Safer practice with Gentamicin

1 Summary

The problems of poor labelling and the lack of access to technical information with the use of injectable medicines increases risk. The risks are associated with the preparation, administration and monitoring. Error in these areas provides an increased risk that can expose patients to avoidable harm.

Gentamicin is a highly effect drug for treating many infections but carries with it, some risk. The most significant risks are renal damage and hearing loss. Renal damage could result in long term renal failure and ultimately death. Deafness can result in varying degrees from tinnitus to total hearing loss. An example of a Summary Product Characteristics document can be found in Appendix A.

Bearing these risks in mind, the prescribing, administration and monitoring processes all carry potential serious consequences for patients if an error was made. Not all drugs carry this level of risk and so there is a need to take extra care in prescribing, administration and monitoring to ensure optimal and safe treatment.

2 Background

2.1 Phase 1 findings

Gentamicin was identified as drug which featured in incident reporting, where there practice issues, including confusion over the monitoring requirements. Through the focus groups and interviews with staff a case study was developed as illustrated below:

<table>
<thead>
<tr>
<th>Case Study: Gentamicin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pilot Trust:</strong></td>
</tr>
<tr>
<td>United Lincolnshire Hospitals NHS Trust</td>
</tr>
<tr>
<td><strong>Area:</strong></td>
</tr>
<tr>
<td>All (CCU, ICU, Oncology &amp; Haematology)</td>
</tr>
<tr>
<td><strong>Background:</strong></td>
</tr>
<tr>
<td>Gentamicin is a powerful antibiotic and carries risk of renal damage and deafness if the patient has too high a concentration. This needs management through blood testing for levels at regular intervals. 4 methods are used in the Trust:</td>
</tr>
<tr>
<td>• Daily doses (mg/kg) following a haemogram</td>
</tr>
<tr>
<td>• Divided doses (twice or three times a day, often for patients with renal impairment)</td>
</tr>
<tr>
<td>• Divided low dose (as above but for endocarditis)</td>
</tr>
<tr>
<td>• One off prophylactic dose to coincide with an invasive intervention</td>
</tr>
<tr>
<td><strong>Proposed Changes:</strong></td>
</tr>
<tr>
<td>The Trust has guidelines that can be improved to capture the various methods used. The favoured daily dose regimen is not covered by a manufacturing licence, but is commonly used in NHS trusts, so reference sources such as the BNF show primary use as a divided dose. Development of a prescribing and monitoring system using stickers on drug charts.</td>
</tr>
<tr>
<td><strong>Statement of Problem (Issue):</strong></td>
</tr>
<tr>
<td>Protocol and Monitoring process for Gentamicin is complicated and confused by the variety of regimes used. Potential for error and therefore risk to incorrect dosing is significant.</td>
</tr>
<tr>
<td><strong>Potential Benefit:</strong></td>
</tr>
<tr>
<td>Reduced risk from complex calculations</td>
</tr>
<tr>
<td>Reduced risk from complex preparation</td>
</tr>
<tr>
<td>Simplified preparation of cytotoxic drugs</td>
</tr>
<tr>
<td>Standardisation of treatment dosing</td>
</tr>
<tr>
<td>Standardisation of education and training</td>
</tr>
</tbody>
</table>
2.2 Aim and key benefits

To investigate and demonstrate that purchasing medicines that include technical information about prescribing, preparation and administration will reduce the clinical risk. The desired benefits are:

- Reduced risk when making calculations of creatinine clearance
- Reduced risk when making dose calculations
- Reduced risk of failing to monitor levels effectively
- Reduced risk of overdosing or sub-therapeutic dosing
- Standardised approach across the Trust and in conjunction with the microbiology service used

2.3 Workstream summary

Please see Appendix B

3 Objectives

1. To identify risk reduction measures in relation to the injectable therapy with labelled and packaged information, preparation and use.
2. To propose and implement patient safety improvements for the use of Gentamicin.
3. To estimate the costs associated with proposed risk solutions.
4. To identify barriers which might hinder the implementation of a purchasing for safety initiative and propose solutions where appropriate.

4 Methods and measures

4.1 Workstream design:

The workstream lead was selected through their involvement in phase 1 of the project and interest in the subject area.

