AUDIT OF ASEPTIC SERVICES
Darlington Memorial Hospital
16th November 2018

This report should be read in conjunction with the attached summary of results and also with the Quality Assurance of Aseptic Preparation Services Standards document (5th edition), which gives detailed standards for each section. Numbers in brackets refer to these standards.

SERVICE PROFILE

There has been little variation in the workload for the Aseptic Unit when compared to the last audit. The hospital supplies injectable medicines for both Darlington and Durham sites. The majority of cytotoxic injectables are outsourced, with approximately 30% prepared in-house by the Aseptic Unit. Monoclonal antibodies are both outsourced and prepared onsite. A low volume of Intrathecal chemotherapy is also prepared at this site. Outsourced stock is assessed and released by aseptic staff.

No Parenteral Nutrition (PN) preparations are provided for neonatal or paediatric patients. Adult PN is outsourced and managed by the Aseptic Unit.

At the last audit, a Band 4 technician vacancy had been replaced by additional ATO 3 post and this arrangement is working well. The unit's pharmacist staffing resource remains problematic but the Band 7 Pharmacist on maternity has now returned which has enabled the accountable pharmacist to focus on non-operational matters including the PQS. The Lead Pharmacist for Cancer Management still provides strategic advice to the unit and is nearing the end of his two year secondment, at which point it is anticipated that he potentially may return to operational aseptic duties and the aseptic staffing resource once will once again be able to be removed from the Trust Risk Register. It was noted that the Trust has plans to utilise one of the Authorised Pharmacists at a specialist Lung Cancer Clinic. The impact of this on aseptic pharmacist resource is recognised and will be planned and managed for.

There have been no significant changes to staffing. The Chief Pharmacist was acting Chief Pharmacist at the previous audit. However at the time of the audit sickness was viewed as an issue with the senior technician, a key staff member being absent.

MINIMISING RISK WITH INJECTABLE MEDICINES

The Injectable Medicines Policy is contained within the Trusts Medicines Policy. Injectable medicines are evaluated prior to organisational introduction by the Drug and Therapeutics Committee at which members from the Aseptic Services team are involved. It is noted that this is well controlled. Rebecca Coon is the current Medications Safety Officer (MSO). The organisational structure should be amended to reflect this change. Efforts should be made to maintain the excellent risk management strategies implemented by the previous MSO including the outstanding review, as recommended at the last audit, against the High Risk Injectable Medicines List defined by UKMI/PASG (3.1.3).

As aforementioned the majority of aseptically prepared injectables are outsourced. Good use is made of regional purchasing contracts. The unlicensed medicines quality assessment process has been documented in a procurement procedure but it remained in draft at the time of audit. It is welcomed that the Authorised Pharmacist has implemented a standardised

QA Assessment checklist however this needs to be formalised to ensure the quality of any outsourced aseptic products is maintained (3.2.3).

No additions are made to PN and all PN is outsourced. The policy explicitly states that PN additions are prohibited.

Use of concentrated potassium chloride solutions is limited to ICU and complies with NPSA requirements and is commended.

All preparation uses closed systems and all expiries are limited to one week as required in standards.

The Trust Risk Register is well employed by the Aseptic Unit. It is commended that the unit have utilised the risk register to gain funding for a clod room in addition to extra staffing resource. Due to sickness and secondment the risk for aseptic service resources is still high and so capacity remains on the Trust Risk Register (see Management).

A parenteral Nutrition policy has been developed and a Technical Agreement between Baxter who provide outsourced PN was available. It is recognised that the amendment of this policy has been taken though to a clinical standard. This is commended.

No open procedures are undertaken. Eye drops are sourced from 'Specials' manufacturers.

Errors and incidents across the organisation are documented, investigated and monitored by the Safeguarding (Ulysses) system. The Medication Safety Officer is a pharmacist and is involved in this process.

INTRATHECALS

Arrangements for preparation of intrathecal chemotherapy comply with national guidance.

