Intrathecal Chemotherapy: Pharmacy Cytotoxic Production Procedure

1. PROCEDURE INTENT/OVERVIEW

This procedure provides instructions for the Intrathecal Chemotherapy Authorised Production Personnel to safely check, prepare, store and release intrathecal chemotherapy.

2. SCOPE

Intrathecal Chemotherapy Authorised Production Pharmacists and Pharmacy Assistants / Pharmacy Technicians.

3. PROCEDURE DETAIL

3.1 Intrathecal Prescription Verification.

The Intrathecal Chemotherapy Authorised Production Pharmacist must verify the following:

3.1.1 Intrathecal medication has been prescribed by an Intrathecal Chemotherapy Authorised Doctor who is listed on the Intrathecal Register.

3.1.2 Intrathecal chemotherapy has been prescribed on the appropriate pre-printed or electronic intrathecal prescription chart and there are NO handwritten alterations. N.B. Handwritten prescriptions will not be accepted.

3.1.3 Intrathecal chemotherapy prescribed complies with the chemotherapy protocol i.e. the correct chemotherapy medication has been prescribed at the correct dose on the correct day. Prescribed medication is appropriate for intrathecal administration i.e. methotrexate, cytarabine or hydrocortisone.

3.1.4 Doses of intrathecal chemotherapy must be standardised as per the protocol to minimise the risk of handwritten amendments occurring

3.1.5 The following intrathecal doses have been approved for use:

- Cytarabine 100mg when prescribed as a single agent
- Cytarabine 40mg when prescribed in combination with intrathecal methotrexate
- Methotrexate 12 mg, 12.5 mg or 15mg (according to relevant protocol).
- Hydrocortisone 50mg

3.1.6 Intrathecal Chemotherapy Authorised Clinical Pharmacist has reviewed and verified the prescription.

3.1.7 The time and location of administration have been planned according to policy:

- Intrathecal preparations should ONLY be administered within normal working hours i.e. 09:00 to 17:00 hrs Monday to Friday in preapproved locations for the administration of intrathecal chemotherapy.
- Preparations should be made as close as possible to the time required as the preparations are preservative free and route of administration is high risk.

3.1.8 Correct patient, correct medication, correct dose, correct concentration of medication, correct time, and correct route.

3.2 Product Segregation – to be maintained during the entire production process

The Intrathecal Chemotherapy Authorised Production Pharmacist must:

3.2.1 Ensure every effort has been made not to prescribe other parenteral chemotherapy on the same day as intrathecal chemotherapy. If this cannot be avoided then seek advice given below under '3.11 Release of Intrathecal Chemotherapy'.

3.2.2 Ensure that intrathecal preparations are kept separate from all other cytotoxic preparations during assembly, preparation, labelling, storage and supply.

3.2.3 Ensure storage is in designated intrathecal chemotherapy containers and no other products are packed in the same container.

3.2.4 Ensure all vinca alkaloids i.e. vincristine, vinblastine and vinorelbine are dispensed in a 50-100 mL sodium chloride 0.9% minibag and labelled 'For Intravenous Use Only. Fatal if given by any other route', to minimise the risk of the inadvertent intrathecal administration.

3.3 Batch Sheets and Labels

The Intrathecal Chemotherapy Authorised Pharmacy person will enter patient details in dispensing software and ensure:

3.3.1 An approved intrathecal product is selected (e.g. methotrexate, cytarabine, hydrocortisone)

3.3.2 Where there are multiple concentrations for intrathecal use the Intrathecal Chemotherapy Authorised Production Pharmacist must confirm that the correct concentration has been selected.

- The correct dose has been entered into the dispensing software
- The vial(s) with the correct concentration, and preservative free have been selected
- Batch sheet is pre-approved and printed on yellow paper (N.B: preparations for other routes are printed on white paper)
- The appropriate numbers of labels have been generated for the required product(s).

3.4 Pre-assembly Checks

On the scheduled day of administration, the patient platelet count must be above 50 x 10^9/L. If the platelet count is below 50 x 10^9/L the Intrathecal Chemotherapy Authorised Production Pharmacist must liaise with the Intrathecal Chemotherapy Authorised Clinical Pharmacist prior to proceeding.