Stakeholders:

Lead: Robyn Thompson, Principal Pharmacist

Team: Rick Dickinson, Risk Manager
      Liz Gilbert, Principal Pharmacist (Risk)
      Nick Adams, Principal Pharmacist
      Lisa Price, Information Pharmacist
      Bethan Stoddart, Microbiologist
      Ruth Wilne, Principal Pharmacist (Procurement)

4.2 Evaluation(s):

Phase 1 interviews and focus groups identified that there were risks to patient safety. These issues are based around the following points:

- Confusion over the regimen being used
- Monitoring requirements
- Dose calculations
- Responsibilities of staff involved
• Variance in practice between trusts impacting on rotating training doctor’s understanding

Using risk assessment techniques, priorities for action can be identified. The National Patient Safety Agency produced guidelines on risk assessing injectable medicines practice. The criteria applied to gentamicin use is shown in appendix B. The risk level was considered as a moderate risk using this tool, however the issues of monitoring requirements, variance in practice and confusion about regimen are not included and therefore a higher level of risk exists.

Using an adaptation of a Failure Mode Event Analysis tool, risks were identified that take into account patient safety and also the systematic approach in place to recognise error and intervene to mitigate against harm. This assessment can be seen in Appendix C.

One of the additional benefits of this tool, is the ability to re-assess the risk when actions are completed and so demonstrate the risk reduction measures as well. The solutions that have been developed aim to provide a set of tools to reduce risk and improve safer practice.

Problem 1 – Correct dosage
Underdosing - if too little of a drug is prescribed it may mean that the treatment is “sub-therapeutic” or not therapeutic enough to treat the patient in an ideal way. Overdosing – if too much of the drug is prescribed, it may mean that the patient will be harmed, causing renal damage or hearing impairment, potentially leading to long term damage and even death.

Solution development
The solution needs to ensure that the right dose is prescribed. For gentamicin there are 2 important parameters, one is the patients renal function and the other is the patients ideal body weight. Current guidelines do not include ideal body weight.

Actions required
• A dose calculation tool that will ensure the patients renal status and eliminate those patients who are not appropriate for a once daily dosing regime.
• Revision of the dose calculation in the guideline and provide tables to enable staff to use the principle of dose banding with ideal body weight calculations.
• Development of an intranet based calculator that will eliminate the need for a manual calculation and potential errors that could occur.

Problem 2 – Dosing frequency
Too frequent – could overdose the patient
Too infrequent – could provide sub therapeutic treatment, leading to prolonged illness and or a poor outcome
**Solution development**

The ideal solution needs to explicitly guide the team in the right prescribing and administration frequency.

The current prescription chart is designed for regular doses at a set time and frequency. The daily dosing regime can include 24, 36 or 48 hour intervals, depending on the results of the monitoring that is required.

The solution of using a sticker provides prompts, details the prescribing standards and also supports administration monitoring accuracy. The following sticker design was created by Workstream Lead, in consultation with microbiologists and pharmacists. It has been approved for use by the Trust’s Drug and Therapeutic Committee. A consequence of this design is that no more than 3 doses can be given before a review is made.

### GENTAMICIN

<table>
<thead>
<tr>
<th>Prescription</th>
<th>Administration</th>
<th>Prescription</th>
<th>Administration</th>
<th>Prescription</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date / Time</td>
<td>Time given</td>
<td>Sig</td>
<td>Date / Time</td>
<td>Time given</td>
<td>Sig</td>
</tr>
<tr>
<td></td>
<td>Time of level</td>
<td>Sig</td>
<td></td>
<td>Level value</td>
<td>Sig</td>
</tr>
<tr>
<td></td>
<td>Sig</td>
<td>Level value</td>
<td>Sig</td>
<td>Sig</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Next dose due</td>
<td>Sig</td>
<td>Next dose due</td>
<td>Sig</td>
<td></td>
</tr>
<tr>
<td>Dose @ 7mg/Kg Route LV in 100ml of Sodium Chloride 0.9% over 1 hour</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Signature and V number</td>
<td>Bleep</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Actions required**

- Implement sticker with the revised Antibiotic Policy (when approved) in pilot areas
- Evaluate pilot using questionnaire and an issues log
- Revise (if required) and roll out implementation to the whole Trust.

**Problem 3 – Appropriate monitoring of gentamicin levels**

Unless the regime is appropriately monitored there may be result in overdosage or sub therapeutic treatment. The impact of overdosage as previously described is most significant, potentially causing renal or auditory damage.