The designated lead for overseeing compliance with intrathecal (I/T) guidance within the Trust is Dr Mahmoud, as previously. I/T activity has increased by 40% since the last audit and is now around 35 procedures annually, split between the Durham and Darlington sites.

A selection if IT prescriptions were reviewed: A pharmacist, who had completed the aseptic check on the worksheet, appeared to be outside of the validation period. However on further investigation, all pharmacy staff on the intrathecal chemotherapy register had completed annual refresher training. This was not updated on the hard copy in the training folder (3.1 - I/T Standards). It is recommended revalidation is linked to updating the register; optimally this would be a live database

As with the previous audit, the copy of the prescription on file in pharmacy was very poor. It should be ensured that the copy quality received by pharmacy is improved to minimise the risk of transcription error during preparation activities (6.2 – I/T Standards).

Good separation and transport practice for IT products appeared to be in place.

A maximum 8 hour expiry is allocated to I/T products and the unit is using the Surety neuraxial components.

Vincristine is outsourced and vinblastine and Vinorelbine are prepared in-house. The master label used in-house included the term "potentially" and did not state explicitly "For intravenous use only - fatal if given by other routes". This requires amendment (8.4 - I/T Standards).

PRESCRIPTION VERIFICATION

Non-Medical Prescribers are utilised in the Trust; they are signed off by the authorising consultant. A list of non-medical prescribers exists but was not available for view. This list should be made accessible and visible to staff verifying prescriptions in the aseptics unit (4.1.2). It is recognised, however that the use of chemo care for almost all prescriptions provides a preventative measure from an unauthorised member of staff prescribing. It is recommended the robustness of this system is challenged via audit to ensure chemocare continues to be a barrier to non-authorised personnel prescribing.

Chemotherapy prescriptions are clinically reviewed by an authorised pharmacist. The procedure for prescription verification for Intravenous Chemotherapy (ASEP/002) was reviewed. This procedure had been structured using the QAAPS 5 Standards and linked to training which is good practice.

No Clinical Trials have been prepared in the Unit since the last audit. If the unit intend to prepare Clinical Trials again, a change control should be used to consider all impact of this change, particularly with respect to the document control system (4.1.8), the roles and responsibilities with respect to IMP preparation and how it functions with the Clinical Trial team interface should also be considered. It is accepted the Clinical team have a Clinical Trials procedure, however the Aseptic Unit require a separate procedure which feeds into the PQS. A Technical Agreement may also be considered to be of benefit to define the roles and responsibilities.

All of the pharmacists performing aseptic verification checks have also been trained to clinically check prescriptions. No products are released from the Aseptic Unit until all clinical checks are completed. Oral Chemotherapy is also dispensed and checked by the aseptic team.

The use of Chemocare has resulted in standardisation of prescription formats. There is a robust system in place for ensuring checks are made against the original prescription prior to product release. It is recommended that the unit moves forward with putting additional I/T prescriptions onto Chemocare which will prevent poor copies of prescriptions being used in the aseptic unit.

Mixing of PN bags from tri-chamber bags occurs before the point of administration on the wards by nursing staff. It is recommended that the roles and responsibilities of all the carious disciplines involved in prescribing, preparing, administering and monitoring of PN are documented (4.1.3). This will ensure that the acceptance of responsibility for adequate mixing by nursing staff is documented, as this is a preparation step which is routinely undertaken by pharmacy staff

MANAGEMENT

As with the previous audit, due to secondment of the Lead Pharmacist for Cancer Services, the Accountable Pharmacist now reports directly to the Chief Pharmacist, as required by the standards. Although the Senior Technician is also managed by the Chief Pharmacist she is professionally accountable to Accountable Pharmacist.

It is welcomed that a gap analysis of the updated requirements of Quality Assurance of Aseptic Preparation Services had been implemented via the internal audit procedure however, responsibilities were unclear regarding their scheduling regarding the actions determined as a result of these audits (see PQS).

