Pharmacy File
Site Pharmacy Manual
Dexamethasone 2mg/5ml Oral Solution or Matching Placebo

PHARMACY MANUAL

DRAFT Version 1.7 08-Apr-2014

NOTE: The ASAP trial will remain in a state of hibernation until the UK next encounters a flu pandemic and thus this Pharmacy Manual will remain in draft until the trial is activated. **An updated final version of this Pharmacy Manual will be sent to sites prior to commencement of recruitment.**

Trial Title:	Adjuvant Steroids in Adults with Pandemic Influenza (ASAP)	**EudraCT No:**	2013-001051-12
Investigational Medicinal Product (IMP):	Dexamethasone 2mg/5ml oral solution or matching placebo (75ml bottle)		
Sponsor:	Nottingham University Hospitals NHS Trust		
Co-ordinating Centre:	Nottingham Clinical Trials Unit (NCTU) ☎ 0115 884 4952 (Trial Manager: Clare Brittain) ✉ asap@nottingham.ac.uk		
Chief Investigator	Dr Wei Shen Lim, Nottingham University Hospitals NHS Trust		

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1. Pharmacy Responsibilities

The pharmacy responsibilities for the ASAP trial are as follows:

- Receive IMP from manufacturing unit(s) supplying IMP
- Confirm receipt of IMP using online stock control system
- Store the IMP until distribution to pandemic flu admission points is required
- Maintain storage records (i.e. location, temperature, excursions) whilst IMP is in Pharmacy
- Distribute IMP to pandemic flu admission point(s) as agreed with the Principal Investigator and in accordance with the local Trust's Pandemic Influenza Plan
- Complete/maintain IMP Inventory Log detailing which Participant Packs have been distributed to which admission points within the hospital
- Receive back any unused Participant Packs (retain until authorised by Nottingham Clinical Trials Unit (NCTU) to destroy)
- Complete/maintain IMP Destruction Log
- Destroy any empty/part-used bottles returned to Pharmacy
- File completed Participant Registration Cards in the Pharmacy File

This Pharmacy Manual should be read in conjunction with the current approved trial protocol.

1.1. Pharmacy File

A Pharmacy File must be constructed and maintained for the ASAP Trial. Trial sites may construct their own Pharmacy File in accordance with their local format however this **must** include the following documents:

- Trial Protocol
- This Pharmacy Manual
- Simplified IMPD for the labelling and packaging of the IMP
- SmPC for Dexsol (dexamethasone)
- Patient Information Leaflet
- MHRA Approval letters (including approval for any amendments)
- REC Approval letters (including approval for any amendments)
- IMP Inventory Log*
- Completed Participant Registration Postcards – these should be returned to pharmacy after completion at the flu admission points and will serve as the Patient Accountability Log
- Example prescription
- IMP Destruction Log*
- Correspondence with Coordinating Centre and site
- Record of any unblinding performed
- Temperature records whilst IMP is stored in Pharmacy
- Training material/training logs
- QP release documentations
- Pharmacy Delegation Log

*Logs are provided by NCTU and must be used. However sites are permitted to use their own logs providing all information requested on the NCTU log is captured.

If any of the above documents are stored in a separate location to the Pharmacy File, a File Note specifying the location of the document(s) must be added to the Pharmacy File.

Please contact the Trial Manager at NCTU if you require copies of any of the above documents.

Once the Pharmacy File has been constructed with the above documents please fax the completed 'ASAP Pharmacy File Confirmation' document to the Trial Manager.

1.2. Delegation Log

A designated pharmacist must be named as the Responsible Pharmacist for the trial at each site. During the hibernation phase of the trial the Responsible Pharmacist should sign the delegation log. A copy of this should be sent to the Trial Manager.

Please ensure that the Trial Manager is informed if the details of the Responsible Pharmacist change and forward a copy of the updated delegation log.

Upon activation of the trial, all staff involved in the following activities will be required to complete a short online trial training package:

- Use of online stock control system
- Prescription validation
- Completion of IMP Inventory Log
- Completion of IMP Destruction Log

Once the training package has been completed, pharmacy staff responsible for the receipt, storage, distribution and destruction of study medication should be added to the delegation log and sign to confirm that they have completed the online training.