**Solution development**

The existing tool for monitoring the results of the gentamicin level is the Hartford Gentamicin Nomogram. This tool is reliable and has been used with effect. The problem is not about the tool, but about the accurate documentation of sampling times in relation to administration and the 6-14 hour window for checking the sample. That information needs to be captured on the microbiology blood test request form. In order to capture the detail, the sticker solution above is a method of creating prompts for collecting timings and may prompt the blood sampling required.
The interpretation of the results could also be strengthened using a web based calculator tool. The calculator tool will be able to identify the dosage interval required and the frequency of monitoring. It will also trigger the toxic range to alert the staff member to stop the treatment, seek advice and access an urgent medical review.

**Actions required**
- As Problem 2
- Incorporate into the web based tools identified in Problem 1.
- Implementation Training package, for dissemination into each team.
- Implementation plan for the introduction of the revised antibiotic guidelines.

**Additional actions**
Revision of the antibiotic guideline which incorporates the dosing and monitoring methods. (Shared document with North Lincolnshire and Goole NHS Foundation Trust- Current version is shown in appendix D) This is required in any case due to the review frequency of the policy.

4.3 Measures

The outcome measures are going to be:
- Incident and intervention rate regarding gentamicin.
- Questionnaires during the pilot phase.
- Feedback from users

Long term measures can be monitored using a balanced scorecard approach (see appendix E).

5 Workstream outputs

5.1 Working groups
Phase 1 produced focus groups to identify the issues surrounding the use of gentamicin, providing suggestions to improve practice, followed up with interviews of:
- Consultant Microbiologist
- Pharmacists
- Nursing Leads

As this starting point for phase 2 was building on the initial work, the opportunities for working groups to take forward the actions required was evident.

Outputs to date can be summarized as:
- Gentamicin prescription sticker has been designed and approved for use. Printing has taken place and is now ready to pilot.
- Antibiotic Policy have been revised, with initial efforts made by the team having to conform to comply with North Lincolnshire and Goole NHS Foundation Trust’s requirements. The policy does not include any mention of the sticker system or web based calculator. Further to this, the policy remains a draft document and it is hoped it will be approved at the next
Drug and Therapeutic Committee in early March 2008. The February meeting failed to be convened due to unforeseen circumstances.

- The development work for the calculator tool has been commissioned to the Trust IT development team, and this work is hoped to be completed for testing in March 2008.

5.2 Evaluation

No evaluation can be made as yet, as the implementation of the pilot has not been possible due to the delay in approval of the Antibiotic Policy

6 Recommendations

The list of recommendations is limited as there has not been any evaluation made yet.

Local clinical
Changing practice for a Trust wide risk area and joint working with another Trust can prolong the process in agreeing process and clinical standards. With this in mind, the timescale was not enough to complete all the necessary governance arrangements for the Pilot. Many organisations may not have this challenge. United Lincolnshire Hospitals NHS Trust has a service level agreement with Path Links which is managed by North Lincolnshire and Goole NHS Foundation Trust. In essence, the Microbiology service is provided by another organisation, who are part of a larger network.

Purchasing
Injectable medicines purchase should take into account the provision of tools that enable safer practice, i.e. safety solutions and the quality of information provided with the drug.

NHS PASA
Encourage standardisation of information provision.
Develop a system for current practice standards to be available and accessible for all NHS organisations.
Standardise prescription charts, at least to the acute sector, so that solutions can be considered for all NHS organisations.

Industry
Provide safety solutions as part of the product design for all products, even if they are old or common place in practice.
Use risk assessment tools such as Failure Mode Event Analysis to reduce the risks in practice for all injectable medicines.
Provide accessible tools for complex calculations, e.g. for weight, body mass or surface area.
7 Conclusions

This objectives of the workstream have yet to be considered in light of changes in practice. The Trust intends to continue the work that has already started and will be happy to provide a report on the outputs in due course.

References
Antibiotic Policy, United Lincolnshire Hospitals NHS Trust
1. NAME OF THE MEDICINAL PRODUCT
Cidomycin™ Adult Injectable 80mg/2ml.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each ampoule or vial (2ml) contains Gentamicin Sulphate Ph Eur equivalent to 80mg
Gentamicin base.
For excipients, see section 6.1

3. PHARMACEUTICAL FORM
Solution for Injection.
Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
Gentamicin is an aminoglycoside antibiotic with broad-spectrum bactericidal activity. It is
usually active against most strains of the following organisms: Escherichia coli, Klebsiella
spp., Proteus spp. (indole positive and indole negative), Pseudomonas aeruginosa,
Staphylococi, Enterobacter spp., Citrobacter spp and Providencia spp.
Gentamicin injection and gentamicin paediatric injection are indicated in urinary-tract
infections, chest infections, bacteraemia, septicaemia, severe neonatal infections and other
systemic infections due to sensitive organisms.

