (02) 49110501

If you have any questions please call Dr Ingrid Berling on 0403026477 or 1800676944

Study Protocol

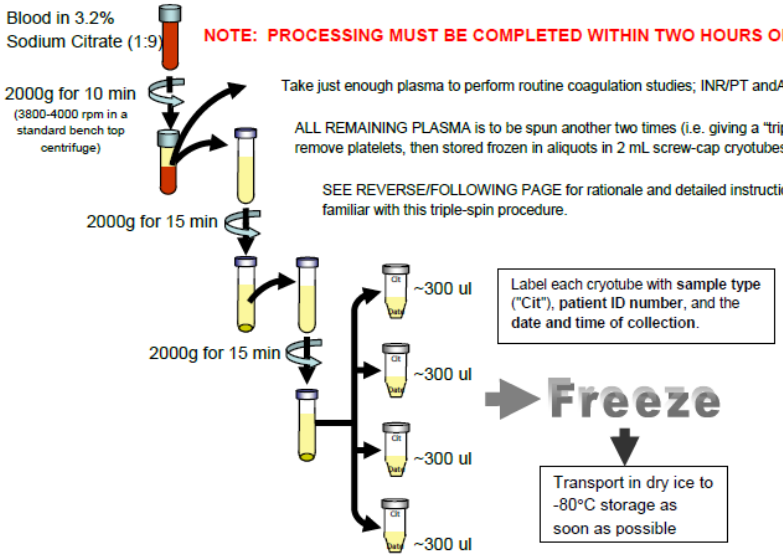
ATOM STUDY: Australian Toxicology Monitoring

Insert hospital Logo

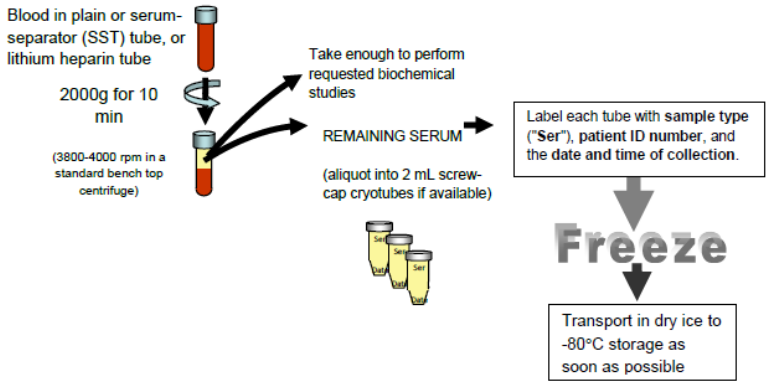
Anticoagulation Project Time & Treatment

Laboratory Protocol

CITRATE PLASMA PROCESSING PROTOCOL



SERUM PROCESSING PROTOCOL



Please send this information sheet to your pathology laboratory with the first serum research sample collected

ATOM STUDY: Australian Toxicology Monitoring

Insert hospital letterhead here

Anticoagulation Project Time & Treatment

Laboratory Protocol

PLASMA PROCESSING RATIONALE AND DETAILED INSTRUCTIONS:

Overview

The plasma collected for this study is used for functional antigen studies using platelet free plasma.

Processing must be completed within 2 hours of collection

Triple spinning is employed to remove all platelets. This platelet-free plasma is then aliquoted into small tubes which must be frozen within 2 hours of collection and moved in dry ice to a -80C freezer as soon as possible.

It is very important that the plasma is processed and frozen as quickly as possible in order to maintain activity of the various factors that we will be assaying.

Collection

5-10 ml of venous blood is collected into tubes containing 3.2% sodium citrate (standard coag collection tubes) at a ratio of 1:9 and mixed well

Processing

1. Centrifuge the citrate tubes at 2000g (3800-4000 rpm in a standard bench top centrifuge) for 10 minutes to separate the plasma from the red and white cells.
2. Take just enough plasma to perform routine coagulation studies: i.e. INR/PT, APTT
3. Carefully removed all remaining upper plasma fraction from the bottom layer of cells using a transfer pipette and transfer the plasma into a fresh sterile 15ml tube.
4. Centrifuge the plasma at 2000g for 10 min.
5. Remove the upper plasma from any pelleted debris and transfer the plasma to a fresh sterile 15 ml tube.
6. Centrifuge the plasma again at 2000g for 10 min.
7. Remove the upper plasma and aliquot it into 2 ml screw cap Eppendorf/Sarsdedt or equivalent cryotubes in ~ 0.3ml aliquots (4 – 10 tubes in total, depending on amount of plasma available). **If you do not have screw-top cryotubes**, then use the smallest tubes available to you.
8. Label each tube with the **patient ID number**, "**Cit**" (indicating that this is a citrate sample) and **date and time of collection** on the side of the tube, and the **patient ID number on the cap**.
9. **Freeze** tubes in an **upright position** (preferably in boxes) and move to –80C storage as soon as possible. TRANSPORT MUST ALWAYS BE IN DRY ICE.

ATOM STUDY: Australian Toxicology Monitoring

Insert hospital letterhead here

Anticoagulation Project Time & Treatment

Laboratory Protocol

Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient and doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are **not discarded** without first discussing with a study coordinator (contact details at the bottom of this page).

Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and coagulation). Please either fax to **(02) 49110501**

OR : Post to Dr Dr Geoff Isbister, Calvery Mater Newcastle, Edith Street, Waratah, NSW, 2298

Sample Transport

Please label these samples as:

"Anticoagulation Project; Study Hold for Dr Isbister"

These samples are to be sent to:

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service,
John Hunter Hospital,
Lookout Road, New Lambton Heights
NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:

The Anticoagulation Project Time & Treatment (aPTT) aims to investigate the pharmacokinetics and dynamics of anticoagulants in overdose. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call Dr Ingrid Berling (Associate investigator) on **0403026477**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 4911 0501

Appendix 5: Dialysis Of Toxins Study (DOTS): "ATOM: DOTS Protocol: Master Version 1: June 2014: page 29- 35

Insert hospital letterhead here

Australian TOxicology Monitoring (ATOM) Study
Dialysis Of Toxins Study (DOTS)
Procedure

AIMS: To investigate the pharmacokinetics and pharmacodynamics of those drug overdoses that require extracorporeal elimination that is intermittent haemodialysis or continuous renal replacement therapy. In particular calculating drug half-life and clearance during the patient's treatment.

INCLUSION:

1/ Any ingestion requiring extracorporeal elimination either intermittent haemodialysis (IHD) or continuous renal replacement therapy (CRRRT).

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves access to the patients' medical records and collecting blood and urine samples at set time points. The patient or next of kin should be informed that extra blood and urine samples will be collected. The majority of these samples will be taken from the haemodialysis lines. These samples will be analysed for drug levels and metabolite levels. The patient will be de-identified.

METHOD:

STEP 1 - Obtain **consent** from the patient. Please ask them to sign **page 4** of the **"Subject Information and Consent form"** and then please fax this page to: **(02) 80160860.**

STEP 2 - Complete the **patient data form 1** and please fax the completed form to **(02) 80160860.**

STEP 3 - Research samples are to be collected in a **serum tube or tube required to measure drug level**. **Note** on all request forms **"Dialysis of Toxins Study (DOTS)"** – research sample. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

STEP 4 – **Patient data sheet 2** – to be completed by staff member completing dialysis. This sheet outlines samples to be collected.

BLOOD SAMPLE TIMING

Please collect 5mL serum samples for drug levels (note certain drugs may require coagulation tube to measure drug levels)

1/ Before commencement of renal replacement therapy:

A/ full blood count
B/ drug level
C/ urine sample (please note volume in data sheet)

2/ During renal replacement therapy: Collect samples as per data sheet 2. Please complete relevant sheet depending on mode of renal replacement therapy used.

3/ Post renal replacement therapy:

A/ collect drug level 4 hours after ceasing IHD and then as clinically indicated.
B/ urine sample (please note volume on data sheet)

If you have any questions please call Dr (insert name) on (insert phone number) or 1800 676 944. Please fax all forms to (02) 80160860

Australian TOxicology Monitoring (ATOM) Study

Dialysis Of Toxins Study (DOTS)

Insert hospital letterhead here

PATIENT DATA SHEET 1

PATIENT STICKER:	DATE AND TIME PRESENTED TO ED: CONSENT OBTAINED: YES / NO	
WEIGHT (KG): HEIGHT (CM):	PAST MEDICAL HISTORY:	
MEDICATIONS:	ACTIVATED CHARCOAL GIVEN: YES / NO DATE/ TIME: DOSE:	
DRUG INGESTED OR ETOH Patient certain of dose: YES / NO	AMOUNT	TIME INGESTED
DATE & TIME DECISION MADE TO COMMENCE IHD:		
VASCULAR CATHETER INSERTION DATE/TIME: SITE: TYPE OF CATHETER AND LENGTH:		

Please fax completed form to (02) 80160860

If you have any questions please call Dr (insert doctor) on (insert phone number)

Australian TOxicology Monitoring (ATOM) Study

Insert hospital letterhead here

Dialysis Of Toxins Study (DOTS)

Data Collection FORM 2 – INTERMITTENT HAEODIALYSIS

To be completed by nurse or doctor collecting samples

PATIENT STICKER:	DATE/TIME IHD COMMENCED:
TYPE OF HAEMODIALYSIS: HD / HF / HP	TYPE OF FILTER:
INTERUPTIONS TO HAEODIALYSIS: YES / NO TIME STOPPED: TIME RECOMMENCED:	REASON FOR INTERUPTION:

Blood samples and effluent samples to collect:

Blood samples: PRE- filter: arterial limb, POST – filter: venous limb (please collect in serum tube unless otherwise specified)

Effluent sample: please collect in urine specimen container at least 5mL

Time	Sample Type	Time collected	Blood flow rate IHD	Dialysate flow rate	UF rate
Time = 0h	PRE-filter (arterial limb)				
	POST-filter (venous limb)				
1 hour	Effluent sample				
2hours	PRE-filter				
	POST- filter				
3 hours	Effluent sample				
4 hours	PRE-filter				
	POST-filter				
5 hours	Effluent sample				

Urine samples:

Measure urine volume every hour and every second hour obtain a 5mL sample for drug levels (shaded)

Time: Start:						
Finish:						
Volume of urine						
Sample collected: Y/N						

Australian TOxicology Monitoring (ATOM) Study

Dialysis Of Toxins Study (DOTS)

Insert hospital letterhead here

Data Collection FORM 2 – CONTINOUS RENAL REPLACEMENT THERAPY

To be completed by nurse or doctor collecting samples

PATIENT STICKER:	DATE/TIME IHD COMMENCED:
TYPE OF RENAL REPLACEMENT THERAPY: PiRRT / CVVHD / CVVHDF / Other:	TYPE OF FILTER:
INTERUPTIONS TO HAEODIALYSIS: YES / NO TIME STOPPED: TIME RECOMMENCED:	REASON FOR INTERUPTION:

Blood samples and effluent samples to collect:

Blood samples: PRE- filter: arterial limb, POST – filter: venous limb (please collect in serum tube unless otherwise specified)

Time	Sample Type	Time collected	Blood flow rate IHD	Dialysate flow rate	UF rate
Time = 0h	PRE-filter (arterial limb)				
	POST-filter (venous limb)				
3 hours	PRE-filter				
	POST- filter				
6 hours	PRE-filter				
	POST-filter				
10 hours	PRE-filter				
	POST-filter				
14 hours	PRE-filter				
	POST-filter				
18 hours	PRE-filter				
	POST-filter				

CONTINUE NEXT PAGE DIALYSIS EFFLUENT and URINE SAMPLES

Australian TOxicology Monitoring (ATOM) Study

Dialysis Of Toxins Study (DOTS)

Insert hospital letterhead here

Data Collection FORM 2 – CONTINOUS RENAL REPLACEMENT THERAPY

Dialysis Effluent

Effluent samples: please collect in urine specimen container at least 5mL.
Please collect a sample from each effluent bag. Once effluent bag full, please note volume and collect a sample.

Time: Start:					
Finish:					
Volume of effluent					
Sample collected: Y/N					

Urine samples:

Measure urine volume every hour and every second hour obtain a 5mL sample for drug levels

Time: Start:						
Finish:						
Volume of urine						
Sample collected: Y/N						

Time: Start:						
Finish:						
Volume of urine						
Sample collected: Y/N						

Please fax completed form to (02) 80160860.
If you have any questions please call Dr (insert name) on (insert phone number)

Australian TOxicology Monitoring (ATOM) Study

Insert hospital letterhead here

Dialysis Of Toxins Study (DOTS)

Laboratory Protocol

Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum

Blood in plain or serum-separator (SST) tube

2000g for 10 min (3800-4000 rpm in a standard bench top centrifuge)

1.6-2mL aliquots of serum (in 2mL screw cap cryotubes if available)

Label each tube with **sample type** ("**Ser**"), **patient ID, date & time of collection**.

Keep samples from each collection time separate in a single specimen bag, along with a copy of the corresponding request form.

Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient and doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are **not discarded** without first discussing with a study coordinator (contact details at the bottom of this page).

3. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and coagulation). Please either fax to **(02) 80160860**

OR:

Post to: Dr Angela Chiew
Prince of Wales Hospital
Emergency Department
Barker Street, Randwick NSW 2031

If you have any questions please call Dr (Insert Doctors name) (principal investigator) on (**insert number**). IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160860

Australian TOxicology Monitoring (ATOM) Study

Insert hospital letterhead here

Dialysis Of Toxins Study (DOTS)

Laboratory Protocol

4. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:

"Dialysis Of Toxins Study (DOTS): **Study Hold for Dr Isbister"**

These samples are to be sent to:

NSW:

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service, John Hunter Hospital,
Lookout Road, New Lambton Heights, NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:

The aims of Dialysis Of Toxins Study (DOTS) is to investigate the pharmacokinetics and pharmacodynamics of those drug overdoses that require extracorporeal elimination. That is either intermittent haemodialysis or continuous renal replacement therapy. In particular calculating drug half-life and clearance during the patient's treatment. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call Dr (Insert Doctors name) (principal investigator) on (**insert number**). IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160860

Appendix 6: Cardiac Arrest & ToxinS: "ATOM: Cardiac Arrest & ToxinS (CATS): Protocol Master Version 1: 10th July 2015": page 36-39"

Insert Hospital Logo

Australian TOxicology Monitoring (ATOM) Study
Cardiac Arrest & ToxinS (CATS)

AIMS: to investigate the incidence of cardiac arrests suspected to be caused by poisonings.

INCLUSION:
1. Any patient presenting with a cardiac arrest or near arrest thought to be related to overdose or poisonings.

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves a structured audit of the types of overdose and outcomes of standard management – ECGs, clinical observation (pulse, BP), taking blood samples and documenting common clinical symptoms. These should be done on admission, 4 hours later and when clinically indicated until discharge.

METHOD:
STEP 1 - Obtain consent from the patient or relatives. Please ask them to sign page 4 of the "Subject Information and Consent form" and then please fax this page to: (02) 80160868 (or email to betty.chan@sesiahs.health.nsw.gov.au)
STEP 2 - For this study extra blood samples will be required to be collected with routine blood tests.
STEP 3 – Perform ECG at the time when blood samples are taken.
STEP 4 - Complete the patient data form and please fax the completed form to (02) 80160868 (or email to above address).
STEP 5 – Research samples are to be collected in a serum tube. Note on all request forms "CATS study" – research samples. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

ECG AND BLOOD SAMPLE TIMES:

Research samples to be collected are 5mL serum samples (SST)

ECG should be done on admission and when clinically indicated.
Please collect a serum tube for research purposes:
1) On admission,
2) 4 – 6 hours post admission bloods
3) As indicated for clinical monitoring.

If you have any questions please call Dr Betty Chan (principal investigator) on 0439 601 068 or IF THIS FAILS please call the ASP/ATOM study line on 0413 286 663 or 1800676944.
Fax number: (02) 80160868

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY **Patient Data Sheet #1 – Cardiac Arrest & ToxinS** **Cardiac Arrest & ToxinS (CATS)**	Insert Logo

PATIENT STICKER:	DATE AND TIME PRESENTED TO ED: CONSENT OBTAINED: YES NO
WEIGHT (KG): HEIGHT (CM):	Please circle: Route: Oral / Intravenous/Other

OVERDOSE MEDICATIONS (& AMOUNTS IF KNOWN)

DATE & TIME OF INGESTION (OR LIKELY TIME RANGE):

SYMPTOMS ON PRESENTATION: (PLEASE CIRCLE) PLEASE INCLUDE A COPY OF ECG WHEN FAXING DATA FORM.

CVS: Rhythm on presentation_____ GCS: _____

HR: BP: pH: Lactate: K: Cr:

Time of cardiac arrest:

Cardiac arrest rhythm: _____ Time to ROSC: _____

Final Outcome_____

REGULAR MEDICATIONS:	PAST MEDICAL HISTORY:

Treatment: (please circle)

IVF (Volume):

INTUBATION & VENTILATION: YES / NO

CHARCOAL: YES / NO, NUMBER OF DOSES (50 G):

INOTROPES: Adrenaline / Noradrenaline / Metaraminol / Others:

SPECIFIC ANTIDOTES & DOSES & APPARENT RESPONSE:

ECMO:

OTHERS:

Australian TOxicology Monitoring (ATOM) Study
Cardiac Arrest & ToxinS (CATS)
Laboratory Protocol

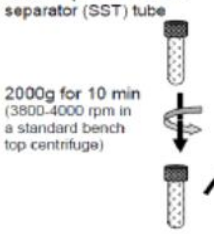
Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum

Blood in plain or serum-separator (SST) tube

2000g for 10 min (3800-4000 rpm in a standard bench top centrifuge)

1.6-2mL aliquots of serum (in 2mL screw cap cryotubes if available)



Label each tube with **sample type** ("**Ser**"), **patient ID**, **date & time of collection**.

Keep samples from each collection time separate in a single specimen bag, along with a copy of the corresponding request form.

Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and methotrexate levels). Please either **fax to (02) 80160868 or email to:** betty.chan@sesiahs.health.nsw.gov.au

3. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:
"CARDIAC ARREST & TOXINS: Study Hold for Dr Isbister"

These samples are to be sent to: **NSW:**

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service,
John Hunter Hospital,
Lookout Road, New Lambton Heights, NSW 2305
*PLACE IMMEDIATELY IN -80

PRINCE OF WALES HOSPITAL

Australian TOxicology Monitoring (ATOM) Study

Study Protocol

Background information about this study:

The Cardiac Arrest & Toxins (CATS) study aims to investigate whether the suspected overdose was the cause of the cardiac arrest and to have a better understanding of the epidemiology of overdoses resulting in cardiac arrest in Australia as well as identifying areas where we can improve in our management of these patients. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call Dr Betty Chan (principal investigator) on **0439 601 068** or **0413 286 663**. IF THIS FAILS please call the ASP/ATOM study line on 1800676944.
Fax number for sending laboratory results: (02) 80160868

Appendix 7: ATOM: Pregabalin Gabapentin Toxicity Project: Master Protocol: Version 1: 16th July 2015.: Page 40-42

Insert hospital logo

Australian TOxicology Monitoring (ATOM) Study
Pregabalin Gabapentin Toxicity Project (PGTP)

AIMS: to investigate the pharmacokinetics and dynamics of pregabalin and gabapentin in overdose.

