B3.1 Management of Multi-Resistant Organisms

B3.1.1 What are the risks?

MROs, which are predominantly bacteria, are resistant to multiple classes of antimicrobial agents. Antibiotic resistance increases the morbidity and mortality associated with infections, and contributes to increased costs of care due to prolonged hospital stays and other factors, including the need for more expensive drugs (Struelens 1998). A major cause of antibiotic resistance is the exposure of a high-density, high-acuity patient population in frequent contact with healthcare workers to extensive antibiotic use, along with the attendant risk of cross-infection (Gold & Moellering 1996; Christiansen et al 2008).

For the purpose of these guidelines, MROs are taken to include:

- all methicillin-resistant *Staphylococcus aureus* — MRSAs cause up to a third of hospital-acquired bloodstream infections (Christiansen et al 2008), with mortality from BSI ranging from 10% to 50% according to the setting (Herwaldt 1999);
- all vancomycin-resistant enterococci with mobile resistance determinants (e.g. VanA, VanB) — the ratio of invasive VRE infection to colonisation appears to be proportionately lower than that of MRSAs (Christiansen et al 2008); and
- a range of Gram-negative bacteria with multiple classes of drug resistance or resistant mechanisms to critically important antibiotics — highly transmissible resistance is a particular feature of antibiotic resistance among the Gram-negative bacteria, especially the Enterobacteriaceae. Multi-drug resistance is also common and increasing among non-fermenting Gram-negative bacteria (e.g. *Pseudomonas aeruginosa* and *Acinetobacter baumannii*) and a number of strains have now been identified that exhibit resistance to essentially all commonly used antibiotics. These organisms are associated with treatment failure and increased morbidity (Christiansen et al 2008).

A two-level approach is necessary for the prevention and control of MROs. This involves implementation of:

- core strategies for MRO prevention and control in any situation where MRO infection or colonisation is suspected or identified (see Section B3.1.2); and
- organism-based or resistance mechanism-based approaches if incidence or prevalence of MROs are not decreasing despite implementation of the core strategies (see Section B3.1.3).

In the event of an MRO outbreak, investigation and control/containment should be conducted as outlined in Section B3.2.

The best practices in these guidelines are based on the assumption that healthcare settings already have basic infection prevention and control systems in place. If this is not the case, healthcare settings will find it challenging to implement the practices recommended for the management of MRSA and VRE. These settings must work with organisations that have infection prevention and control expertise, such as academic health science centres, regional infection control networks, public health units that have professional staff certified in infection prevention and control and local infection prevention and control associations to develop evidence-based programs (PIDAC 2007).

B3.1.2 Core strategies for MRO prevention and control

Successful control of MROs is based on a combination of interventions. These involve continued rigorous adherence to hand hygiene, appropriate use of PPE and implementation of specific transmission-based precautions (isolation of infected or colonised patients, increased environmental cleaning and patient-dedicated equipment) until patients are culture-negative for a target MRO or have been discharged from the facility.

In non-acute healthcare settings, general measures of infection control (particularly hand hygiene by both patients and healthcare workers) may be enough to prevent transmission. However, contact precautions, such as gowns and gloves, may be necessary if the patient is heavily colonised or there is known continuing transmission. Local guidelines and circumstances should determine practice in settings where the patient population is vulnerable (Matlow and Morris 2009).

Organisational measures — such as staff education on prevention and management of MRO transmission, antibiotic stewardship program, and appropriate response to active surveillance cultures — are discussed in Part C.
Hand hygiene

MROs can be carried from one person to another via the hands of a healthcare worker. Contamination can occur during patient care or from contact with environmental surfaces in close proximity to the patient, particularly when patients have diarrhoea and the reservoir of the MRO is the gastrointestinal tract. Effective hand hygiene is therefore the most important measure to prevent and control the spread of MROs. Alcohol-based hand rub of at least 70% v/v ethanol or equivalent has been shown to be effective against MRSA and VRE (Picheansathian 2004).

Personal protective equipment

Both direct patient contact (e.g. routine patient care) and indirect contact (e.g. involving environmental contamination) can lead to contamination of the healthcare worker’s hands and clothing. Appropriate use of gloves has been found to be as effective a strategy as patient isolation in containing MROs, particularly when isolation may not be feasible (Trick et al 2004; Bearman et al 2007). Glove use is more effective when combined with wearing of gowns (Puzniak et al 2002; Srinivasan et al 2002; Hayden et al 2008). Section B1.2.3 provides guidance on the selection of an appropriate gown and Section B1.2.5 on selection of gloves.