At Royal Adelaide Hospital (RAH) Pharmacy preparation may occur before scheduled day of administration.

The intrathecal injections will NOT be released before the day of administration. The Intrathecal Authorised Production Pharmacist will check the patient's platelet count on the scheduled day of administration as above.

3.4.1 **Product segregation must occur** by ensuring that preparation of all other chemotherapy has stopped prior to proceeding with preparation of intrathecal doses.

3.4.2 Pre-approved intrathecal batch sheet is correct.

3.4.3 Ensure: correct patient, correct medication, correct dose, and correct concentration of medication, correct time, and correct route as per the pre-printed or electronic intrathecal prescription. Ensure correct syringe (luer slip).

3.4.4 Pre-approved batch sheet is printed on a yellow paper.

3.4.5 Check label details: **Patient Name, UR Number, Intrathecal Medication, Dose, Location** against both the batch sheet and the original approved prescription and ensure correct **volume, expiry and intrathecal route** are clearly marked on the label.

3.5 Assembly and Checks

Intrathecal Chemotherapy Authorised Production Pharmacist/Assistant/Technician assembles stock in accordance with the batch sheet.

The following items to be assembled in a tub reserved for intrathecal preparations:

3.5.1 The medication (e.g. methotrexate, cytarabine or hydrocortisone) must be:

- preservative free and suitable for intrathecal use
- the correct concentration as per approved batch sheet
- within expiry date (batch number and expiry information are recorded on the batch sheet)
- Suitable sized syringe with a luer slip tip
- 18 G or 21 G needle (as per site practice)
- Syringe cap

Independent check of volume and medication concentration by an Intrathecal Chemotherapy Authorised Production Pharmacist or Technician

3.5.2 The Intrathecal Chemotherapy Authorised Production Pharmacist to reconfirm the assembled items with the batch sheet:

- the batch sheet is pre-approved
- the calculation of medication dose is correct
- the medication is suitable for intrathecal use (Appendix 1) and in date
- the correct materials are assembled (medication, slip syringe and syringe cap)

3.5.3 All checked items to be wiped or sprayed with sterile alcohol 70% and replaced into a designated tub ‘for intrathecal use only’. The checked tub is then passed into the clean room.

3.6 Preparation

3.6.1 In the clean room the Intrathecal Chemotherapy Authorised Production Pharmacist/Technician/Assistant will firstly perform an independent check as below before preparing the intrathecal syringe(s) as per the procedure for preparation of chemotherapy in syringes.

- An independent check of the batch sheet:
  - to confirm concentration and calculation of volume
- An independent check of assembled materials
  - Correct syringe size and luer-slip tip
  - Correct medication, ensuring correct concentration, suitable for intrathecal use (Appendix 1) and in-date
  - Correct syringe cap and needles

3.6.2 The Intrathecal Chemotherapy Authorised Production Operator will mark the prepared syringe with a drug name **(methotrexte, cytarabine or hydrocortisone**), route **(intrathecal) and drug dose** on the outside of the syringe and place the product in the designated tub for intrathecal use and pass out through the hatch.

- At TQEH the Intrathecal Chemotherapy Authorised Production Operator will send out the vials used for the preparation in a sealed bag to allow the Intrathecal Chemotherapy Authorised Production Pharmacist to perform another check of the vial(s) used.
- At RAH the used vials will be disposed of in the clean room as per local practice.

3.7 Post-preparation checks

The Intrathecal Chemotherapy Authorised Production Pharmacist will check:

- the batch sheet with the label and the pre-approved prescription
- the patient information is correct
- the preparation does not contain any air bubbles or particles
- the volume is correct
- the syringe is a luer slip syringe
- the medication and dose recorded on the syringe correspond with the pre-approved batch sheet and the prescription.
- the medication vial formulation is suitable for Intrathecal use (Appendix 1)

3.8 Labelling

The Intrathecal Chemotherapy Authorised Production Pharmacist or Intrathecal Chemotherapy Authorised Assistant/Technician will label the product ensuring:

- The label contains the correct expiry information as per site practice.