INCLUSION:
1. Any patient presenting with a pregabalin poisoning.
2. Any patient presenting with a gabapentin poisoning.

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves a structured audit of the outcomes of standard management – ECGs, clinical observation (pulse, BP), taking blood samples and documenting common clinical symptoms. These should be done on admission, 1h, 2h, h, 6h, 8h, 12h, 16h 24h and then daily if possible and when clinically indicated until discharge.

METHOD:
STEP 1 - Obtain consent from the patient. Please ask them to sign page 4 of the "Subject Information and Consent form" and then please fax this page to: (02) 80160868 (or email to betty.chan@sesiahs.health.nsw.gov.au)
STEP 2 - For this study extra blood samples will be required to be collected with routine blood tests.
STEP 3 – Perform ECG at the time when blood samples are taken.
STEP 4 - Complete the patient data form and please fax the completed form to (02) 80160868 (or email to above address).
STEP 5 – Research samples are to be collected in a serum tube. Note on all request forms "PGTP study" – research samples. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

ECG AND BLOOD SAMPLE TIMES:
Research samples to be collected are 5mL serum samples (SST)

ECG should be done on admission and when clinically indicated.
Please collect a serum tube for research purposes:
1) On admission,
2) 1h, 2h, 4h, 6h, 8h, 12h, 16h 24h and then daily if possible.
3) As indicated for clinical monitoring.

Pregabalin Gabapentin Toxicity Project: Master Protocol: Version 1 : 16th July 2015. Page 1 of 3

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY
Patient Data Sheet #1 – Pregabalin Gabapentin Toxicity Project (PGTP)

Insert hospital logo

PATIENT DATA SHEET

PATIENT Sticker/Details:	Presentation to ED DATE: TIME:
	CONSENT OBTAINED: YES / NO
INGESTION details DATE: TIME:	Weight (KG): Height (CM):
Product (Circle): Pregabalin / Gabapentin DOSE ingested: Certain of Dose Ingested? (Circle): Yes / No	Usual medication: YES / NO Reason for use: Chronic pain / epilepsy / another person's medication INTENTIONAL / ACCIDENTAL ingestion (circle)
CO INGESTIONS : Alcohol: Before / With overdose	CHARCOAL GIVEN: YES / NO TIME and DOSE (eg 50g):

Clinical Effects:

CNS Effects: Min GCS_____ Description (alert, drowsy, unconscious)

G.I. effects:

Delirium: (presence of confusion, agitation, restlessness): YES/NO

Arrhythmia ☐ *Please include copy ECG with Fax*

Other (comments):

Blood Collection: Please collect as many of the samples below as possible.

Pregabalin has a short half-life (4.6 to 6.8 h), therefore timeframe for detection is brief. Suggest collecting in the first 24 hour period where possible – time 1h, 2h, 4h, 6h, 8h, 12h, 16h, 24h; thence daily.

Treatment:

Intubation/ventilation ☐ *Other (eg. Haemodialysis):*

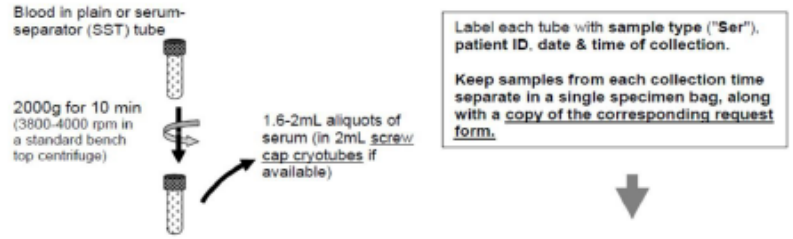
Please fax completed form to (02) 4911 0501 or email Dr Angela Chiew or Betty Chan (Investigators) at:
angela.chiew@sesiash.health.nsw.gov.au or betty.chan@sesiash.health.nsw.gov.au

Insert hospital logo

Australian TOxicology Monitoring (ATOM) Study
Pregabalin Gabapentin Toxicity Project (PGTP)

Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum



Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient and doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are **not discarded** without first discussing with a study coordinator (contact details at the bottom of this page).

3. Sample Transport

Samples should be kept in a single batch on patient discharge.

Please label these samples as:

"Pregabalin/Gabapentin Toxicity Project: Study Hold for Dr Chiew"

Background information about this study:

Pregabalin and gabapentin are commonly prescribed for epilepsy and, chronic and neuropathic pain in Australia. In view of very limited recent research pregabalin may display a potential for abuse among individuals with a history of chronic opiate intake. The Pregabalin Gabapentin Toxicity Project (PGTP) aims to therefore investigate the pharmacokinetics and dynamics of these two drugs in overdose. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call **Dr Betty Chan (Principal investigator) on 0439601068.**
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 4911 0501

Methotrexate Intoxication & Antidotes (MIA): "**Appendix 8:** MIA Protocol: Master Version 1: 10th July 2015." Page 43 – 46.

Insert Hospital Logo

Australian TOxicology Monitoring (ATOM) Study
Methotrexate Intoxication & Antidotes (MIA)

AIMS: to investigate the toxic effects and pharmacokinetics of methotrexate in acute or chronic poisonings.

INCLUSION:
1. Any patient presenting with an acute methotrexate poisoning.
2. Any patient presenting with a chronic methotrexate poisoning.

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves a structured audit of the outcomes of standard management – clinical observation (pulse, BP), taking blood samples and documenting common clinical symptoms and follow up with GP for follow up blood tests at 1 and 2 weeks post ingestion. Bloods should be done every 6 hours for 24 hours and when clinically indicated until discharge.

METHOD:
STEP 1 - Obtain consent from the patient. Please ask them to sign page 4 of the "Subject Information and Consent form" and then please fax this page to: (02) 80160868 (or email to betty.chan@sesiahs.health.nsw.gov.au)
STEP 2 - For this study extra blood samples will be required to be collected with routine blood tests.
STEP 3 - Complete the patient data form and please fax the completed form to (02) 80160868 (or email to above address).
STEP 4 – Research samples are to be collected in a serum tube. Note on all request forms "MIA study" – research samples. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

ECG AND BLOOD SAMPLE TIMES:
Research samples to be collected are 5mL serum samples (SST)

Please collect a serum tube for research purposes:
1) On admission,
2) Every 6 hours post admission bloods for 24 hrs
3) As indicated for clinical monitoring.

If you have any questions please call Dr Betty Chan (principal investigator) on 0439 601 068 or IF THIS FAILS please call the ASP/ATOM study line on 0413 286 663 or 1800676944.
Fax number: (02) 80160868

ATOM: MIA Protocol: Master Version 1: 10th July 2015 Page 1 of 4

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY

Patient Data Sheet #1 – Methotrexate Poisoning

Methotrexate Intoxication & Antidotes (MIA)

Insert hospital logo

PATIENT STICKER:	DATE AND TIME PRESENTED TO ED: CONSENT OBTAINED: YES NO
WEIGHT (KG): HEIGHT (CM):	Please circle: Route: Oral ACUTE / CHRONIC METHOTREXATE POISONING
CURRENT MEDICATIONS:	PAST MEDICAL HISTORY:
DOSE OF METHOTREXATE TAKEN: TIME OF INGESTION:	DOSE OF METHOTREXATE TAKEN WEEKLY: TIME OF LAST DOSE METHOTREXATE INGESTION:
SYMPTOMS ON PRESENTATION: (PLEASE CIRCLE) Haematology: Neutropenia (N =), Anaemia (Hb =), Thrombocytopenia (Platelet =). GIT: Stomatitis / Mucositis / Nausea / Vomiting / Abdominal pain CNS: Confusion / Delirium. Others: Renal failure / hepatitis / dyspnoea / dermatitis	
CO INGESTION :DRUG	AMOUNT / TIME INGESTED
Initial Cr: Time taken:	FOLINIC ACID: YES / NO. Time & date: DOSE OF FOLINIC ACID:
CHARCOAL: YES / NO. Time & Date:	GLUCARPIDASE: YES / NO. Time & date: DOSE OF GLUCARPIDASE:
Treatment: Haemodialysis: IHD / CVVHD / CVVHDF; Steroid type & dose: Others: GCSF /	

Australian TOxicology Monitoring (ATOM) Study
Methotrexate Intoxication & Antidotes (MIA)
Laboratory Protocol

1. Serum

Blood collection: Please take blood at baseline for FBC, EUC, liver function & methotrexate level. Methotrexate levels should be performed every 6 hours in the first 24 hours if possible. Repeat FBC & EUC at day 7 and 14.

Please send the serum samples collected for methotrexate levels to your referral hospital.

2. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and methotrexate levels). Please either **fax to (02) 80160868 or email to:** betty.chan@sesiahs.health.nsw.gov.au

Background information about this study:
The Methotrexate Intoxication & Antidotes (MIA) study aims to investigate acute methotrexate poisoning and its response to antidotes. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call Dr Betty Chan (principal investigator) on **0439601068**. IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160868

Insert hospital logo

Australian TOxicology Monitoring (ATOM) Study
Methotrexate Intoxication & Antidotes (MIA)

To Family Doctor,

This patient was admitted to _____ Hospital following an acute overdose of methotrexate on _____. He has agreed to be recruited into our methotrexate study to help us to have a better understanding of acute methotrexate poisoning.

I would appreciate if you can perform a FBC and EUC on day 7 and then 14 following the overdose to determine if there is any significant methotrexate related myelosuppresion.

Please send a copy of the pathology results to Dr Betty Chan by either email to betty.chan@sesiahs.health.nsw.gov.au or fax: 02-80160868. I can be contacted on mob: 0439601068 if you wish to discuss any matter regarding the methotrexate poisoning or the study.

If you have any further queries regarding this proposal, please do not hesitate to contact me.

Yours sincerely

Betty Chan
Head of Clinical Toxicology Unit.
Prince of Wales Hospital
MBBS, FACEM, PhD

Appendix 9: Sotalol, Propranolol, Atenolol, Metoprolol: "ATOM: SPAM Protocol Master Version 1: June 2016": page 47 – 50

Insert hospital logo

Australian TOxicology Monitoring (ATOM) Study

SPAM (Sotolol, Propranolol, Atenolol, Metoprolol)

AIMS: To investigate the pharmacokinetics & dynamics of beta-blockers in overdose. In particular the management of beta-blocker toxicity including the benefits & risks of inotropes & high dose insulin euglycaemia therapy (HIE).

INCLUSION:
1/ Any patient taking an intentional overdose of a beta-blocker
2/ Any patient taking an accidental overdose of a beta-blocker

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves using serum already collected & obtaining additional serum samples, while the patient is in hospital. Patients' will be informed that extra blood samples will be taken. At the most we will collect 4 extra blood samples per 24 hours. The majority of these samples will be taken with the patient's routine bloods. Hence there are minimal risks from this study, only that of collecting an extra blood sample. The patients will be de-identified. Samples are tested for drug levels. Once the study is completed the samples are destroyed. As a part of this study we will also be accessing the patient's medical records. This study will allow us to better understand the toxicity of beta-blockers in overdose.

METHOD:

STEP 1 - Obtain **consent** from the patient. Please ask them to sign **page 4** of the **"Subject Information & Consent form"** & then please fax this page to: **(02) 80160860.**
STEP 2 - Complete the patient data form & please fax the completed form to **(02) 80160860**
STEP 3 - Research samples are to be collected in a **serum tube. Note** on all request forms **"SPAM"** – research sample. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

ECG & BLOOD SAMPLE TIMES:

Research samples to be collected are 5mL serum samples (SST)
ECG should be done on admission & when clinically indicated.
Blood collection: Please collect as many of the samples below as possible:
Suggest collecting in the first 24-hour period where possible – on admission, 2h, 4h, 6h, 12h, 18h, 24h & then 6 hourly while in Intensive Care or High Dependency Unit. Then daily after 3 days.

Any questions please call Dr Colin Page on 0404044732 or 1800 676 944.
Please fax all forms to (02) 80160860

ATOM: SPAM Protocol: Master Version 1 June 2016 1

Study Protocol

Insert hospital logo	Australian TOxicology Monitoring (ATOM) Study Sotolol, Propranolol, Atenolol & Metoprolol (SPAM) Patient Data Sheet
PRESENTATION TO HOSPITAL: **DATE:** **TIME:**	**Patient Sticker/Details:**
CONSENT OBTAINED: Yes / No	
INGESTION DETAILS **DATE:** **TIME:**	**WEIGHT:** **HEIGHT:**
DRUG, DOSE & NUMBER INGESTED:	**USUAL MEDICATION:** Yes / No **INDICATION:** e.g. Hypertension **INTENTIONAL / ACCIDENTAL**
CO INGESTIONS: Drugs or Alcohol	**CHARCOAL GIVEN:** Yes / No **TIME & DOSE:**
CLINICAL EFFECTS: **Minimum GCS:** **Seizures:** Yes / No **Minimum pulse:** **Minimum blood pressure:** **Arrhythmia:** Yes / No Please include ECG **Other end organ toxicity** e.g. renal impairment/ Please specify.	
MANAGEMENT: **INTUBATION/VENTILATION:** Yes / No **INOTROPES:** Yes / No **If yes, which inotropes & maximum dose used** **High Dose Insulin Euglycaemia (HIE):** Yes / No **If yes, maximum dose insulin used & duration** **OTHER TREATMENTS: e.g. Calcium, atropine, glucagon**	

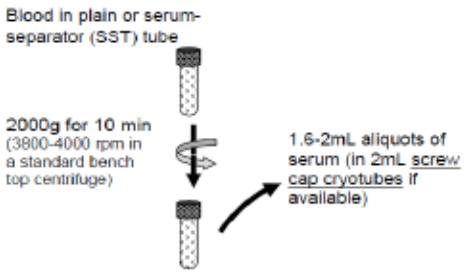
Please fax completed form to (02) 80160860 or scan & email to cpage@bigpond.net.au. If you have any questions, please call Dr Colin Page on 0404044732 or 1800676944

ATOM: SPAM Protocol: Master Version 1 June 2016 2

Australian TOxicology Monitoring (ATOM) Study
SPAM Laboratory Protocol

Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum



Label each tube with **sample type** ("**Ser**"), **patient ID, date & time of collection.**

Keep samples from each collection time separate in a single specimen bag, along with a copy of the corresponding request form.

Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient & doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are not discarded without first discussing with a study coordinator (contact details at the bottom of this page).

3. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology & coagulation).
Please either fax to (02) 80160860

OR :

Post to: Dr Colin Page
Emergency Department
Princess Alexandra Hospital
Ipswich Road
Woolloongabba QLD 4102

If you have any questions please call **Dr Colin Page (QLD) on 0404044732.**
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160860

ATOM: SPAM Protocol: Master Version 1 June 2016 3

Australian TOxicology Monitoring (ATOM) Study
Australian Paracetamol Project
Laboratory Protocol

4. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:

"SPAM ATOM STUDY: Study Hold for Dr Isbister (NSW) or Dr Goce Dimeski (QLD)"

These samples are to be sent to:

FOR NSW SAMPLES

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service, John Hunter Hospital,
Lookout Road, New Lambton Heights, NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

FOR QLD SAMPLES

For Dr Goce Dimeski
Chief Scientist
c/o Chemical Pathology
Princess Alexandra Hospital
Woolloongabba
QLD 4102
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:

The SPAM study aims to investigate the pharmacokinetics & dynamics of beta-blockers in overdose. In particular we want to examine the benefits & risks of various management options in beta-blocker toxicity. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call **Dr Colin Page (QLD) on 0404044732.**
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160860

Appendix 10: VAlproate Toxicity Study (VATS): "ATOM: VAT Protocol Master Version 1: 20th June 2016": page 51 - 55

Insert hospital logo

Australian TOxicology Monitoring (ATOM) Study

VAlproate Toxicity Study (VATS)

Procedure

AIMS: to investigate the pharmacokinetic and dynamics of Valproate in acute and chronic toxicity

INCLUSION:

1/ Any patient presenting with an acute immediate or extended release Valproate poisoning (accidental or intentional)

2/ Any patients presenting with suspected chronic Valproate toxicity including patients on therapeutic Valproate with:

i. Decreased level of consciousness not adequately explained by other pathology and/or

ii. Raised ammonia levels

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves a structured audit of the outcomes of standard management including ECGs, clinical observation (heart rate, blood pressure, Glasgow coma score), taking blood samples, and documenting clinical symptoms. Collection of blood samples for EUC, LFT, FBC, Ammonia, Valproate levels and Venous Blood Gas (VBG) should be collected on admission, 2h, 6h, 12h, 18h, 24h then twice daily or more frequently if clinically indicated.

METHOD:

STEP 1 - Obtain consent from the patient. Please ask them to sign page 4 of the "Subject Information and Consent form" and then please fax this page to: (02) 80160868 (or email to kylieprncardle@gmail.com)

STEP 2 - For this study extra blood samples will be required to be collected. Consider inserting an extra cannula to collect blood samples to avoid repeated venipuncture.

STEP 3 - Complete the patient data form and please fax the completed form to (02) 80160868 (or email to above address).