Isolation

Placing colonised or infected patients in single rooms, cohort rooms or cohort areas as a component of a multifaceted infection control policy can reduce acquisition rate and infection with MROs in acute-care settings. Cohorting patients with the same strain of MRO has been used extensively for managing outbreaks of specific MROs, including MRSA, VRE, extended spectrum beta-lactamase (ESBL)-producing bacteria, and Pseudomonas aeruginosa. However, it is not always appropriate to cohort patients with the same MRO species if they have a different resistance mechanism or phenotype (e.g. if one has a community-acquired strain of likely panton-valentine leukocidin (PVL)-positive MRSA and the other has a hospital-acquired strain of MRSA).

In long-term care facilities, isolation and cohorting may not be possible, so hand hygiene with appropriate routine use of gloves for individual resident and environmental contact is preferred (Trick et al 2004).

Due to the varying nature of healthcare facilities, it is not feasible to provide a generic policy on the movement of patients with MROs. This needs to occur at a local level and be relevant to the patient’s treatment plan. These policies should not limit access to treatment and should consider the social implications of managing a patient with an MRO.

Environmental cleaning

In acute-care areas where the risk of patient vulnerability and risk of cross infection due to the presence of an MRO is high, contact precautions should be followed. This will require all patient surrounds and frequently touched objects (e.g. bedrails, trolleys, bedside commodes, doorknobs, light switches or tap handles, ensuite facilities) to be cleaned with a suitable detergent and disinfected with a TGA-registered hospital grade disinfectant.

As outlined in Section B1.4 this process must involve either:

- a 2-step clean, which involves a physical clean using detergent solution followed by use of a chemical disinfectant; or
- a 2-in-1 clean in which a combined detergent/disinfectant wipe or solution is used and mechanical/manual cleaning action is involved.

Sole reliance on a disinfectant without mechanical/manual cleaning is not recommended.

Patient equipment

Standard precautions concerning patient-care equipment are very important in the care of patients with MROs. Patient-care devices (e.g. electronic thermometers) may transmit infectious agents if devices are shared between patients. To reduce the risk of transmission, disposable or patient-dedicated equipment is preferred. Section B1.5 provides more detailed information on reusable instruments and equipment.

Monitoring

Monitoring of the incidence of target MRO infection and colonisation should continue after these interventions are implemented. If rates do not decrease, more interventions may be needed to reduce MRO transmission as outlined in Section B3.1.3.

Recommendation
24 Implementation of core strategies in the control of MROs (MRSA, MRGN, VRE)  

Implement transmission-based precautions for all patients colonised or infected with an MRO, including:

- performing hand hygiene and putting on gloves and gowns before entering the patient-care area;
- using patient-dedicated or single-use non-critical patient-care equipment;
- using a single-patient room or, if unavailable, cohorting patients with the same strain of MRO in designated patient-care areas; and
- ensuring consistent cleaning and disinfection of surfaces in close proximity to the patient and those likely to be touched by the patient and healthcare workers.

Patient-care tip

When patients are placed on transmission-based precautions due to infection or colonisation with an MRO, efforts should be made to ensure patients continue to receive adequate medical care, and to counteract potential psychological adverse effects of isolation such as anxiety and depression, and feeling of stigmatisation.

B3.1.3 Organism-specific approach

When the incidence or prevalence of MROs is not decreasing despite implementation of the core strategies outlined above, further measures to control transmission need to be considered. A risk management approach focuses on:

- the type of MRO (e.g. prioritisation of available isolation facilities according to MRO);
- the healthcare area (e.g. intensive care or haematology/oncology units have higher risks of transmission);
- patient factors (e.g. whether the consequences of infection are severe);
- available resources (e.g. whether screening a certain patient population is feasible); and
- whether interventions to interrupt transmission are available (e.g. decolonisation for MRSA).

Further measures may include:

- **targeted screening** — timely active screening to identify colonised patients combined with the use of contact precautions for the care of colonised patients has been followed by a significant reduction in the rates of both colonisation and infection of patients with MRSA (Calfee and Farr 2002; Pop-Vicas and D-Agata 2005). Screening involves collecting specimens from the patient and subsequent laboratory analysis of these samples. In a risk assessment approach to screening, considerations include the endemicity of the MRO, the prevalence of MRO infection, and the likelihood of MRO carriage. Clinicians and the infection control professional should be informed of both negative and positive screening results promptly. If screening returns a positive sample, contact precautions should be applied and appropriate use of isolation and cohorting facilities should be implemented.