EXPIRY TIMES per site		
Drug name	RAH	TQEH
Cytarabine	30 days	12 hours
Hydrocortisone	24 hours	12 hours
Methotrexate	30 days	12 hours

- The label specifies the route: INTRATHECAL
- The patient details are correct: Name, UR number and Location
- The medication is correct: Correct Agent, Dose and Volume
- An additional yellow label For Intrathecal Use ONLY has been applied.

Note: if the Assistant/Technician labels the product, then the Intrathecal Chemotherapy Authorised Production Pharmacist will then check that all of the above details are correct before packaging.

3.9 Packaging

The Intrathecal Chemotherapy Authorised Production Pharmacist will then package the product ensuring:

- The intrathecal product is placed into a sealed clear plastic bag which is clearly labelled on both sides indicating 'For Intrathecal Use ONLY' and purple 'Cytotoxic' label if applicable.

This is then sealed into a black plastic bag labelled with:

- the label on the product – including patient name, UR number, drug name, dose, volume, expiry, route, ward/clinic(or location)
- a yellow 'For Intrathecal Use ONLY' label and purple 'cytotoxic' label (if applicable) on both sides of the black bag
- a Store at room temperature label

3.10 Storage of Finished Product

The Intrathecal Chemotherapy Authorised Production Pharmacist will then store the labelled, packaged intrathecal preparation:

- In a dedicated container which is not used for any other purpose and is clearly labelled 'For Intrathecal Use Only', stored and transported separately from all other medication.

3.11 Release of Intrathecal Medication

- The intrathecal medication is released to the Intrathecal Chemotherapy Authorised Doctor after confirming:
  - The collecting doctor is on the Intrathecal Register
  - Patient particulars are correct
  - The patient's platelet count is above 50 x 10^9/L
  - The patient is not having any intravenous chemotherapy on the same day or if intravenous chemotherapy is to be administered on the same day proof is provided that the administration has commenced (e.g. the chemotherapy administration chart is sighted).
- Release occurs as close to administration time as possible to ensure intrathecal medication is not kept on a ward.
- The Intrathecal Chemotherapy Authorised Production Pharmacist and then the Intrathecal Chemotherapy Authorised Doctor (or Nurse) sign the release on both the production copy and original intrathecal prescription.
- Under exceptional circumstances another Intrathecal Chemotherapy Authorised Practitioner may collect the intrathecal medication from Production to deliver to the Intrathecal Chemotherapy Authorised Doctor. The Intrathecal Chemotherapy Authorised Production Pharmacist must :
  - Ensure that the collecting practitioner (nurse, doctor or pharmacist) is on the Intrathecal Register
  - Ensure that the collecting practitioner signs the production copy of the prescription noting the reason why the authorised doctor is unable to collect the intrathecal medication.

3.12 Cancellation of Intrathecal Administration

If intrathecal chemotherapy administration is cancelled after its release from Pharmacy Production it is returned to Production for destroying and notation in the Pharmacy Production records.

3.13 Ensure that all staff involved with the administration of intrathecal chemotherapy comply with the CAHLN Intrathecal Policy, procedures and associated documents.

Report any non-compliance to the Haematology/Oncology Management Team.

Report any near misses or errors on the Safety Learning System (SLS).

4. DEFINITIONS / ACRONYMS

Intrathecal Chemotherapy Authorised Doctor

A medical doctor, consultant or registrar, who has been certified within CALHN as competent to prescribe or administer intrathecal chemotherapy after successful completion of the intrathecal chemotherapy training and competency assessment programme.

Intrathecal Chemotherapy Authorised Nurse

A chemotherapy nurse who has been certified within CALHN to verify intrathecal chemotherapy after successful completion of the intrathecal chemotherapy training and competency assessment programme.

Intrathecal Chemotherapy Authorised Clinical Pharmacist

A competent haematology oncology clinical pharmacist, who has been certified within CALHN, to clinically verify intrathecal chemotherapy after successful completion of the intrathecal chemotherapy training and competency assessment programme.