4.2 Posology and method of administration
ADULTS:
Serious infections: If renal function is not impaired, 5mg/kg/daily in divided doses at six
or eight hourly intervals. The total daily dose may be subsequently increased or decreased
as clinically indicated.
Systemic infections: If renal function is not impaired, 3-5mg/kg/day in divided doses
according to severity of infection, adjusting according to clinical response and body weight.
Urinary tract infections: As "Systemic infections". Or, if renal function is not impaired, 160mg once daily may be used.

CHILDREN:
Premature infants or full term neonates up to 2 weeks or age: 3mg/kg 12 hourly. 2 weeks to 12 years: 2mg/kg 8 hourly.

THE ELDERLY:
There is some evidence that elderly patients may be more susceptible to aminoglycoside toxicity whether secondary to previous eighth nerve impairment or borderline renal dysfunction. Accordingly, therapy should be closely monitored by frequent determination of gentamicin serum levels, assessment of renal function and signs of ototoxicity.

RENAL IMPAIRMENT:
Gentamicin is excreted by simple glomerular filtration and therefore reduced dosage is necessary where renal function is impaired. Nomograms are available for the calculation of dose, which depends on the patient's age, weight and renal function. The following table may be useful when treating adults.

<table>
<thead>
<tr>
<th>Blood Urea (mg/100ml)</th>
<th>Creatinine clearance (GFR) (ml/min)</th>
<th>Dose &amp; frequency of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40</td>
<td>6 - 7</td>
<td>&gt; 70</td>
</tr>
<tr>
<td>40 - 100</td>
<td>6 - 17</td>
<td>30 - 70</td>
</tr>
<tr>
<td>100 - 200</td>
<td>17 - 34</td>
<td>10 - 30</td>
</tr>
<tr>
<td>&gt; 200</td>
<td>&gt; 34</td>
<td>5 - 10</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*60mg if body weight <60kg. Frequency of dosage in hours may also be approximated as serum creatinine (mg%) x eight or in si units, as serum creatinine (umol/l) divided by 11. If these dosage guides are used peak serum levels must be measured. Peak levels of gentamicin occur approximately one hour after intramuscular injection and intravenous injection. Trough levels are measured just prior to the next injection. Assay of peak serum levels gives confirmation of adequacy of dosage and also serves to detect levels above 10mg/l, at which the possibility of ototoxicity should be considered. One hour concentrations of gentamicin should not exceed 10mg/l (but should reach 4mg/l), while the pre dose trough concentration should be less than 2mg/l.

The recommended dose and precautions for intramuscular and intravenous administration are identical. Gentamicin when given intravenously should be injected directly into a vein or into the drip set tubing over no less than three minutes. If administered by infusion, this should be over no longer than 20 minutes and in no greater volume of fluid than 100ml.

4.3 Contraindications
Hypersensitivity; Myasthenia Gravis.

4.4 Special warnings and precautions for use
Otoxicity has been recorded following the use of gentamicin. Groups at special risk include patients with impaired renal function, infants and possibly the elderly.

Consequently, renal, auditory and vestibular functions should be monitored in these patients and serum levels determined so as to avoid peak concentrations above 10mg/l and troughs above 2mg/l. As there is some evidence that risk of both ototoxicity and nephrotoxicity is related to the level of total exposure, duration of therapy should be the shortest possible compatible with clinical recovery. In some patients with impaired renal function there has been a transient rise in blood-urea-nitrogen which has usually reverted to normal during or following cessation of therapy. It is important to adjust the frequency of dosage according to the degree of renal function.

Gentamicin should only be used in pregnancy if considered essential by the physician (see
section 4.6 Pregnancy and Lactation.
Gentamicin should be used with care in conditions characterised by muscular weakness. In cases of significant obesity gentamicin serum concentrations should be closely monitored and a reduction in dose should be considered.