STEP 4 - Research samples are to be collected in a serum tube. Note on all request forms "VATS" – research samples. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

BLOOD SAMPLE TIMES:

Research samples to be collected are 5mL serum samples (SST)

Please collect a serum tube for research purposes at these times:

a) On admission

b) 2h, 6h, 12h, 18h, 24h and then twice daily if possible

c) As indicated for clinical monitoring

If you have any questions please call Dr Kylie McArdle (principal investigator) on **0425256578**.
IF THIS FAILS please call the ASP study line on 1800676944.
Please fax completed forms to (02) 80160868

ATOM: VATS Protocol Master Version 1: 20th June 2016. Page 1 of 5

Insert hospital logo	AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY VAlproate Toxicity Study (VATS) Patient Data Sheet #1 – Valproate Toxicity

PATIENT STICKER:	DATE AND TIME PRESENTED TO ED: CONSENT OBTAINED: YES / NO	
WEIGHT (KG): HEIGHT (CM):	CHARCOAL GIVEN: YES / NO TIME AND DOSE:	
CURRENT MEDICATIONS:	PAST MEDICAL HISTORY:	
ACUTE INGESTION: Yes / No SLOW RELEASE PREPARATION: Yes / No DOSE OF VALPROATE TAKEN: TIME OF INGESTION: CERTAIN OF DOSE INGESTED (Circle): Yes / No	CHRONIC THERAPEUTIC USE: Yes / No INDICATION: Epilepsy / Chronic Pain / Mood Disorder SLOW RELEASE PREPARATION: Yes / No DOSE OF VALPROATE TAKEN DAILY: TIME OF LAST DOSE VALPROATE INGESTION:	
CO INGESTION: DRUG	AMOUNT:	TIME INGESTED:
SYMPTOMS ON PRESENTATION: (PLEASE CIRCLE) CNS: Decreased level of consciousness / Confusion / Delirium / Seizures / Ataxia / Visual disturbances CVS: QT prolongation / Hypotension / Tachycardia / Other: GIT: Nausea / Vomiting / Abdominal pain Metabolic: Hypernatreamia / Acidosis / Hyperlactateamia / Hypoglyceamia HEAM: Thrombocytopeania / Neutropeania		
MANAGEMENT: Intubation: YES / NO ICU or HDU Admission: YES / NO CT BRAIN: YES / NO RENAL REPLACEMENT THERAPY: YES / NO	OTHER THERAPIES ADMINISTERED: L-Carnitine: Other:	

Study Protocol

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY

Patient Data Sheet #2 – Valproate Toxicity

VAlproate Toxicity Study (VATS)

Insert hospital logo

Time (indicative times given but write actual times)	Blood Sample/ VBG	HR	BP	Level of Coma (Awake or GCS)	CNS or Abdominal symptoms	Other Comments (Other treatments given and patient response)
Baseline *						
1hr						
2hr						
6hr						
12hr						
18hr						
24hr						

Initial Valproate level: Time taken:	Initial Ammonia level: Time taken:
Initial Platelets: Time Taken:	Initial VBG: pH PCO2 PO2 HCO3- BE Lactate

If you have any questions please call Dr Kylie McArdle (principal investigator) on **0425256578**.
IF THIS FAILS please call the ASP study line on 1800676944.
Please fax completed forms to (02) 80160868

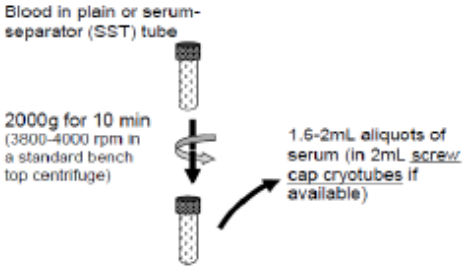
Australian TOxicology Monitoring (ATOM) Study

VAlproate Toxicity Study (VATS)

Laboratory Protocol

Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum



Label each tube with **sample type ("Ser"), patient ID, date & time of collection.**

Keep samples from each collection time separate in a single specimen bag, along with a copy of the corresponding request form.

Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient and doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are **not discarded** without first discussing with a study coordinator (contact details at the bottom of this page).

3. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and coagulation). Please either fax to **(02) 80160868**

OR:

Post to: Dr Kylie McArdle
Department of Clinical Toxicology and Pharmacology
Calvary Mater Hospital Newcastle
Locker Mail Bag 7
Hunter Region Male Centre NSW 2310

If you have any questions please call Dr Kylie McArdle (principal investigator) on **0425256578**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160868

Australian TOxicology Monitoring (ATOM) Study

VAlproate Toxicity Study (VATS)

Laboratory Protocol

4. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:

"Valproate Toxicity Study (VATS): Study Hold for Dr Isbister(NSW) or Dr Goce Dimeski (QLD)""

These samples are to be sent to:

NSW:

FOR NSW SAMPLES

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service, John Hunter Hospital,
Lookout Road, New Lambton Heights,
NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

QLD:

FOR QLD SAMPLES

For Dr Goce Dimeski
Chief Scientist
c/o Chemical Pathology
Princess Alexandra Hospital
Woolloongabba
QLD 4102
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:
The aim of this study is to investigate the pharmacokinetic and pharmacodynamics of Valproate in acute and chronic toxicity. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call Dr Kylie McArdle (principal investigator) on **0425256578**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160868

Appendix 11: LIPID study: "ATOM: LIPID Protocol: Version 1 June 2016": page 56 - 59

Please insert hospital	**Australian TOxicology Monitoring (ATOM) Study** **LIPID Study**

AIMS: To investigate the effect of Intralipid on drug levels in overdose. This will involve any drug overdose in which Intralipid has been given as part of the patient's management. In particular, we will determine drug levels prior to Intralipid and after to determine the effectiveness of Intralipid in the management of acute poisoning.

INCLUSION:
1/ Any patient who has taken an intentional overdose and has Intralipid as part of their treatment
2/ Any patient who has taken an accidental overdose and has Intralipid as part of their treatment

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves using serum already collected & obtaining additional serum samples, while the patient is in hospital. Patients' or their relative will be informed that extra blood samples will be taken. At the most we will collect 2 extra blood samples per 24 hours. The majority of these samples will be taken with the patient's routine bloods. Hence there are minimal risks from this study, only that of collecting an extra blood sample. The patients will be de-identified. Samples are tested for drug levels. As a part of this study we will also be accessing the patient's medical records. This study will allow us to better understand the use of Intralipid in managing overdoses.

METHOD:

STEP 1 - Obtain consent from the patient. Please ask them to sign page 4 of the "Subject Information & Consent form" & then please fax this page to: **(02) 8016 0860.**
STEP 2 - Complete the patient data form & please fax the completed form to **(02) 8016 0860**
STEP 3 - Research samples are to be collected in a serum tube. Note on all request forms "ATOM: LIPID" – research sample. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

ECG & BLOOD SAMPLE TIMES:
Research samples to be collected are 5mL serum samples (SST)
ECGs should be done on admission & when clinically indicated.
Blood collection: Please collect as many of the samples below as possible:
1/ On admission (pre intralipid)
2/ Immediately post intralipid bolus
3/ 1 hr post intralipid bolus

4/ As clinically indicated

If there are any questions please call Dr Therese Becker on 0400 338 786
Please fax all forms to (02) 80160860

ATOM: LIPID Protocol: Version 1 June 2016 1

Study Protocol

Australian TOxicology Monitoring (ATOM) Study Patient Data Sheet – LIPID Study	
PRESENTATION TO HOSPITAL: DATE: TIME:	Patient Sticker/Details:
CONSENT OBTAINED: Yes / No	
INGESTION DETAILS DATE: TIME:	WEIGHT: HEIGHT:
DRUG, DOSE & NUMBER INGESTED:	USUAL MEDICATION: Yes / No INDICATION: e.g. Hypertension INTENTIONAL / ACCIDENTAL
CO INGESTIONS: Drugs or Alcohol	CHARCOAL GIVEN: Yes / No TIME & DOSE:
CLINICAL EFFECTS: Minimum GCS: Seizures: Yes / No Minimum pulse: Minimum blood pressure: Arrhythmia: Yes / No Please include ECG Other end organ toxicity e.g. renal impairment/ Please specify.	
MANAGEMENT: INTRALIPID: Time and dose INTUBATION/VENTILATION: Yes / No INOTROPES: Yes / No If yes, which inotropes & maximum dose used High Dose Insulin Euglycaemia (HIE): Yes / No If yes, maximum dose insulin used & duration OTHER TREATMENTS: e.g. Calcium, atropire, glucagon	

Please fax completed form to (02) 8016 0860 or scan & email to therese.becker@health.nsw.gov.au

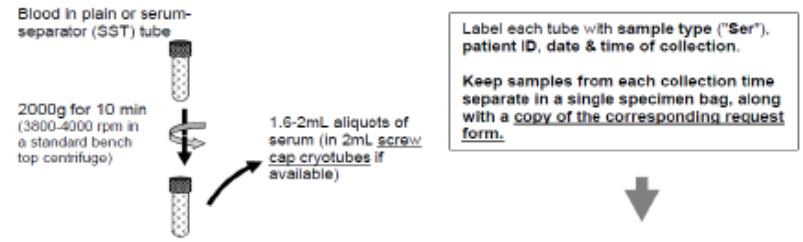
If you have any questions, please call Dr Therese Becker on 0400338786

Australian TOxicology Monitoring (ATOM) Study: LIPID Study

Laboratory Protocol

Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum



Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient & doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are not discarded without first discussing with a study coordinator (contact details at the bottom of this page).

3. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology & coagulation). Please either fax to (02)80160860

OR :

Post to: Dr Therese Becker
Emergency Department
Prince of Wales Hospital
Barker Street
RANDWICK 2031

If you have any questions please call **Dr Therese Becker 0400 338 786**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160860

ATOM: LIPID Protocol: Version 1 June 2016 3

Australian TOxicology Monitoring (ATOM) Study

LIPID Project

Laboratory Protocol

4. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:

"LIPID ATOM STUDY: Study Hold for Dr Isbister (NSW) or Dr Goce Dimeski (QLD)"

These samples are to be sent to:

FOR NSW SAMPLES

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service, John Hunter Hospital,
Lookout Road, New Lambton Heights, NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

FOR QLD SAMPLES

For Dr Goce Dimeski
Chief Scientist
c/o Chemical Pathology
Princess Alexandra Hospital
Woolloongabba
QLD 4102
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:

The LIPID study aims to investigate the use of Intralipid in overdose and determine its effectiveness. In particular we will determine drug levels in overdose prior to Intralipid and after to determine exactly how Intralipid affects drug levels. If you have any questions or queries, please do not hesitate to contact us on the numbers provided below.