Clinical Pharmacy Chemotherapy Order Verification

Clinical pharmacist verification involves the systematic assessment of the suitability of the patient to receive a particular chemotherapy. Subsequently, there is a systematic assessment of the medication order to ensure the chemotherapy is prescribed at the correct dose and frequency for a particular route of administration.

Intrathecal Chemotherapy Authorised Production Pharmacist

A competent haematology oncology production pharmacist who has been certified within CALHN to safely prepare, check and release intrathecal chemotherapy after successful completion of the intrathecal chemotherapy training and competency assessment programme.

Cytotoxic Production Authorised Pharmacy Technician/Assistant

A competent cytotoxic production technician/assistant who has been certified to label, assemble and prepare intrathecal chemotherapy after successful completion of the intrathecal chemotherapy training and competency assessment programme.

Intrathecal Chemotherapy Trainer

An appropriate doctor, pharmacist and nurse, who have been nominated to certify practitioners within their respective professions as being competent to prescribe, supply, verify or administer intrathecal chemotherapy within CALHN.

Intrathecal Chemotherapy Register

A register which is held and maintained by the Intrathecal Co-ordinator that contains a list of medical, nursing and pharmacy practitioners who have been authorised as being competent to either prescribe, supply, verify or administer intrathecal chemotherapy.

Intrathecal Chemotherapy Register Co-ordinator

An appropriate administrator who has been selected by the Haematology Head of Unit to receive Intrathecal Certificates by the Intrathecal Chemotherapy Trainers. The role of the Intrathecal Register Co-ordinator is to manage the Intrathecal Register by ensuring the names of practitioners who have completed training are added to the register in a timely fashion. Also, correspondence must be made to those practitioners who are due for re-training. Where re-training has not been completed, the name of the relevant practitioner must be removed from the register.

Intrathecal Chemotherapy Training Certificate

A certificate that is completed by a Intrathecal Trainer containing information which will be added to the Intrathecal Register. The completed certificate must contain the practitioners name, their roles and responsibilities, their date of completion of training and their date of re-training which will be within 2 years of addition to register or as per instruction by the appropriate CALHN Intrathecal Chemotherapy Trainer.

Intrathecal chemotherapy

Any chemotherapy or other anti-cancer medication to be delivered directly into the cerebrospinal fluid via either lumbar puncture or intraventricular injection into an Ommaya reservoir.

5. SUPPORTING MATERIAL

5.1 Appendices

Appendix 1: Approved Intrathecal Preparations

Appendix 2: Approved batch sheets (TQEH and RAH specific)

Appendix 3: Approved labels (TQEH and RAH specific)

5.2 Resources and Forms

Hyperlink to Intrathecal Chemotherapy Registers CALHN Cancer Services

6. REFERENCES

Department of Health (2008) Health Service Circular Updated National Guidance on the Safe Administration of Intrathecal Chemotherapy [Issued under HSC 2008/001, 11 August 2008], available at: http://www.dh.gov.uk/en/Publicationsandstatistics/Lettersandcirculars/Healthservicecirculars/DH_086870 - Google Search

NHS Trust, Portsmouth Hospitals Intrathecal Chemotherapy policy for Oncology and Haematology. Issue 13, September 2013

Scottish Executive Health Department (2005) Guidance for the Safe Use of Cytotoxic Chemotherapy [Issued under NHS HDL (2005) 29, 4 July 2005], available at: http://www.sehd.scot.nhs.uk/mels/HDL2005_29.pdf

Standards for Chemotherapy in South Australia November 2010, available at: http://www.sahealth.sa.gov.au/wps/wcm/connect/89ec480045a68ae78fdeaf9f9859b7b1/Standards+for+Chemotherapy+Services+in+South+Australia+January+2011.pdf?MOD=AJPERES&CACHEID=89ec480045a68ae78fdeaf9f9859b7b1

7. HEALTH AND SAFETY

7.1 Work Health and Safety

The responsible manager must ensure the worker who undertakes this instruction receives adequate information, induction, training, direction / supervision and support to fulfil their responsibilities in line with requirements documented in this procedure.