- **decolonisation** — interventions may be topical — whole body washes (using chlorhexidine) and topically applied antimicrobial agents (e.g. mupirocin); systemic — orally administered antibiotics (tetracyclines, fusidic acid, ciprofloxacin, rifampin and trimethoprim-sulfamethoxazole); and combinations of systemic and topical therapy.

- **surveillance and timely feedback** — increased surveillance may be appropriate to monitor the effect of interventions designed to control particular MROs. Surveillance information should be fed back to health care workers and facility management promptly.

Screening

Currently there is no consensus nationally or internationally about the most appropriate manner to conduct screening for MROs. Control measures specific to local factors should be determined and endorsed by the healthcare facility management structure, and the screening protocols for MROs should be influenced by the:

- local prevalence of the MRO;
- the reason for admission of the patient;
- the risk status of the unit to which they are admitted; and
- the likelihood that the patient is carrying an MRO.

As a minimum standard to reduce the risk of transmission of MROs, it is recommended that the following approaches to screening be implemented. Expert direction and resources allocation is required for effective MRO screening.
The decision to screen for VRE and MRGN is optional and should be made on the basis of local epidemiology, necessity for screening and resource factors. The following tables provide guidance for screening based on patient risk factors for these organisms. Other risk groups may be defined by local experience, based on screening initiatives or outbreak epidemiology.

For example some facilities have found that screening patients who are recent hospital admissions from international facilities into Australian facilities have increasingly been shown to be positive for MRGN. While this is an area for future research, currently, healthcare facilities could consider screening these patients on admission, particularly in areas where MROs are found to be prevalent in transferred patients.

Table B3.1: Suggested approach to screening for MRSA

<table>
<thead>
<tr>
<th>Organism</th>
<th>Screen who</th>
<th>Screen when</th>
<th>Sample collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA</td>
<td>Patients at high risk of carriage:</td>
<td>Screened routinely at the time of admission unless they are being admitted directly to isolation facilities and it is not planned to attempt to clear them of MRSA carriage</td>
<td>Multiple sites including one from the nose and a mucosal surface</td>
</tr>
<tr>
<td></td>
<td>- those who are known to have been previously infected or colonised with MRSA</td>
<td></td>
<td>Reasonable sites to swab include nares, skin lesions and wounds, sites of catheters, catheter urine, groin/perineum, tracheostomy and other skin break in all patients, and sputum from patients with a productive cough</td>
</tr>
<tr>
<td></td>
<td>- frequent re-admissions to any healthcare facility</td>
<td></td>
<td>Where maximum sensitivity is required, consideration should be given to adding a throat swab. The umbilicus should be sampled in all neonates</td>
</tr>
<tr>
<td></td>
<td>- transfers from other acute care facility</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- residence in long term care facilities</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- patients with chronic wounds</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- recent inpatients at hospitals known or likely to have a high prevalence of MRSA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- locales or populations where community-acquired strains of MRSA are prevalent</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Healthcare workers epidemiologically linked to single-strain outbreak in health care facility

After confirmation of epidemiological evidence 2 weeks after decolonisation therapy

Patients in high-risk units

ICU/high dependency unit (admission and discharge)
Spinal unit
Burns unit
Pre-operative clinics
Patients with planned prosthetic surgery (joint replacement, cardio-thoracic surgery)

All patients on admission, discharge and once weekly

Management

Apply stringent hand hygiene, contact precautions (gloves and gown) and core strategies outlined in B.3.1.2 including isolating and cohorting patients, increased environmental cleaning and dedicated patient equipment.

Patients positive for MRSA have an electronic alert placed on their case record for easy identification on readmission.

Consider topical plus/minus systemic decolonisation for:

Healthcare workers epidemiologically linked to transmission
Patients having prolonged hospitalisation
Patients with chronic conditions likely to be readmitted (e.g. haemodialysis).
Patients before undergoing high-risk elective surgery such as cardiac and implant surgery

Table B3.2: Suggested approach to screening for VRE and MRGN dependent on local acquisition rates

<table>
<thead>
<tr>
<th>Organism</th>
<th>Suggested targeted screening dependent on local acquisition rates</th>
<th>Frequency of screening</th>
<th>Sample collection</th>
</tr>
</thead>
</table>
### VRE