4.5 Interaction with other medicinal products and other forms of interaction
Concurrent administration of gentamicin and other potentially ototoxic or nephrotoxic drugs should be avoided. Potent diuretics such as etacrylic acid and furosemide are believed to enhance the risk of ototoxicity whilst amphotericin B, cisplatin and ciclosporin are potential enhancers of nephrotoxicity. Any potential nephrotoxicity of cephalosporins, and in particular cephaloridine, may also be increased in the presence of gentamicin. Consequently, if this combination is used monitoring of kidney function is advised. Neuromuscular blockade and respiratory paralysis have been reported from administration of aminoglycosides to patients who have received curare-type muscle relaxants during anaesthesia. Indomethacin possibly increases plasma concentrations of gentamicin in neonates. Concurrent use with oral anticoagulants may increase the hypotherbinamaenic effect. Concurrent use of bisphosphonates may increase the risk of hypocalcaemia. Concurrent use of the Botulinum Toxin and gentamicin may increase the risk of toxicity due to enhanced neuromuscular block. Antagonism of effect may occur with concomitant administration of gentamicin with either neostigmine or pyridostigmine.

4.6 Pregnancy and lactation
There are no proven cases of intrauterine damage caused by gentamicin. However, in common with most drugs known to cross the placenta, usage in pregnancy should only be considered in life threatening situations where expected benefits outweigh possible risks. In the absence of gastro-intestinal inflammation, the amount of gentamicin ingested from the milk is unlikely to result in significant blood levels in breast-fed infants.

4.7 Effects on ability to drive and use machines
Not known.

4.8 Undesirable effects
Side-effects include vestibular damage or hearing loss, particularly after exposure to ototoxic drugs or in the presence of renal dysfunction. Nephrotoxicity (usually reversible) and occasionally acute renal failure, hypersensitivity, anaemia, blood dycrasias, purpura, stomatitis, convulsions and effects on liver function occur occasionally. Rarely hypomagnesia on prolonged therapy and antibiotic-associated colitis have been reported. Nausea, vomiting and rash have also been reported. Central neurotoxicity, including encephalopathy, confusion, lethargy, mental depression and hallucinations, has been reported in association with gentamicin therapy but this is extremely rare.

4.9 Overdose
Haemodialysis and peritoneal dialysis will aid the removal from blood but the former is probably more efficient. Calcium salts given intravenously have been used to counter the neuromuscular blockade caused by gentamicin.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Gentamicin is a mixture of antibiotic substances produced by the growth of micromonospora purpurea. It is bactericidal with greater antibacterial activity than streptomycin, neomycin or kanamycin. Gentamicin exerts a number of effects on cells of susceptible bacteria. It affects the integrity of the plasma membrane and the metabolism of RNA, but its most important effects is inhibition of protein synthesis at the level of the 30s ribosomal subunit.

5.2 Pharmacokinetic properties
Gentamicin is not readily absorbed from the gastro-intestinal tract. Gentamicin is 70-85% bound to plasma albumin following administration and is excreted 90% unchanged in urine. The half-life for its elimination in normal patients is 2 to 3 hours. Effective plasma concentration is 4-8 µg/ml. The volume of distribution (vd) is 0.3 l/kg. The elimination rate constant is:
- 0.02 hr⁻¹ for anuric patients *
- 0.30 hr⁻¹ normal
* Therefore in those with anuria care must be exercised following the usual initial dose, any subsequent administration being reduced in-line with plasma concentrations of gentamicin.

5.3 Preclinical safety data
Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Disodium Edetate
Water for Injections
2M Sodium Hydroxide
1M Sulphuric Acid

6.2 Incompatibilities
In general, gentamicin injection should not be mixed. In particular the following are incompatible in mixed solution with gentamicin injection: penicillins, cephalosporins, erythromycin, heparins, sodium bicarbonate. * Dilution in the body will obviate the danger of physical and chemical incompatibility and enable gentamicin to be given concurrently with the drugs listed above either as a bolus injection into the drip tubing, with adequate flushing, or at separate sites. In the case of carbenicillin, administration should only be at a separate site.
* Carbon dioxide may be liberated on addition of the two solutions. Normally this will dissolve in the solution but under some circumstances small bubbles may form.