If you have any questions please call **Dr Therese Becker 0400 338 786**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160860

Appendix 12: Herbicide Intoxication & Pharmacokinetic (HIP) study: "ATOM: HIP Protocol: Version 1: 21st June 2016": page 60 – 63

Insert hospital logo

Australian TOxicology Monitoring (ATOM) Study
Herbicide Intoxication & Pharmacokinetic (HIP) Study
Procedure

AIMS: to investigate the clinical course and outcomes of patients who ingestion herbicides

INCLUSION:

1/ Any patient presenting with an acute ingestion of a herbicide such as MCPA, Bromoxynil, Glyphosate or Paraquat.

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves using serum already collected & obtaining additional serum samples, while the patient is in hospital. Patients' will be informed that extra blood samples will be taken. At the most we will collect 2 extra blood samples per 24 hours. The majority of these samples will be taken with the patient's routine bloods. Hence there are minimal risks from this study, only that of collecting an extra blood sample. The patients will be de-identified. Samples are tested for drug levels. Once the study is completed the samples are destroyed. As a part of this study we will also be accessing the patient's medical records. This study will allow us to better understand the toxicity of herbicides when ingested.

METHOD:

STEP 1 - Obtain consent from the patient or their relative if too unwell. Please ask them to sign page 4 of the "Subject Information and Consent form" and then please fax this page to: (02) 80160860 (or email to Angela.Chiew@health.nsw.gov.au)

STEP 2 - For this study extra blood samples will be required to be collected.

STEP 3 - Complete the patient data form and please fax the completed form to (02) 80160860 (or email: Angela.Chiew@health.nsw.gov.au).

STEP 4 - Research samples are to be collected in a serum tube. Note on all request forms "ATOM: HIT" – research samples. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

BLOOD SAMPLE TIMES:

Research samples to be collected are 5mL serum samples (SST)

Please collect a serum tube for research purposes at these times:

a) On admission

b) 4 h after presentation

c) As indicated for clinical monitoring. If the patient requires dialysis a researcher will discuss with you further samples and the Dialysis Of Toxins Study (DOTS): protocol

If you have any questions, please call Dr Angela Chiew (principal investigator) on **0412575580**
IF THIS FAILS please call the ASP study line on 1800676944.
Please fax completed forms to (02) 80160860

ATOM: HI Protocol Master Version 1: 21st June 2016. Page 1 of 4

Study Protocol

Insert hospital logo	AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY Patient Data Sheet: Herbicide Intoxication & Pharmacokinetic (HIP) Study

PATIENT STICKER:	DATE AND TIME PRESENTED TO ED: CONSENT OBTAINED: YES / NO	
WEIGHT (KG): HEIGHT (CM):	CHARCOAL GIVEN: YES / NO TIME AND DOSE:	
CURRENT MEDICATIONS:	PAST MEDICAL HISTORY:	
Name of herbicide ingested (brand name): Active ingredients and concentration in product: Amount ingested:		
CO INGESTIONS: DRUG	AMOUNT:	TIME INGESTED:
SYMPTOMS ON PRESENTATION: (PLEASE CIRCLE) MOUTH: erythema/ ulcers/ swelling GIT: Nausea / Vomiting / Abdominal pain CNS: Decreased level of consciousness/ Confusion / Delirium / Seizures / Ataxia / Visual disturbances CVS: Hypotension / Tachycardia / Other: Metabolic: Acidosis / Hyperlactatemia / Hypoglycemia Resp: Tachypnoea/ hypoxia		
MANAGEMENT: Intubation: YES / NO ICU or HDU Admission: YES / NO Dialysis: YES / NO	OTHER THERAPIES ADMINISTERED: Inotropes required: Other:	

PLEASE FAX COMPLETED DATA SHEET TO 0280160860

ATOM: HI Protocol Master Version 1: 21st June 2016. Page 2 of 4

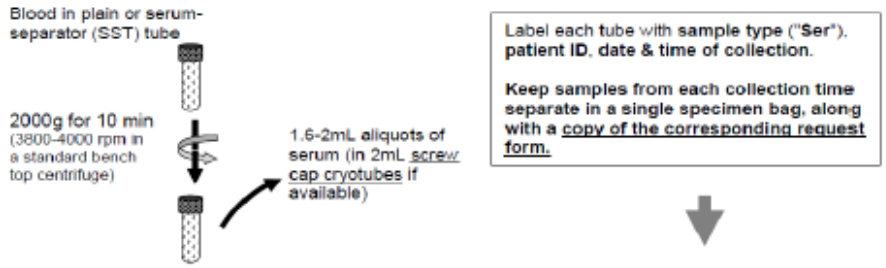
Australian TOxicology Monitoring (ATOM) Study

Herbicide Intoxication & Pharmacokinetic (HIP) Study

Laboratory Protocol

Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum



Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient and doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are **not discarded** without first discussing with a study coordinator (contact details at the bottom of this page).

3. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and coagulation). Please either fax to **(02) 80160860**

OR:

Post to:
Post to: Dr Angela Chiew
Prince of Wales Hospital
Emergency Department
Barker Street, Randwick NSW 2031

If you have any questions, please call Dr Angela Chiew (principal investigator) on **0412575580**
IF THIS FAILS please call the ASP study line on 1800676944.
Please fax completed forms to (02) 80160860

Australian TOxicology Monitoring (ATOM) Study

Herbicide Intoxication & Pharmacokinetic (HIP) Study

Laboratory Protocol

4. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:

"Herbicide Intoxication & Pharmacokinetic (HIP) Study: Hold for Dr Isbister(NSW) or Dr Goce Dimeski (QLD)""

These samples are to be sent to:

NSW:

FOR NSW SAMPLES

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service, John Hunter Hospital,
Lookout Road, New Lambton Heights, NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

QLD:

FOR QLD SAMPLES

For Dr Goce Dimeski
Chief Scientist
c/o Chemical Pathology
Princess Alexandra Hospital
Woolloongabba
QLD 4102
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:

The aim of this study is to investigate the pharmacokinetic and pharmacodynamics of herbicides following an acute ingestion. In particular, looking at the clinical outcomes and comparing this to blood concentrations. If you have any questions or queries, please do not hesitate to contact us on the numbers provided below.

If you have any questions, please call Dr Angela Chiew (principal investigator) on **0412575580**
IF THIS FAILS please call the ASP study line on 1800676944.
Please fax completed forms to (02) 80160860

Appendix 13: MEtformin TOXicity study (METOX): "ATOM: METOX Protocol Master Version 1: 21st June 2016" page 64 – 68

Insert hospital logo

Australian TOxicology Monitoring (ATOM) Study
MEtformin TOxicity study (METOX)
Procedure

AIMS: to investigate the pharmacokinetics and dynamics of Metformin in acute and chronic toxicity

INCLUSION:

1. Any patient presenting with an acute Metformin ingestion (accidental or intentional)

EXCLUSION: Age < 14 years

WHAT IS INVOLVED: This study involves a structured audit of the outcomes of standard management including, clinical observation (heart rate, blood pressure, Glasgow coma score), taking blood samples, taking urine samples (or effluent samples if undergoing renal replacement therapy) and documenting clinical symptoms.

Collection of blood samples for blood gas (arterial or venous), lactate, blood sugar levels (BSL), and EUC should be collected on admission, 2h, 6h, 12h, 18h, 24h. Patients NOT admitted to ICU or HDU would then have twice daily blood sample collection for these specified tests, or more frequently if clinically indicated. Patients admitted to ICU or HDU would have 6h blood sample collection for blood gas, metformin level, and blood sugar level, and 12h blood sample collection for EUC, or more frequently if required. An additional serum sample tube (SST) will also be collected at EACH of these times as the "research sample" for evaluation of Metformin drug levels. Collection of urine samples for metformin levels should ideally be collected at 0h, 12h, 24h then twice daily at time of blood collection. Patients on renal replacement therapy will have additional circuit blood and effluent samples taken for measurement of Metformin and lactate levels.

METHOD:

STEP 1: Obtain **consent** from the patient. Please ask them to sign **page 4** of the **"Subject Information and Consent form"** and then please fax this page to: **(02) 80160868** (or email to **kyliepmcardle@gmail.com)**

STEP 2: Complete the **patient data sheet** 1 and please fax completed form to (02) 80160868 or email to above address

STEP 3: For this study extra blood and urine samples will be required to be collected. Consider inserting an extra cannula to collect blood samples to avoid repeated venipuncture. Research blood samples are to be collected in a **serum tube. Note** on all request forms **"METOX"** – research samples. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

STEP 4: Research urine samples are to be collected in **urine specimen containers**. Note on all request forms **"METOX"** research samples.

STEP 5: Complete the **patient data sheet 2** for the first 24hrs of clinical observation and patient sampling.

STEP 6: If patient requires renal replacement therapy the investigators will provide you with additional protocol and patient data sheets. (Please call investigators on number below)

STEP 8: All completed data sheets to be faxed or emailed to the above contacts on patient discharge.