A quality meeting (3 to 1) is held involving the Chief Pharmacist, the Accountable Pharmacist and the Senior Technician. The intention is for these meetings to be monthly however minutes reviewed showed meetings occurred in January, April, June, September and October. As this is the method of reviewing regulatory change and providing senior management oversight, it is recommended that efforts are made to ensure the meetings occur on a monthly basis (5.2.4) . The meeting has consisted of only two staff since October, due to sickness.

Minutes from the meetings from the 14th of September were reviewed. Whilst the meeting's agenda is comprehensive, the minutes contained little detail around the actions confirmed at the meetings. It would be useful to add more details to these minutes with respect to outcomes discussed to enable progress to be tacked between meetings.

Significant improvements in the PQS were observed. This could further be improved and monitored by integrating Key Performance Indicator metrics and quality indicators for review at quality meetings (5.2.3).

The capacity plan for September 2018 was reviewed; however previous month's data were not available for review. Maintaining monthly capacity plans are beneficial for trending and determining when interventions are required (5.5.5).

It is commended the capacity plan had been utilised to demonstrate to the Trust board how the unit was operating at risk with the current issues with pharmacist resource, which was subsequently added to the Trust Risk Register after which more funding was secured.

Procurement and QA of outsources activity is time heavy however outsourced products have a longer expiry which is beneficial for increasing flexibility for ward use. The capacity plan did not include any time for management of the PQS (5.2.2). It is recommended the plan is updated to include time for this critical factor.

An accompanying policy to detail the actions in the event of any trend was recommended last year, however was not yet in place. It is recommended this is completed.

Preparation out of house does not occur.

FORMULATION, STABILITY AND SHELF-LIFE

A comprehensive file of stability data continues to be maintained electronically with assessment occurring via the accountable pharmacist however a procedure for stability assessment is required to formalise the local application of stability data (6.3.1).

The Lead Pharmacist for Cancer Management is working toward an innovative robotic solution to updating the SMPC data. This is commended.

FACILITIES AND EQUIPMENT

The use of the Trust Register had been employed to secure funding for a new cold room, used to stock the outsourced products and those made in-house. The unit is commended on the implementation of the cold room. It is recommended the comprehensive validation document for the cold room should be used to formalise a Validation Master Plan and to detail planned and preventative maintenance for all critical equipment (7.1.3).

The aseptic facility is in good condition and being well maintained. The work flow is good with a logical order. The storage areas in the support rooms were tidy and clear segregation was observed in cupboards and fridges.

The isolator room in use, houses two negative pressure isolators which are alternated on a weekly basis. They remain switched on with no set back. (See Aseptic Processing)

The positive pressure isolator had been removed from use as the current strategy within the aseptic unit is to prepare chemotherapy only. Only one of the negative pressure isolators are in use at any one time: As they are due for replacement next year,it is recommended that consideration should be given to the use of the facility for CIVAS products which would require a positive isolator to replace one of the negative pressure isolators.

Both negative pressure isolators are serviced via a six monthly PPM maintenance visit
It should be ensured that reports from external contractors are reviewed and formal acceptance should be documented in a timely manner. This includes the quarterly report from Stockton QC Laboratory. The most recent SQC report from the 14th September 2018 and the one previous to that could not be located on the day of the audit. Both final reports would have been expected to be received at the time of audit. It was unclear if they had been reviewed. This requires urgent attention as the Accountable Pharmacist is required to accept reports from service and maintenance visits to ensure the correct level of testing has been applied, in accordance with the standards and that they equipment or facility is acceptable for use (7.2.6).
It is recommended a procedure is implemented for the review and acceptance of service or maintenance visits, this will ensure that any comments requiring action are fed in to the pharmaceutical quality system where a change is required .

Changing and hand washing arrangements are as at the previous audit. The use of boots in the isolator room has continued.

PHARMACEUTICAL QUALITY SYSTEMS

It is recognised that the unit has made significant progress with the Pharmaceutical Quality System since the previous audit. The substantial improvements are commended. The continued emphasis on the pharmaceutical quality system is encouraged to sustain this progress.