6.3 Shelf life
3 years
6.4 Special precautions for storage
Do not store above 25°C. Do not refrigerate or freeze.

6.5 Nature and contents of container
Cidomycin Adult Injectable is supplied in ampoules and vials.

6.6 Special precautions for disposal and other handling
Not applicable.

7. MARKETING AUTHORISATION HOLDER
Aventis Pharma
Broadwater Park
Denham
Uxbridge
Middlesex UB9 5HP

8. MARKETING AUTHORISATION NUMBER(S)
PL 0109/5065R

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION
24th January 1991

10. DATE OF REVISION OF THE TEXT
July 2005
Legal category: POM
## Appendix B – NPSA risk assessment tool

### Proforma 2: Risk assessment of individual injectable medicine products prepared in clinical areas

<table>
<thead>
<tr>
<th>Clinical area:</th>
<th>Directorate:</th>
<th>Hospital site:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>All</td>
<td>All</td>
<td>10/7/07</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Name and strength of prepared injectable product</th>
<th>Diluent</th>
<th>Final volume</th>
<th>Bag or syringe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin 0.9% NaCl 100mls Bag</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Therapeutic risk</td>
<td>Where there is a significant risk of patient harm if the injectable medicine is not used as intended.</td>
</tr>
<tr>
<td>2 Use of a concentrate</td>
<td>Where further dilution (after reconstitution) is required before use, i.e. slow iv bolus not appropriate.</td>
</tr>
<tr>
<td>3 Complex calculation</td>
<td>Any calculation with more than one step required for preparation and/or administration, e.g. microgram/kg/hour, dose unit conversion such as mg to mmol or % to mg.</td>
</tr>
<tr>
<td>4 Complex method</td>
<td>More than five non-touch manipulations involved or others including syringe-to-syringe transfer, preparation of a burette, use of a filter.</td>
</tr>
<tr>
<td>5 Reconstitution of powder in a vial</td>
<td>Where a dry powder has to be reconstituted with a liquid.</td>
</tr>
<tr>
<td>6 Use of a part vial or ampoule, or use of more than one vial or ampoule</td>
<td>Examples: 5ml required from a 10ml vial or four x 5ml ampoules required for a single dose.</td>
</tr>
<tr>
<td>7 Use of a pump or syringe driver</td>
<td>All pumps and syringe drivers require some element of calculation and therefore have potential for error and should be included in the risk factors. However it is important to note that this potential risk is considered less significant than the risks associated with not using a pump when indicated.</td>
</tr>
<tr>
<td>8 Use of non-standard giving set/device required</td>
<td>Examples: light protected, low adsorption, in-line filter or air inlet.</td>
</tr>
</tbody>
</table>

### Total number of product risk factors

5* Six or more risk factors = high-risk product (Red). Risk reduction strategies are required to minimise these risks. Three to five risk factors = moderate-risk product (Amber). Risk reduction strategies are recommended. One or two risk factors = lower-risk product (Green). Risk reduction strategies should be considered.
<table>
<thead>
<tr>
<th>Risk assessment undertaken by:</th>
<th>Name of pharmacist:</th>
<th>Name of clinical practitioner:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rick Dickinson</td>
<td>Nick Adams</td>
<td></td>
</tr>
</tbody>
</table>

*Although a moderate risk using this assessment criteria, the risk is greater due to variance in dose ranges, the monitoring requirements and the potential impact on patients if toxic levels occur (deafness and renal failure).*
**Appendix C - FMEA risk assessment**

Describe the process or system you wish to analyse:

<table>
<thead>
<tr>
<th>What could go wrong?</th>
<th>What controls or barriers exist?</th>
<th>Consequence of impact (1-5)</th>
<th>How likely for failure mode to: (1-5)</th>
<th>Risk Priority (CxOxD)</th>
<th>Critical Score (CxO)</th>
<th>Recommended Actions</th>
<th>Responsible person and target date</th>
<th>Action taken</th>
<th>Assess scores when action completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrong dose prescribe -ed</td>
<td>Weight related dose calculation included in the antibiotic guidelines</td>
<td>Toxic treatment level</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>24</td>
<td>8</td>
<td>Web-based calculation tool to be created, tested and approved for use</td>
<td>RT – March 2008</td>
</tr>
<tr>
<td>Administered at wrong interval</td>
<td>Prescription completion</td>
<td>Over-dosage</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>48</td>
<td>12</td>
<td>Sticker system to prompt frequency of dosage/next dose and monitoring schedule – Pilot pan trust</td>
<td>RT – March 2008</td>
</tr>
<tr>
<td></td>
<td>Pharmacy validation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring of levels</td>
<td>Nomogram in antibiotic guidelines</td>
<td>Sub-therapeutic treatment</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>27</td>
<td>9</td>
<td>Revised antibiotic guidelines to be approved and implemented</td>
<td>RT – March 2008</td>
</tr>
<tr>
<td>Not monitored appropriately</td>
<td>Antibiotic guidelines</td>
<td>Toxic treatment level</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>36</td>
<td>12</td>
<td>Sticker system as above</td>
<td>As above</td>
</tr>
<tr>
<td></td>
<td>Pharmacist and Microbiologist intervention</td>
<td>Inadequate treatment level</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>27</td>
<td>9</td>
<td>Standardised approach by Microbiologists</td>
<td>DTC – March 2008</td>
</tr>
</tbody>
</table>
Appendix D – Existing antibiotic guideline extract