If you have any questions please call Dr Kylie McArdle (principal investigator) on **0425256578**. IF THIS FAILS please call the ASP study line on 1800676944. Please fax ALL forms to **(02) 80160868 or email to kyliepmcardle@gmail.com**

ATOM: METOX Protocol Master Version 1: 21st June 2016. Page 1 of 5

Study Protocol

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY: MEtformin TOXicity study (METOX)

Insert hospital logo

PATIENT DATA SHEET #1 – INGESTION INFORMATION

PATIENT STICKER:	**DATE AND TIME PRESENTED TO ED:** **CONSENT OBTAINED: YES / NO**	
WEIGHT (KG): **HEIGHT (CM):**	**CHARCOAL GIVEN: YES / NO** **TIME AND DOSE:**	
CURRENT MEDICATIONS:	**PAST MEDICAL HISTORY:**	
ACUTE INGESTION: Yes / No **EXTENDED RELEASE PREPARATION:** Yes / No **DOSE TAKEN:** **TIME OF INGESTION:** **CERTAIN OF DOSE INGESTED (Circle):** Yes / No **COMBINATION MEDICATION:** Yes / No **OWN MEDICATION:** Yes / No	**THERAPEUTIC USE:** Yes / No **INDICATION:** Diabetes /Polycystic Ovarian Syndrome/Other **EXTENDED RELEASE PREPARATION:** Yes / No **DOSE METFORMIN TAKEN DAILY:** **FREQUENCY OF DOSING:** **BASELINE CREATININE (if known):**	
COINGESTION OR CONCURRENT :DRUG	**AMOUNT:**	**TIME INGESTED:**

SYMPTOMS ON PRESENTATION: (PLEASE CIRCLE)

CVS: Hypotension / Tachycardia / Cardiac Arrest / Other:

GIT: Nausea / Vomiting / Abdominal pain

Metabolic: Acidosis (pH <7.35) / Hyperlactatemia (Lactate >2mmol/L) / Hypoglycemia (BSL <3.5mmol/L)

CNS: Decreased level of consciousness/ Confusion / Delirium / Agitation

OTHER:

If you have any questions please call Dr Kylie McArdle (principal investigator) on **0425256578**. IF THIS FAILS please call the ASP study line on 1800676944. Please fax ALL forms to **(02) 80160868 or email to kyliepmcardle@gmail.com**

Study Protocol

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY: MEtformin TOXicity study (METOX) PATIENT DATA SHEET #2 – SCHEDULE OF BLOOD AND URINE SAMPLES	Insert hospital logo

PATIENT STICKER	Please note confirmation of blood and urine sampling on the table below together with basic clinical parameters at the time of sampling. **BSL not required separately if recorded as part of blood gas*

BLOOD SAMPLING PROCEDURE AND TIMES

Please undertake the following blood tests at the specified times to be completed at the admitting hospital. Please collect an additional 5ml into a serum sample tube (SST) for the "Research sample" and note on the request form "METOX research sample". Please send the attached Laboratory protocol with the sample and request form.

- 0h, 2h, 6h, 12h, 24h (or more frequently if clinically indicated): Blood gas (including Lactate), BSL*, Research Sample (METOX Study), EUC
- After 24h and NOT admitted to HDU/ICU: twice daily EUC, blood gas (including lactate), BSL*, Research Sample (METOX study)
- After 24hr and admitted to HDU/ICU:6h EUC, blood gas (incl lactate), BSL, Research sample (METOX study)
- If on renal replacement therapy additional serum samples will be required: see data sheet #4

URINE SAMPLING PROCEDURE AND TIMES

Please collect urine sample for research purposes at the following times. Research samples to be collected are 5mls urine into a urine specimen container, and note on the request form "METOX research sample".

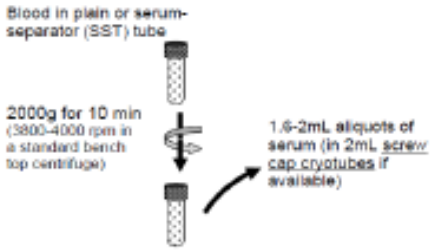
- 0h, 12h, 24h
- After 24h and NOT admitted to HDU/ICU: twice daily if possible
- After 24h and admitted to HDU/ICU : 6h corresponding with blood sampling times if possible
- If on renal replacement therapy additional effluent samples will be required: see data sheet #4

Time (write actual times)	Blood Sample	Urine Sample	HR	BP	Awake or GCS	Abdominal symptoms	Other Comments / Treatments
0hr							
2hr							
6hr							
12hr							
18hr							
24hr							
30h (ICU ONLY)							
36h							
42h (ICU ONLY)							
48h							
54h (ICU ONLY)							
60h							

Australian TOxicology Monitoring (ATOM) Study
MEtformin TOXicity study (METOX)
Laboratory Protocol

Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum



Label each tube with **sample type ("Ser"), patient ID, date & time of collection.**

Keep samples from each collection time separate in a single specimen bag, along with a copy of the corresponding request form.

Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient and doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are **not discarded** without first discussing with a study coordinator (contact details at the bottom of this page).

3. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology and coagulation).
Please either fax to **(02) 80160868**

OR:

Post to: Dr Kylie McArdle
Department of Clinical Toxicology and Pharmacology
Calvary Mater Hospital Newcastle
Locker Mail Bag 7
Hunter Region Male Centre NSW 2310

If you have any questions please call Dr Kylie McArdle (principal investigator) on **0425256578**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160868

Australian TOxicology Monitoring (ATOM) Study
MEtformin TOXicity study (METOX)
Laboratory Protocol

4. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:

"MEtformin TOXicity study (METOX): Study Hold for Dr Isbister or Dr Goce Dimeski (QLD)"

These samples are to be sent to:

NSW:

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service, John Hunter Hospital,
Lookout Road, New Lambton Heights,
NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

QLD:

For Dr Goce Dimeski
Chief Scientist

c/o Chemical Pathology
Princess Alexandra Hospital
Woolloongabba
QLD 4102
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:
The aim of this study is to investigate the pharmacokinetic and pharmacodynamics of Metformin in acute and chronic toxicity. If you have any questions or queries please do not hesitate to contact us on the numbers provided below.

If you have any questions please call Dr Kylie McArdle (principal investigator) on **0425256578**.
IF THIS FAILS please call the ASP study line on **1800676944**.
Fax number for sending laboratory results: (02) 80160868

Appendix 14: MEtformin TOXicity study (METOX): " METOX Supplementary Protocol Master Version 1: 21st June 2016" page 69 – 71

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY: MEtformin TOXicity study (METOX)

Insert hospital logo

SUPPLEMENTAL PATIENT DATA SHEET: CONTINUOUS RENAL REPLACEMENT THERAPY [CRRT]

PATIENT STICKER:	**DATE/TIME IHD COMMENCED:**
TYPE OF RENAL REPLACEMENT THERAPY: **PiRRT / CVVHD / CVVHDF / SLED** **Other:**	**TYPE OF FILTER:**
INTERUPTIONS TO HAEODIALYSIS: YES / NO **TIME STOPPED:** **TIME RECOMMENCED:**	**REASON FOR INTERUPTION:**
ANTICOAGULATION USED: **Heparin / Citrate / Other:**	**VASCATH:** **Site:** **Gauge:** **Length:**

BLOOD SAMPLES TO COLLECT:

Blood samples: Please collect 5ml in serum sample tube and mark pathology form with **"Research sample: METOX" and the source of the sample (PRE-arterial or POST-venous filter)**

Effluent sample: please collect in urine specimen container at least 5mL and mark pathology form with **"Research sample: METOX" and the source of the sample (IHD Effluent)**

Time	Sample Type	Time collected	Blood flow rate IHD	Dialysate flow rate	UF rate
Time = 0h	PRE-filter (arterial limb)				
	POST-filter (venous limb)				
3 hours	PRE-filter				
	POST- filter				
6 hours	PRE-filter				
	POST-filter				
10 hours	PRE-filter				
	POST-filter				
14 hours	PRE-filter				
	POST-filter				
18 hours	PRE-filter				
	POST-filter				

CONTINUE NEXT PAGE: DIALYSIS EFFLUENT and URINE SAMPLES

If you have any questions please call Dr Kylie McArdle (principal investigator) on **0425256578**. IF THIS FAILS please call the ASP study line on 1800676944. Please fax ALL forms to **(02) 80160868 or email to kyliepmcardle@gmail.com**

ATOM: METOX Supplementary Protocol Master Version 1: 21st June 2016.

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY: MEtformin TOXicity study (METOX)

SUPPLEMENTAL PATIENT DATA SHEET: CONTINUOUS RENAL REPLACEMENT THERAPY [CRRT]

Insert hospital logo

DIALYSIS EFFLUENT SAMPLES

Effluent sample: please collect in urine specimen container at least 5mL and mark pathology form with **"Research sample: METOX" and the source of the sample (IHD Effluent)**

Please collect a sample from each effluent bag. Once effluent bag full, please note volume and collect a sample.

Time: Start:					
Finish:					
Volume of effluent					
Sample collected: Y/N					

URINE SAMPLES:

Urine samples: please collect in urine specimen container at least 5mL and mark pathology form with **"Research sample: METOX"**

Measure urine volume every hour and every second hour obtain a 5mL sample for drug levels if possible

Time: Start:						
Finish:						
Volume of urine						
Sample collected: Y/N						

Time: Start:						
Finish:						
Volume of urine						
Sample collected: Y/N						

If you have any questions please call Dr Kylie McArdle (principal investigator) on **0425256578**. IF THIS FAILS please call the ASP study line on 1800676944. Please fax ALL forms to **(02) 80160868 or email to kyliepmcardle@gmail.com**

ATOM: METOX Supplementary Protocol Master Version 1: 21st June 2016.