The Principal Investigator is responsible for maintaining an oversight of the delegation of activities.

1.3. Training Log

At the point of trial activation, training will be delivered using online training resources. All training must be recorded; further information on the recoding of training will be added at the point of trial activation.

2 Site Details

2.1 Principal Investigator

Name and contact details of the Principal Investigator at site will be added here prior to trial activation.

2.2 Sponsor

Nottingham University Hospital NHS Trust.

2.3 Co-ordinating Centre

Nottingham Clinical Trials Unit (NCTU)
☎ 0115 884 4952
✉ asap@nottingham.ac.uk

2.4 Location of participants

Randomisation takes place and the first dose (Day 1) of the IMP is given at the Pandemic Flu Admission Point(s) within the hospital according to the Trust's Pandemic Flu Plan.

The remaining doses (Days 2 to 5) are given on ward / Intensive Care Unit (ICU) / at home.

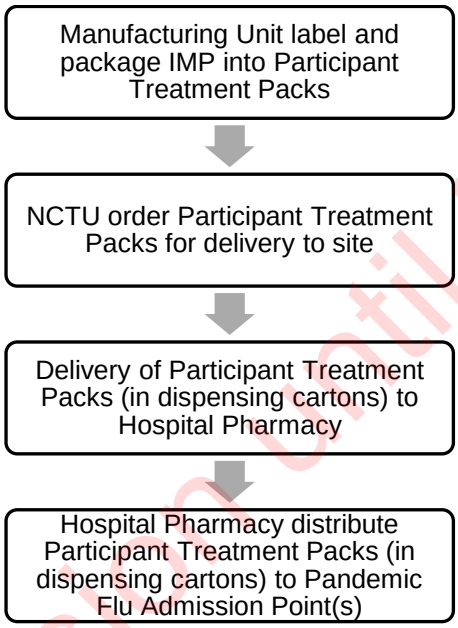
2.5 Location of IMP(s)

IMP will only be delivered to the site once the trial has been activated and recruitment is about to commence.

The IMP forms part of a Participant Treatment Pack that will be delivered (packaged into dispensing cartons) to Pharmacy.

Dispensing cartons (each containing 6 Participant Treatment Packs) will be issued from Pharmacy to the Admissions Point(s) where patient recruitment will occur. Participant Treatment Packs will be dispensed to the trial participants by a nurse or doctor upon randomisation.

Participant Packs should transfer with the Participant to the ward / ITU and/or with the patient home for the duration of the 5 days treatment.



3 Storage, handling & management of IMP

3.1. Description of IMP

Dexamethasone 2mg/5ml Oral Solution (Dexsol Manufacturing Authorisation: PL 00427/0137) 1 x 75ml and matching placebo.

Manufacturing units have been set up to overlabel the bottles of dexamethasone and placebo with a blackout label to completely cover and obscure the original label and package the IMP

The secondary pack (Participant Treatment Pack) is clear plastic and packed in such a way that the bottle label can be read through the pack. Therefore the secondary pack will remain unlabelled.

The Participant Treatment Packs are assembled in numerical order into cardboard tertiary dispensing cartons. Each dispensing carton contains 6 Participant Treatment Packs. These dispensing cartons

are designed to be issued complete to the Admissions Point(s) at the hospital. Pictures of the Participant Pack (and contents) and the cardboard dispensing carton can be found in Appendix A.

Each Participant Treatment Pack contains:

- 75ml bottle of Dexamethasone Oral solution 2mg/5ml or matching placebo.
- 'Instructions for taking your medicine at home' leaflet
- 5ml spoon
- ASAP Trial Wristband

In addition, the outside of the Participant Treatment Pack has the following attached:

- Prescription Label (see section 3.9 below for information on using this label)
- Participant Registration Postcard (see Appendix B). This is completed by the clinical staff dispensing the IMP at the Admission Point and will be used to register trial participants on the online trial system.

Each participant will receive a single bottle of IMP packed into a Participant Treatment Pack. Every bottle has a unique Participant Identification Number assigned to it.