Workers following this procedure have a duty of care for taking reasonable steps to protect their own health and safety and not adversely affecting another person while at work.

Below is the hyperlink to the SA Heath WHS&IM home page:

SA Health Workforce Health Home Page

The following hyperlink takes you to Inside Central WH&S Home Page

7.2 Infection Control Commonly Used Procedures Are Listed Hereunder

Standard Precautions
Transmission-based Precautions
Blood and Body Substance Spills
Principles of Assessment and Management
Hand Hygiene
Blood and Body Spill Procedure
Disposing of Sharps Instruments

8. KEY WORDS

Intrathecal chemotherapy, Intrathecal Production, Pharmacy/pharmacist, Intrathecal register, National Standard 4, National Standard 5

9. VERSION TRACKING

Revision of this document subsequent to date of printing or downloading may render hard copy text obsolete. Check Version Number on the eCentral System.			
Version	**Effective From**	**Change Summary**	**Effective To**
1.0	February 2014	Initial Version	February 2017

10. AUTHORISATION

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END OF INSTRUCTION

Appendix 1 - Approved Intrathecal Preparations

***METHOTREXATE**
Methotrexate 5mg/2mL (DBL)

*Licensed for Intrathecal Use

****CYTARABINE**
Cytarabine 100mg/5mL (Pfizer)

** Only brand licensed for Intrathecal Use

*****HYDROCORTISONE**
Hydrocortisone Sodium Succinate (Solu-Cortef) ACT-O-VIALS 100mg (Pfizer)
Hydrocortisone Sodium Succinate (Solu-Cotef) Vials 100mg (Pfizer)

*** Not Licensed for Intrathecal use – No hydrocortisone product is. However it is used in Australia.

END OF APPENDIX 1

Appendix 2 - Example of TQEH Batch Sheet

Pharmacy Services

ASEPTIC BATCH SHEET

[redacted] MRN. [redacted] Ward: NE1B (Haem/Onc OPD NE1B)

Reference: [redacted] Route: Intrathecal Date: 18/11/2013

Methotrexate (Tqeh, Intrathecal Non-Adult) 12mg/4.8mL Injection 1

Generic	Brand	Strength	Form	Pack Desc	Quantity	Volume (mL)	Batch	Expiry Date
Ingredients								
Methotrexate	DBL, 614400C00	5mg/2mL	INTRATHECAL 5 INJ		12 Milligram	4.80	_____	

Method

CAUTION: CHECK CONCENTRATION OF MASTER PROTOCOL
1. Assemble Required equipment
Methotrexate (DBL) 5mg vials - FOR INTRATHECAL USE
10mL Slip syringe
18G and 21G Needles
2. Concentration 2.5mg/mL thus Volume required = _____mL
3. Aseptically draw up the required volume of methotrexate using the required syringe
4. Aseptically cap a red syringe combi stopper on the syringe

Dispensed by : _____ at_____ Assembled by : _____ at_____
Prepared by: _____ at_____ Labelled by: _____ at_____
Released By: _____ at_____

Affix Sample Label Here

Actual label to be stuck here

This item was prepared 1 time(s)

Prepared By: _____ (Signature) Date: _____ Time: _____

Checked By: _____ (Signature) Date: _____ Time: _____

Example of R.A.H. Work Sheet for Methotrexate 12 mg Intrathecal Injection

Government of South Australia
Central Northern Adelaide Health Service

Royal Adelaide Hospital - Pharmacy Department
Cytotoxic Production Service

WORK SHEET

Prescription number: **11114**

Patient last name: SAMPLE **First name:** J

URN: 12345 **Ward:** DC

Date prepared: 02/12/2013

Batch number **12130001** **Number to make = 1**

Detailed Drug Name	*Calculated Dose*	***Required volume***
METHOTREXATE Intrathecal	**12.0 mg**	**4.8 mL**