<table>
<thead>
<tr>
<th>High risk units</th>
<th>For endemic VRE screen on admission to intensive care unit, discharge and once weekly</th>
<th>Multiple sites including rectal or perianal swabs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive care unit</td>
<td></td>
<td>Reasonable sites include groin, wounds and respiratory secretions or tracheal aspirates depending on the infectious agent</td>
</tr>
<tr>
<td>Nephrology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haematology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid organ transplant unit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients epidemiologically linked to single-strain outbreak in health care facility</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Patients at high risk of carriage

- Dialysis patients
- Recent hospitalisation in any health care facility
- Critical illness in intensive care units
  - Long duration of stay and severity of illness
- Chronic disease and impaired functional status
- Patients with urinary catheters
- Prolonged or broad-spectrum antibiotic use, particularly vancomycin

### MRGN

<table>
<thead>
<tr>
<th>High risk units</th>
<th>Multiple sites including rectal or perianal swabs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive care unit</td>
<td>Reasonable sites include nares, groin, wounds and respiratory secretions or tracheal aspirates depending on the infectious agent</td>
</tr>
<tr>
<td>Solid-organ transplant unit</td>
<td></td>
</tr>
<tr>
<td>Speciality centres (e.g. burns, neurosurgery)</td>
<td></td>
</tr>
<tr>
<td>Patients epidemiologically linked to single-strain outbreak in health care facility</td>
<td></td>
</tr>
</tbody>
</table>

#### Patients at high risk of carriage

- Those with recent broad spectrum antibiotic therapy (carbapenem, quinolones, and 3rd and 4th generation cephalosporins)
- Long duration of stay and severity of illness
- Chronic disease and impaired functional status
- Presence of invasive medical devices

### Management

**Staff screening and decolonisation is not recommended for VRE and MRGN**

Apply stringent hand hygiene, contact precautions (gloves and gown) and core strategies outlined in B.3.1.2 including isolating, cohorting, increased environmental cleaning and dedicated patient equipment. Patients positive for VRE or MRGN should have an electronic alert placed on their case record for easy identification on readmission.
MRO clearance

Based on the 2005 Multi-Resistant Organism Screening and Clearance Recommendations the following criteria should be satisfied prior to certifying that a patient has cleared a particular MRO:

- more than 3 months elapsed time from the last positive specimen;
- all wounds healed, no indwelling medical devices present;
- no exposure to any antibiotic or antiseptic body wash for at least 2 weeks prior to screening;
- in the case of MRSA, no exposure to specific anti-MRSA antibiotic therapy in the past three months; and
- consecutive negative screens from above screening sites on two separate occasions OR evaluation of a single set of screening swabs with a broth amplification technique.

Some patients with VRE may appear to ‘clear’ with time but relapse with antibiotic therapy. Where VRE or MRGN are prevalent, admission and interval screening in specialised units is an important way to detect new or relapsed VRE or MRGN colonisation.

These criteria are based on evidence related to MRSA. It is recognised that there is variation in clearance methods between jurisdictions, but currently there is insufficient evidence to recommend the most effective method of demonstrating clearance of a particular MRO. This is an area that warrants further research. The important issue appears to be sampling the patient on more than two occasions separated in time. This period should not be less than 3 weeks but is typically months.

Examples of successful approaches

With an incidence rate of 1.09 per 100,000 population in 2006, Western Australia (WA) has consistently reported low rates of acquisition of MRSA compared to other states in Australia (Ferguson 2007). Tables B3.3 and B3.4 provide examples of approaches that have been successful in reducing rates of cross-transmission in hospitals in WA. It is acknowledged that approaches will vary across jurisdictions, depending on the setting (e.g. available resources and access to laboratory techniques).

Table B3.3: Example of a successful strategy to prevent endemicity of MRSA in a tertiary hospital in WA
<table>
<thead>
<tr>
<th>Patient screening</th>
<th>Infection control precautions</th>
<th>Decolonisation strategies</th>
<th>Sample collection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients hospitalised or in long-term care facility outside WA in previous 12 months</td>
<td>Core strategies plus Contact precautions:</td>
<td>Topical plus/minus systemic</td>
<td>Multiple sites including the nose and a mucosal surface</td>
</tr>
<tr>
<td>Healthcare workers who have worked outside WA in 12 months prior to commencing employment in WA</td>
<td>Single room or cohort</td>
<td>Healthcare workers</td>
<td>Reasonable sites to swab include nares, throat and wounds</td>
</tr>
<tr>
<td>Patients / healthcare workers epidemiologically linked to single-strain outbreak in healthcare facility</td>
<td>Gown and gloves</td>
<td>Patients having prolonged hospitalisation</td>
<td></td>
</tr>
<tr>
<td>Patients from WA long-term care facilities</td>
<td></td>
<td>Patients with chronic conditions likely to be readmitted</td>
<td></td>
</tr>
<tr>
<td>Patients in high-risk units:</td>
<td></td>
<td>Clearance only after negative screening swabs on at least three occasions over a ten week period</td>
<td></td>
</tr>
<tr>
<td>ICU/high dependency unit (admission and discharge)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spinal unit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burns unit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-operative clinics</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patients positive for MRSA have an electronic alert placed on case record for easy identification on readmission.