2.3.2 Aminoglycosides
Aminoglycosides are used systemically in one of two ways:

Multiple daily dosing bd/tds
In multiple daily dosing (bd/tds regimens), trough levels should be less than 2, and preferably less than 1 in prolonged treatment eg endocarditis. Levels should be collected immediately pre-dose. Peak levels should ideally be 5 - 10 mg/L and be collected one hour post-dose.

Once a Day Aminoglycosides (Gentamicin/Tobramicin)
Once daily administration of a single large dose of aminoglycoside enables rapid achievement of effective levels and may be less toxic. In addition it is easier to calculate the correct dose and monitor levels.

Contraindications
This schedule is NOT appropriate for the following:
Children especially neonates
Patients who are pregnant
Patients with endocarditis, cystic fibrosis, gross ascites or major burns.
Patients with an eGFR <20 (serum creatinine >200) should not be treated without prior discussion with the microbiologist.

Dosing schedule
Initial dose
This must be approximately 7mg/kg body weight (refer to table below) administered by iv. infusion over 1 hour in 100ml 0.9% Sodium Chloride or 5% glucose. Doses other than 7mg/kg cannot be interpreted from the nomogram.

The dose should be written in the ‘once only’ section of the prescription chart.

Subsequent doses
Do not give a second dose until level confirmed from first dose. This will indicate the frequency of dosing as either 24 hourly or less frequently.

Note that changes are made in dosing interval – the dose remains constant at 7mg /kg.

Serum level monitoring
Take a sample between 6 and 12 hours after the start of the infusion. The following information must be clearly stated on the request form:
Time infusion started
Time sample was taken
Dose administered

Cautions with once daily Aminoglycoside
Renal toxicity with gentamicin is more likely in the elderly, those who are septic or on other potentially nephrotoxic drugs e.g. NSAID, ACE inhibitors or diuretics, regardless of initial creatinine. In such patients, the continued need for gentamicin should be reviewed daily and should not generally exceed 3 days.

Once a day Aminoglycosides (Hartford Nomogram)
The table below may be used to calculate the dose of aminoglycosides required. It gives typical body weights based on height and the corresponding aminoglycosides dose. If there is a difference between the dose calculated from the actual body weight and the dose from the table below, the dose calculated directly from body weight is preferable. It applies to adults only.
Select the patient’s height from the left hand column and check that their actual weight is within the range given in the appropriate male or female column. The dose and injection volume (of 80mg/2ml strength) is then given in the column to the right of the weight range. This should be diluted in 100ml of 0.9% Sodium Chloride or 5% glucose and administered by infusion over one hour. For patients outside these weight ranges for a particular height, it may be necessary to adjust the dose. Consult pharmacy for advice.
Once Daily Aminoglycosides Nomogram
Q24h Dose every 24 hours
Q36h Dose every 36 hours
Q48h Dose every 48 hours

NOTE: If dose, time of administration and time of sampling are on request form, the pharmacy will do the calculations for you.
### Appendix E – Balanced Scorecard

#### Benefits

<table>
<thead>
<tr>
<th>Objective</th>
<th>Measure</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safer treatment provision</td>
<td>Reduced claims, incidents and complaints</td>
<td>Risk assessment rating reduced</td>
</tr>
<tr>
<td>Cost effective treatment</td>
<td>Antibiotic usage audit</td>
<td>Compliance with policy</td>
</tr>
<tr>
<td>Staff time saving</td>
<td>Level of intervention by Pharmacists and Consultant Microbiologists</td>
<td>Intervention rates reduced</td>
</tr>
</tbody>
</table>

#### Patient Outcomes

<table>
<thead>
<tr>
<th>Objective</th>
<th>Measure</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient experience</td>
<td>Complaint and claim rates</td>
<td>No complaints or claims</td>
</tr>
<tr>
<td>Patient safety</td>
<td>Incident rates</td>
<td>No harm incidents occur</td>
</tr>
<tr>
<td>Effective treatment</td>
<td>Clinical outcomes framework</td>
<td>Improved mortality and morbidity</td>
</tr>
</tbody>
</table>