There is currently no quality manual for the unit which makes it difficult to monitor the effectiveness of current systems (8.1.2) This would be a helpful tool, not only for compliance with the standards and training of staff but also to enable understanding of the resources required to maintain the Quality System, particularly for people working outside of the unit (such as the Chief Pharmacist) which could then be used to gain further resources.

The capacity plan lacks time dedicated to the PQS. This is a critical element and protected time is strongly recommended (see management).

There is no overarching procedure which defines responsibility for writing, verifying and approving and archiving documentation. This should be formalised (8.2.2.1).

Significant improvements have been made to the deviation system since last year's audit. The change control procedure details implementation and review of planned deviations.

Change Controls were reviewed. The system necessitates that each time a change control is required the entire SOP is printed, addition of an appendix to the SOP is recommended to aid document control.

One change control considered two changes. One for the inclusion of sporicidal wipe and two further alcohols wipes at the second stage of disinfection in addition to investigating the

use of triple/double wrapped packs in the unit. It is recommended one type of planned deviation is assessed per change control to facilitate implementation and traceability.

The current change control form considers impact on particular areas however the list is not comprehensive. A separate appendix to include a checklist of different impacts to consider is recommended to ensure consistent and systematic decisions are made. The auditor will send an example to assist with this.

The change control form contains a section for action which is welcomed however this could be further improved by adding a target date for actions (this could feed into an electronic data base and a RAG system used, ensuring outstanding actions are visible). Actions should be tracked, discussed, recorded and fed back into the deviation system where appropriate, at the monthly management meetings.

The system for recording unplanned deviations (Quality Exception Reports) was reviewed. The forms require selection of whether the deviation relates to a planned or unplanned deviation. This should be removed: Planned deviations should be recorded as Change Controls and unplanned as Quality Exception. A SOP for completing unplanned deviations (Quality Exceptions) is strongly recommended (8.4).

The current system lacks detail; there is no severity assessment and the level of investigation is not commensurate to the risk. Many recent deviations related to particles in final products. One deviation related to an operator preparing products without an up-to-date broth test following a period of absence. Although the latter had much greater risk associated, there was no differentiation between the assessment of that and those deviations associated with particles in the bag. No root cause had been determined and no corrective or preventative actions were assigned (8.2.5.2). It is recommended the current system is reviewed and an SOP written to ensure personnel understand the scope of the procedure. A severity risk assessment is recommended to quantify and standardise the investigation.

Assignation of a reference numbers would be beneficial when referencing change controls or Quality Exception Reports in any other element of the PQS. Consideration should be given the introduction of a log to aid this.

A technical agreement is now in place between Baxter and the Unit which is commended.

Although all SOPs reviewed were in date, the electronic database used to determine when SOPs were scheduled for review had not been updated; it is recommended this is reviewed. Approved SOPs are uploaded onto the intranet where they are then distributes to groups; it is recommended that it is ensured that all procedures as listed in chapter 8 of QAAPS exist and are in date (8.4).

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A selection of worksheets and associated prescriptions were reviewed including Irinotecan Infusion 300mg in glucose 5% where the worksheet stated “withdraw 15ml” on two occasions. Both had been crossed out and changed to “0ml”. Both had been signed and dated however routine hand amending worksheets does not comply with data integrity principles and should be minimised. Discussion with staff highlighted that it was more common practice not to remove any volume when preparing Irinotecan doses. The system should be based on routine practice thus the worksheet requires review to ensure it is more applicable to practice. Additionally the layout of the worksheets does not make it easy to see that each starting material has been checked. The first boxes to be completed chronologically must be signed by the operators who make the products, which does not promote workflow (8.5.2).

This was evidenced by the absence of signatures on worksheet for Pembrolizumab 200mg Infusion volume checks, which is a critical parameter. It is recommended current worksheets are reviewed and amended to reflect current practice where applicable so as to improve clarity and minimise the risk of errors (8.5.4).

At the time of the last audit the unit was not participating in the PASG error monitoring scheme, the error monitoring record form has now been amended to fit this scheme for ease of feedback which the unit plan to do for the first time next month. This is encouraged.

The recall procedure has been successfully challenged via a simulated recall since the last audit.