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY: MEtformin TOXicity study (METOX)

SUPPLEMENTAL PATIENT DATA SHEET: INTERMITTANT HAEMODIALYSIS

Insert hospital logo

To be completed by nurse or doctor collecting samples

PATIENT STICKER:	DATE/TIME IHD COMMENCED:
TYPE OF HAEMODIALYSIS: HD / HF / HP	TYPE OF FILTER:
INTERUPTIONS TO HAEODIALYSIS: YES / NO TIME STOPPED: TIME RECOMMENCED:	REASON FOR INTERUPTION:

BLOOD AND EFFLUENT SAMPLES TO COLLECT:

Blood samples: Please collect 5ml in serum sample tube and mark pathology form with "Research sample: METOX" and the source of the sample (PRE or POST filter)

Effluent sample: please collect in urine specimen container at least 5mL and mark pathology form with "Research sample: METOX" and the source of the sample (IHD Effluent)

Time	Sample Type	Time collected	Blood flow rate IHD	Dialysate flow rate	UF rate
Time = 0h	PRE-filter (arterial limb)				
	POST-filter (venous limb)				
1 hour	Effluent sample				
2hours	PRE-filter				
	POST- filter				
3 hours	Effluent sample				
4 hours	PRE-filter				
	POST-filter				
5 hours	Effluent sample				

URINE SAMPLES FOR COLLECTION:

Measure urine volume every hour and every second hour obtain a 5mL sample for drug levels (shaded) if possible.

Time: Start:						
Finish:						
Volume of urine						
Sample collected: Y/N						

If you have any questions please call Dr Kylie McArdle (principal investigator) on 0425256578. IF THIS FAILS please call the ASP study line on 1800676944. Please fax ALL forms to (02) 80160868 or email to kyliepmcardle@gmail.com

ATOM: METOX Supplementary Protocol Master Version 1: 21st June 2016.

Appendix 15: ATOM: SODA Protocol: CHW Version 1: 10TH March 2017 page 72 - 75

Please insert hospital

Australian TOxicology Monitoring (ATOM) Study

SODium Channel Blockers & BicArbonate (SODA)

AIMS: To investigate the effect of sodium bicarbonate as an antidote in sodium channel blocker poisoning. This will include any drug overdose that shows evidence of cardiac sodium channel blockade on the ECG where the patient receives sodium bicarbonate as part of their management. We will aim to determine the effectiveness, dose and format (bolus versus infusion) of sodium bicarbonate in shortening the QRS, managing cardiac arrhythmias and improving haemodynamic status. This study will allow us to better understand the use of sodium bicarbonate in treating severe sodium channel blockade in overdose.

INCLUSION:

1/ Any patient who has taken an intentional overdose of a sodium channel blocker and has evidence of sodium channel blockade on the ECG (ie QRS > 110 ms) and receives sodium bicarbonate as part of their management

2/ Any patient who has taken an accidental overdose of a sodium channel blocker and has evidence of sodium channel blockade on the ECG (ie QRS > 110 ms) and receives sodium bicarbonate as part of their management

EXCLUSION: Age < 14 year

WHAT IS INVOLVED

A retrospective and prospective study will be undertaken of patients who are have taken a sodium channel blocker overdose.

This study involves using serum already collected & obtaining additional serum samples, while the patient is in hospital. In particular drug levels prior to sodium bicarbonate and after will be measured. Patients' or their relative will be informed that extra blood samples will be taken. At the most we will collect 4 extra blood samples per 24 hours. The majority of these samples will be taken with the patient's routine bloods. Hence there are minimal risks from this study, only that of collecting an extra blood sample. The patients will be de-identified. Samples are tested for drug levels (therefore the drugs taken must be known). Once the study is completed the samples are destroyed.

METHOD:

STEP 1 - Obtain consent from the patient. Please ask them to sign page 4 of the "Subject Information & Consent form" & then please fax this page to: (02) 8016 0860.

STEP 2 - Complete the patient data form & please fax the completed form to (02) 8016 0860

STEP 3 - Research samples are to be collected in a serum tube. Note on all request forms

"ATOM: SODA" – research sample. Please send the "Laboratory Protocol" to your pathology laboratory with the first research serum sample collected.

ECG & BLOOD SAMPLE TIMES:

Research samples to be collected are 5mL serum samples (SST)

ECG should be done on admission & after each bolus of sodium bicarbonate and if any change in clinical status

Blood collection: Please collect as many of the samples below as possible:

1/ On admission (pre sodium bicarbonate)

2/ Immediately post bicarbonate bolus

3/ 1 hr post sodium bicarbonate bolus

4/ 4hr post bicarbonate bolus

5/ As clinically indicated

If there are any questions please call Dr Therese Becker on 0400 338 786

Please fax all forms to (02) 80160860

ATOM: SODA Protocol: CHW Version 1: 10TH March 2017 Page 1 of 4

AUSTRALIAN TOXICOLOGICAL MONITORING (ATOM) STUDY

Patient Data Sheet #1 –

SODium Channel Blockers & BicArbonate Study (SODA)

NSW poisons Information Centre the children's hospital at Westmead

PATIENT STICKER: MRN DOB HOSPITAL	DATE AND TIME PRESENTED TO ED: CONSENT OBTAINED: YES NO
WEIGHT (KG): HEIGHT (CM):	Drug/s ingested and Dose:
REGULAR MEDICATIONS:	PAST MEDICAL HISTORY:

SYMPTOMS ON PRESENTATION: (PLEASE CIRCLE) PLEASE INCLUDE A COPY OF ECG WHEN FAXING DATA FORM.

CVS: Cardiac rhythm: Sinus / Junctional / Complete heart block

GCS: HR: BP: pH: Lactate: Cr:

CNS: Confusion / Delirium / Coma / seizure

Others: Renal failure / hepatitis / dyspnoea

Treatment: (please circle) SODIUM BICARBONATE: BOLUS: YES / NO

Number of doses and timing:

INFUSION: YES / NO Date & Duration:

INTUBATION & VENTILATION: YES / NO

Ventilator Settings:

Mode: RR: TV Pressure support

CHARCOAL: YES / NO, NUMBER OF DOSES and timing (50 G):

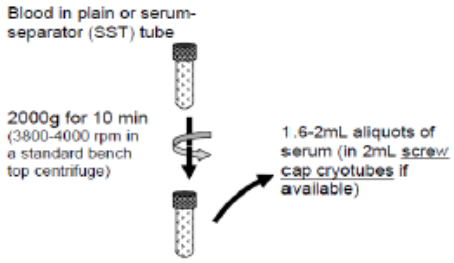
INOTROPES: adrenaline / Noradrenaline / Metaraminol /Vasopressin / HIET (doses)

Australian TOxicology Monitoring (ATOM) Study: SODA Study

Laboratory Protocol

Please send this information sheet to your pathology laboratory with the first serum research sample collected.

1. Serum



Label each tube with **sample type ("Ser"), patient ID, date & time of collection.**

Keep samples from each collection time separate in a single specimen bag, along with a copy of the corresponding request form.

Freeze as soon as possible and transport in dry ice (or other suitable frozen transport) to -80°C storage. **NOTE: please freeze all available (earlier) left-over samples, even if they have been left unfrozen for several days, noting the date and time of freezing on the request forms.**

2. Left over serum/ plasma from earlier time points

The most important samples are the first ones taken, when the patient & doctor may not be aware of the study. Even if these samples have not been processed according to the procedures above, we can obtain important information from them. Therefore, please ensure that samples from this patient are **not discarded** without first discussing with a study coordinator (contact details at the bottom of this page).

3. Results from your lab

If time permits we would appreciate copies of all results (biochemistry, haematology & coagulation).
Please either fax to **(02) 80160860**

OR :

Post to: Dr Therese Becker
Emergency Department
Prince of Wales Hospital
Barker Street
RANDWICK 2031

If you have any questions please call **Dr Therese Becker 0400 338 786**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160860

Australian TOxicology Monitoring (ATOM) Study

SODA Project

Laboratory Protocol

4. Sample Transport

Samples should be sent in a single batch on patient discharge.

Please label these samples as:

"SODA ATOM STUDY: Study Hold for Dr Isbister (NSW) or Dr Goce Dimeski (QLD)"

These samples are to be sent to:

FOR NSW SAMPLES

For Dr Geoff Isbister

Specimen Reception,
Hunter Area Pathology Service, John Hunter Hospital,
Lookout Road, New Lambton Heights, NSW 2305
PLACE IMMEDIATELY IN -80 FREEZER

FOR QLD SAMPLES

For Dr Goce Dimeski
Chief Scientist
c/o Chemical Pathology
Princess Alexandra Hospital
Woolloongabba
QLD 4102
PLACE IMMEDIATELY IN -80 FREEZER

Background information about this study:

- The Sodium channel blockers and bicarbonate study (SODA) aims to identify patients who have taken a sodium channel blocker overdose and have been treated with sodium bicarbonate.
- We would like to determine the effectiveness, dose and format (bolus versus infusion) of sodium bicarbonate in terms of shortening QRS prolongation, managing cardiac arrhythmia or improve haemodynamic status.
- A prospective and retrospective study will be undertaken of patients who are have taken a sodium channel blocker overdose.
- The following data will be collected
  - Initial ECG, observations, blood gas
  - Doses and timing of sodium bicarbonate given
  - Other interventions : eg intubation and ventilation (including ventilator settings),dialysis, other antidotes, charcoal
  - Subsequent ECG's, observations, blood gases and EUC post sodium bicarbonate
  - Serum drug levels where appropriate

If you have any questions please call **Dr Therese Becker 0400 338 786**.
IF THIS FAILS please call the ASP study line on 1800676944.
Fax number for sending laboratory results: (02) 80160860