3.2. Storage conditions of IMP

Storage conditions of the IMP are described on the IMP label as follows:

'**Store below 30°C. Do not refrigerate or freeze'**

No temperature monitoring of the IMP is required at the Admission Point(s). This is detailed in the simplified-IMPD which has been approved by the MHRA as part of the clinical trial authorisation.

The tertiary cardboard dispensing cartons provide light protection. The Participant Treatment Packs must not be stored out of the tertiary dispensing carton. Participant Treatment Packs should only be removed from the dispensing carton once a participant has given consent to participate in the trial. This should be done at the Admission Point(s).

IMP should be stored in the Pharmacy until it is required at the Admission Point(s). Temperature monitoring of the IMP in the pharmacy should be according to local procedures. Any deviations (i.e. outside the temperature range 8-30°C) should be reported to the NCTU. It is expected that any temperature monitoring records will be held centrally by Pharmacy and access granted upon request.

All correspondence relating to temperature deviations should be filed in the Pharmacy File.

3.3. Storage space requirements

The IMP will not be delivered to Pharmacy until the trial and the site have been activated.

The approximate dimensions of the tertiary dispensing carton (containing 6 Participant Packs) is 12.5cm (width) x 33cm (height) x 6cm (depth). See also Appendix A for a picture of the carton.

It is anticipated that the maximum size of any single delivery of IMP will be 8 x Tertiary Dispensing Cartons.

3.4. Source of IMP

Rosemont Pharmaceuticals Ltd (Yorkdale Industrial Park, Braithwaite Street, Leeds, Yorkshire, LS11 9XE) will manufacture the Dexamethasone 2mg/5ml Oral Solution (Dexsol Manufacturing Authorisation: PL 00427/0137) and the matching placebo.

Manufacturing units have been set up to receive the active and placebo supplies from Rosemont and overlabel and package the IMP.

The supply of IMP will then be delivered to study sites from one of these manufacturing units.

QP certification will be retained by the sponsor and made available to study sites electronically. Details will be provide at point of trial activation.

Supplies will be ordered by Nottingham CTU following liaison with the site research team.

3.5. Cost of IMP

IMP is supplied free of charge.

3.6. Delivery and receipt of goods

NCTU will provide confirmation of site activation status once all pre-activation checks have been completed.

An initial delivery of IMP will be sent to the site once the trial has been activated. The quantity of IMP to be delivered will only be determined once the trial has been activated and details of the pandemic are known.

Receipt of the IMP at site must be confirmed using the online stock control system. Only those set up with a site user login can access the system for confirming the receipt of the IMP. This will be granted by the NCTU.

A link to and instructions for using the online stock control system will be added here once the trial has been activated.

The IMP should also be added to the IMP Inventory Log. See section 3.7.

3.7. Accountability

An IMP Inventory Log is supplied for recording the IMP received in Pharmacy and the distribution of the IMP from Pharmacy to the Admission Point(s).

Individual Participant Treatment Pack usage is recorded on the ASAP Participant Registration Card (see Appendix B) attached to the Participant Treatment Pack.
The following process is in place for the ASAP Participant Registration Card:

- The ASAP Participant Registration Card is completed at the point of dispensing by a member of the clinical team at the Admission Point(s).
- The completed Participant Registration Card is posted in the ASAP Letterbox at the Admission Point(s).
- Participant Registration Cards are collected daily by the ASAP Data Clerk/Research Nurse and the data from the card is entered onto an online Registration System.

Completed Participant Registration Cards will then be sent by the ASAP Data Clark/Research Nurse to Pharmacy as a record of accountability and filed in the Site Pharmacy File.

3.8. Obtaining further supplies

Local procedures should be in place for assessing stock levels at the Admission Point(s). Staff at Admission Point(s) should notify Pharmacy when stock is running low and re-supply from the Pharmacy is required.

NCTU will manage stock levels at sites and reorder stock according to site recruitment. Sites will be informed that IMP has been ordered and the site will be advised of the delivery date.

Any requests for further stock should be made to the NCTU.

If required, NCTU will arrange for further stock to be delivered from the manufacturing unit.

3.9. Prescribing

The following label (sticker) is attached to the outside of the Participant Treatment Pack. It may be used as an example of the prescription requirement (for the prescription card) or removed and attached to the Treatment Card according to local practice.