PERSONNEL TRAINING AND COMPETENCY ASSESSMENT

Competency requirements were reviewed for a rotational pharmacist and a Band 4 Technician, both training files were maintained well and up to date.

Aspects of the competency training program were excellent, however a formalised system for the background underpinning knowledge, for example use of the TSET Training module is required (9.3.1). Formalising the requirements to become competent to perform particular roles such as authorised pharmacist, checking technician etc. via a checklist would also be of benefit.

The auditors spoke to the rotational pharmacist. She was knowledgeable about all the aspects of her role in the unit.

ASEPTIC PROCESSING

Preparation of cytotoxic is undertaken in a negative pressure isolator and this alternates on a weekly basis as the unit houses two isolators. As noted at the previous audit preparation of monoclonal antibodies is undertaken. Although it is recognised that segregation and time separation is being employed, it is recommended that the practice is reviewed against the Yellow Cover Document to ensure that it is justified. The second isolator forms contingency only, therefore it is recommended that consideration is given to the purchase of a positive pressure isolator to enable CIVAS preparation to be undertaken in preference to replacing like for like (see Facilities and Equipment).

The potential use of double or triple wrapped disposables was to be considered as part of a wider change control for implementation of a sporicidal disinfection step. It was not reviewed within the change control although it had been considered, with AMD visiting the site with samples and a decision made not to progress due to perceived wastage.

Since the last audit the unit have employed the use of a resheathing block which is commended.

As seen in the previous audit, needles were not always separated before being transferred into the clean room. This requirement should be incorporated into the appropriate SOP (10.1.3.4).

Implementation of the sporicidal disinfection step was successful with Redditch Sporicidal wipes being the wipes used (see cleaning).

Process validation is undertaken using a universal operator broth kit which has been judged suitable to cover all types of manipulations. As a consequence of last year's audit the

number of Kits had been increase to two consecutively to represent the number of manipulations undertaken in one session by one operator

Operator validations were monitored effectively and staff were informed when due to undertake a validation exercise. However there was one significant deviation where product had been made and subsequently released by an operator who was not validated despite directions from senior staff that they were not to make. This had not been investigated and assigned preventative actions (see PQS).

MONITORING

The programme of monitoring employs sessional settle plates and finger dabs as well as weekly monitoring of all areas. Critical zones are monitored sessionally with settle plates and finger dabs. Results were good with very few exceptions within a year period. The unit uses the regional programme of three end-of-session broth tests and one sterility test per month. There have been no failures.

The MRS system is employed to notify the unit of out of specification microbiological results. The results were reviewed online via MRS. Whilst the system details appropriate cleaning for any microorganisms identified in a grade A environment; this is not recorded departmentally or fed back into the deviation system for investigation: as such potential preventative actions are not assigned.

A procedure for investigations of microbiological out of specification deviations is required. Trends are monitored via the 3 to 1 meetings; however it is difficult with so few exceptions to have an oversight of any true trends. It is recommended a database for microbiological non-conformances is established to improve oversight for trending with respect to isolators, operators, servers and identifications. An annual review not currently performed, this should be remedied, particularly for reassessment of alert limits (11.1.2).

The last two quarterly reports from Stockton QC Laboratory were not available (see Facilities and Equipment).

CLEANING AND SANITISATION

Cleaning is performed by the aseptic unit staff. Sterile disposable mop heads are stored in the collation room and mop shanks kept in the change area. Ready-to-use disinfectants are sprayed directly onto the areas to be cleaned. There is no use of buckets and no requirement for monitoring of in-use dilutions of agents.

It is recommended consideration is given to use of a tachy mat before entering the first change to reduce risk of carry in of large particles on footwear.

Cleaning is performed regularly in conjunction with the Cleaning SOP. The unit uses two rotational biocidal disinfections and has implemented the sporicidal disinfection step via change control and use of Redditch Sporicidal wipes. Stopwatches were placed at the point of sporicidal disinfection and were being used as required. Cleaning logs were reviewed and were satisfactory. Bioburden monitoring had occurred as part the transfer validation. This is commended.