Infusion solution and volume

Diluent to add (for infusor)
0 mL

Manufacturer's lot no.
S024400AA

Manufacturer's name
PFIZER PTY LTD

Prepared by:
Final Product Checked by:
Volume checked by:

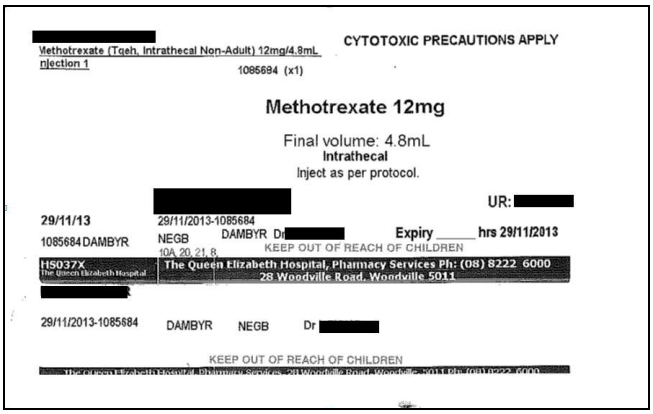
METHOTREXATE 12 mg INTRATHECAL
PREPARATION METHOD- R.A.H. PHARMACY
CAUTION: Check concentration is Methotrexate 5 mg/2 mL
1. Assemble required equipment:
- Methotrexte (DBL) 5 mg/2 mL vials (For intrathecal use)
- 5 mL Luer SLIP syringe and syringe cap
- 18 G needles
2. Aseptically withdraw 4.8 mL methotrexate 5 mg/2 mL injection solution into 5 mL luer SLIP syringe via 18 G needle.
3. Aseptically attach sterile syringe cap to syringe.

Batch sheet checked:	at	hrs
Dispensed by:	at	hrs
Assembled by:	at	hrs
Assembly checked by:	at	hrs
Labelled by:	at	hrs
Released by:	at	hrs

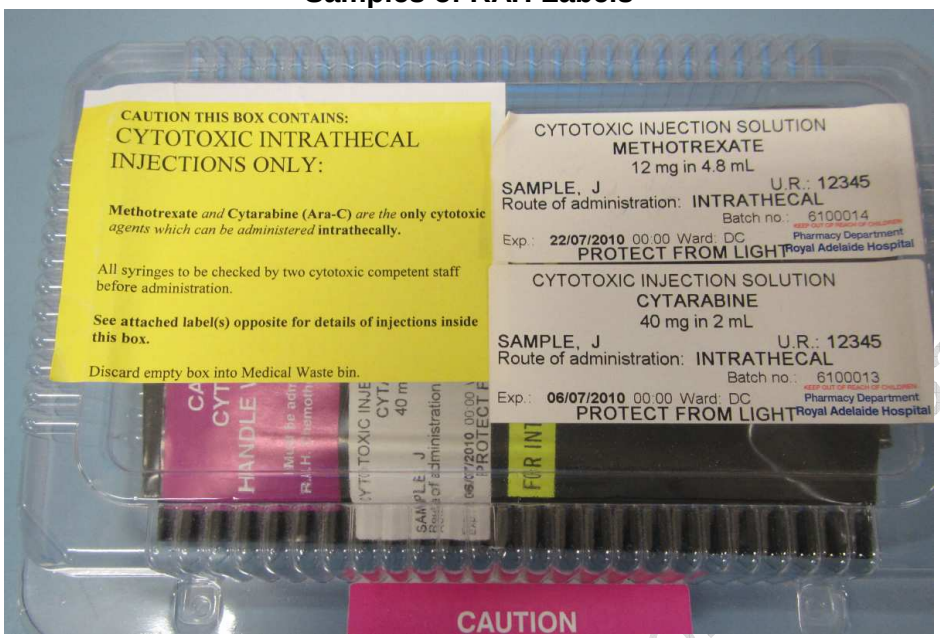
END OF APPENDIX 2

Appendix 3 - Samples of Labels

Samples of TQEH Labels



Samples of RAH Labels



END OF APPENDIX 3