#### Pathways/ Processes

<table>
<thead>
<tr>
<th>Objective</th>
<th>Measure</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appropriate prescribing</td>
<td>Antibiotic usage audit</td>
<td>Correct dose and interval prescribing</td>
</tr>
<tr>
<td>Appropriate administration</td>
<td>Documentation audit</td>
<td>Correct dose and interval administration</td>
</tr>
<tr>
<td>Effective monitoring</td>
<td>Web-based calculator usage rate</td>
<td>Correct monitoring and interpretation of results</td>
</tr>
</tbody>
</table>

#### Capability

<table>
<thead>
<tr>
<th>Objective</th>
<th>Measure</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate training</td>
<td>Included in relevant induction program</td>
<td>Nurses, doctors and pharmacists are trained when they start</td>
</tr>
<tr>
<td>Competent workforce</td>
<td>Intervention rates</td>
<td>Reduced need for intervention</td>
</tr>
<tr>
<td>Safety culture</td>
<td>MaPSaF</td>
<td>Improved safety culture</td>
</tr>
</tbody>
</table>
Appendix F – Workstream brief
Workstream 3: Technical information (Staff information)

Stakeholders:

Lead: Robyn Thompson, Principal Pharmacist

Team: Rick Dickinson, Risk Manager
Liz Gilbert, Principal Pharmacist (Risk)
Nick Adams, Principal Pharmacist
Lisa Price, Information Pharmacist
Bethan Stoddart, Microbiologist
Ruth Wilne, Principal Pharmacist (Procurement)

Others – to be determined

Problem:

Poor labelling and poor availability and access to technical information of how to use medicines increases risk associated with preparation, administration and monitoring of injectable medicines – leading to errors

Subject and settings:

Provision of information for staff.

Injectable Medicine of Choice:

Gentamicin

Aim:

To investigate and demonstrate that purchasing medicines that include technical information about preparation and administration will reduce the clinical risk and medication error associated with lack of effective information on label and in package to inform staff of technical information associated with the use of the injectable medicine.

Key research questions:

1. What risk reduction measures need to be identified and evaluated in relation to injectable therapy?
2. What criteria and information need to be specified for staff information leaflet?
3. How else can information be made available?
4. What are the associated costs and how can they be estimated?
5. How can patient safety improvements be implemented?
6. How can manufacturers contribute to this issue in delivering patient safety?
7. What are the National actions required, and what barriers do exist?
8. How can this contribute to designing a purchasing for safety framework and checklists in pharmaceuticals?
9. Can a common approach be employed in sharing work across the 3 pilot Trusts?

Objectives:

5. To identify high risk injectable medicines that would require staff information leaflets as a risk reduction strategies
6. To identify risk reduction measures in relation to the injectable therapy with labelled and packaged information preparation and use
7. To propose and implement patient safety improvements for the use of Gentamicin.
8. To estimate the costs associated with proposed risk solutions
9. To identify barriers which might hinder the implementation of a purchasing for safety initiative and propose solutions where appropriate.

Project deliverables & milestones:

1. Review the systems in place to manage Gentamicin and develop solutions to the risks associated with its use.
2. Consider methods for provision of information to staff
3. Consider the key information set required for reconstitution and administration
4. Survey staff to find a preferred content, format and style to staff information leaflets or similar
5. Pilot the use of the Gentamicin solutions proposed, with the appropriate implementation and selection of location(s) to pilot.
7. Evaluate the effectiveness of proposed changes in practice.
8. Provide a report on the outputs from the workstream
9. Provide a process map to illustrate the steps taken as part of this workstream
10. Methodology for evaluating progress and benefits against baseline/benefits tracking tool.

Milestones:

Oct 2007 Start Objective 1-2; Set up work stream, identify stakeholders, agree brief and action plan; Plan Objective 3
Nov 2007 Start Objective 3, Complete Objectives 1-3, plan and start Objectives 4-5
Dec 2007 Complete Objective 4, plan and start Objectives 5-6
Jan 2008 Complete Objectives 5-6, plan and start Objectives 7-10
Feb 2008 Complete Objectives 7-10

Measures:

To be identified during Objective 1 of the workstream
Challenges to the workstream

1. MHRA regulation
2. Manufacturer- licensing process prolongation
3. Sourcing options need to be evaluated when a service is being purchased (pre-prepared products) implying time and complexity to the process