At the time of the audit, making for the day had finished so preparation was not observed, however aseptic technique was observed for the Kit 301. The operator was observed using the same side of the alcohol wipe for the top and middle parts of components. The SOP for transfer disinfection requires review to clairify the stroke direction with IMS, although it is

accepted the risk is minimised in the isolator room due to implementation of the sporicidal step in the support room (12.5.1).

Sterile bins were in use as a result of recommendation from the previous audit Cytotoxic residue testing has been completed in November 2018 with Etoposide and Paclitaxel. Clarification around the range of agents to be tested 6 monthly was discussed.

STARTING MATERIALS, COMPONENTS AND OTHER CONSUMABLES

Starting materials are sterile and hold a marketing authorisation.

One unlicensed starting material had been used since the last audit. Alumtuzumab (Genzyme), it had been quality assessed however the assessment form is not an approved document. It is recommended this is approved (see Minimising Risk with Injectable Medicines).

A system via email updates has been implemented to ensure the SmPC is updated when required, although there are limitations to the system and a novel robotic approach is being investigated.

All components are sterile and CE marked. Recently procurement of these items has been changed, with the unit now required to order through Synchronicity who obtains stock from Cardia. No risk had been identified through this change, although implementation via a change control would have documented this.

Presence of a CE mark is checked and the batch number recorded when products are transferred from store to the collation room such that an audit trail is available for all components in use in the unit.

PRODUCT APPROVAL

The product approval process could be improved by implementation of a daily log checklist to ensure the pharmacist releasing the product has assurance that all parameters in the unit are satisfactory (14.10).

In the event of failure the fate of the product is documented on the worksheet and a reference is given to the product reject form in the comments section. Failures are reviewed at the 3 to 1 meeting.

The improvements in the units error monitoring is recognised but requires further development (see PQS)

STORAGE AND DISTRIBUTION

Temperature monitoring of fridges is continuously performed via the Building Management System and by the use of data loggers; Tempods. Calibration for a Tempod used in a fridge in the support room was reviewed, It was found to be satisfactory. It is recognised extensive work, including temperature mapping had been completed in the commissioning of the new cold room (see Facilities and Equipment).

All products are wrapped in a primary plastic wrapping, then an additional light protective secondary wrapping, which is then placed in a zip lock bag. Transport boxes are sturdy and secure, with clear instructions on how to contact the unit if one should be found unexpectedly. It is recommended in use validation of the transport boxes to included

seasonal variation. is preformed to ensure distribution conditions are maintained throughout the journey (15.3.2).

Both products prepared in the aseptic unit and outsourced products are transported to other Trust sites. In the case of Shotley Bridge, a taxi company is used to undertake this transportation.

A documented risk assessment and gap analysis against the distribution standards of Chapter 15 was not reviewed but accepted to be completed. As with the previous audit there were discussions around the requirement that staff involved in the transport chain are aware of their responsibilities and for training with assessment to be given (15.3.9, particularly with respect to Taxi and Trust drivers. This requires review as it is still outstanding. A gap analysis with justification where required may be suitable.

There is currently no procedure for handling complaints although it was stated they were handled by the Datix system. It is recommended this is formalised to feed back into the Quality Exception system to ensure appropriate investigation is performed (15.4.2, 15.4.3) .

INTERNAL AND EXTERNAL AUDIT

The most recent edition of QAAAPs provided a basis for the internal audit SOP which was reviewed. Although much improved since the previous audit, the timing of the quarterly schedule was unclear. In addition the Accountable Pharmacist had delegated responsibilities to the lead technician but was unaware of the schedule in her absence. It is recommended that audit is driven as part of the quality system and actions stemming from internal audit are added to a database with a time for completion assigned in order to ensure any outstanding actions can be reviewed, discussed at the 3 to 1 meetings, thus ensuring the Chief Pharmacist has full knowledge of the risks (16.10).

The response to the last external audit has been excellent with significant improvements clearly tracked and witnessed across all areas. Where slippage is observed it is recommended these actions are completed.