The Participant ID number should be added to the label. This can be found on the label on the IMP bottle in the Participant Treatment Pack.

ASAP **Prescribing**	**A S A P Trial Participant ID No: _____** **Dexamethasone/placebo** **6mg in 15ml for 5 days**		Time / Date	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5
			0800					
	Route: **oral**	**Day 1 give ANYTIME** **Day 2 to Day 5 give AM**						
	Signature:							
	Print Name:							

The Participant Pack contains a 'Instructions for taking your medicine at home' leaflet and a 5ml spoon. Additional copies of the leaflet will be supplied to the Pharmacy to use in case the packed leaflet is misplaced.

3.10. Dispensing

Dispensing of the Participant Treatment Pack is done by the nurse or doctor at the Admission Point(s).

The clinical staff at the Admission Point(s) will receive trial training and will be instructed to complete the Patient Registration Card and also add Participant Name and Dispensing Date on the IMP bottle label at the time this is issued to the participant.

3.11. Post-trial arrangement for IMP

After completion of the study medication (total 5 days), if patients subsequently require steroid treatment as part of standard care, it may be prescribed in the usual manner.

3.12. Returned IMP

Any empty or part used bottles may be disposed of immediately as there is no requirement for participant level accountability to be performed.

Any unused Participant Treatment Packs should be returned to Pharmacy from the Admission(s) Points. Unused packs returned to pharmacy should be recorded in the 'Comments' column on the IMP Inventory Log adjacent to the appropriate Participant ID number. Permission must be sought from NCTU for the disposal of unused Participant Treatment Packs (see section 3.13).

3.13. Disposal of IMP

Permission to dispose of unused Participant Packs must be sought from the NCTU. Unused Participant Packs should be retained until permission is given by the NCTU for them to be disposed of.

Once approval for disposal has been received from NCTU, unused packs should be disposed of at site according to local Trust Procedures. An IMP Destruction Log is supplied and should be used for recording the disposal of any IMP.

Note: sites may use their own Destruction Log if it will improve the local running of the trial, however this must contain all of the information requested on the Destruction Log supplied by NCTU.

4 Unblinding of treatment code

Unblinding will be performed centrally. Details of the procedure will be provided to sites at Trial activation.

A record of any unblinding should be maintained in the Pharmacy File.

5 Monitoring and Ausit

Monitoring and/or audit visits may take place throughout the study, therefore please ensure all documentation and records are kept up to date at all times. Should a visit be required, the Trial Manager will contact the site in advance to arrange this.

6 Archiving

The site is responsible for archiving of site-specific documents. The ASAP Trial Pharmacy File should be archived along with the essential trial documentation. This should be securely retained for a least 5 years after the end of the trial. Participating sites will be sent a letter specifying the permissible disposal date. If local policy is to archive the Pharmacy File in a separate location to the Investigator Site File (ISF), the location of the Pharmacy File must be documented in the ISF. Instructions for retrieval of the Pharmacy File should also be included, where applicable.

Appendix A - IMP Packaging – DRAFT PACKAGING ONLY

The tertiary cardboard dispensing carton is shown in Figure 1. This contains 6 Participant Treatment Packs and will be placed at the Admission Point(s) where the IMP will be dispensed to participants.

Figure 1: Tertiary dispensing carton for IMP

An example Participant Treatment Pack is shown in Figure 2.

Figure 2: Participant Pack

Appendix B - Participant Registration Card

The below Participant Registration Card is attached to the outside of the Participant Treatment Pack and will be completed at point of dispensing medication to trial participant.

ASAP ADJUVANT STEROIDS IN ADULTS WITH PANDEMIC INFLUENZA

PARTICIPANT REGISTRATION CARD

Complete ALL information below

Participant's Trial ID: *(found on bottle label)* | | | | | |

Participant's name:	
Date of birth:	
Gender:	
Hospital ID: *NHS or hospital no.*	
Type of consent: *Tick one box only*	Participant ☐ or Clinician ☐
Medicine issued by: *Add initials only*	_____
Issue date: _____	Time:*(24hr)*: _____

FOR RESEARCH STAFF USE ONLY

Participant registered on database? ☐ *Tick box*

Initials: _____ *Add initials only*

Registration Card DRAFT 10-Mar-2014