**Table B3.4: Example of a successful strategy to prevent endemicity of VRE in a tertiary hospital in WA**
Patients epidemiologically linked to single-strain outbreak in health care facility
- Dialysis patients monthly
- High risk units (admission and discharge)
  - Intensive care unit
  - Nephrology
  - Haematology
  - Solid organ transplant unit
  - Transfers from hospitals outside WA

Patients positive for VRE have electronic alert placed on case record for easy identification on readmission.

Decolonisation not possible

Healthcare workers not screened

Footnotes:

B3.1.4 Antibiotic stewardship

Over the last 40 years, the prevalence of MROs such as MRSA has risen alarmingly, initially mainly in hospitals but now increasingly in the community. There is good evidence that overall rates of antibiotic resistance correlate with the total quantity of antibiotics used, as determined by the number of individuals treated, prior exposure and the average duration of each treatment course. Some antibiotics promote the development of resistance more readily than others, depending in part on the breadth of their antibacterial spectrum. In individuals, the risk of colonisation and infection with MROs correlates strongly with previous antibiotic therapy.

Unnecessary antibiotic use for self-limiting or non-infective illness and inappropriate antibiotic choice, dose or duration of therapy drives the selection of resistant bacteria, disrupts normal bacterial flora and increase the risk of colonisation with resistant organisms. There is a lag period between acquisition of an MRO and its detection; during this period, the infection may spread between patients if risk factors for acquisition are not considered carefully. Clinicians may be under pressure to prescribe broad-spectrum agents against likely pathogens in an environment where MROs are common, thereby further increasing the development of resistant organisms.

As many as 25–50% of antibiotic regimens prescribed in hospitals may be inappropriate. The reasons for the continued unnecessary and/or inappropriate use of antibiotics, in the face of increasing antibiotic resistance and availability of well-established evidence-based treatment guidelines, are varied.

Antibiotic stewardship programs involve a systematic approach to optimising the use of antibiotics (see Section C5). Effective hospital antibiotic stewardship programs have been shown to decrease antibiotic use and improve patient care. Along with infection control, hand hygiene and surveillance, antibiotic stewardship is considered a key strategy in local and national programs to decrease MROs and HAIs.

Note: This section is drawn from ACSQHC (2009) National Report on Antibiotic Stewardship.

B3.1.5 Risk-management case study

VRE outbreak in a large tertiary-care referral hospital

Two months after the first index case of VRE was detected in the intensive care unit of a large teaching hospital, 68 patients had become either infected or colonised with an epidemic strain of vanB vancomycin-resistant Enterococcus faecium, despite standard infection control procedures. Subsequently, 169 patients in 23 wards were found to be colonised with a single strain of vanB vancomycin-resistant E. faecium. Introducing additional control measures rapidly brought the ...
outbreak under control. Hospital-wide screening found 39 previously unidentified colonised patients, with only 7 more non-segregated patients being detected in the next 2 months. The outbreak was terminated within 3 months due to a well-resourced, multifaceted approach.

Source: Based on Christiansen et al (2004).

<table>
<thead>
<tr>
<th>Eliminating risks</th>
<th>In this situation, it is not possible to eliminate risk immediately, so it must be managed.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identifying risks</td>
<td>In this case, the risk has been identified as cross-transmission of VRE.</td>
</tr>
<tr>
<td>Analysing risks</td>
<td>The source of the risk is multidrug resistance coupled with a vulnerable patient population (intensive care unit). Each time there is contact with an infected patient there is potential for cross-transmission to the healthcare worker and/or other patients.</td>
</tr>
<tr>
<td>Evaluating risks</td>
<td>The balance of likelihood and consequences identify this as a ‘very high risk’ situation requiring immediate response.</td>
</tr>
<tr>
<td>Treating risks</td>
<td>Immediate measures to control the outbreak may include;</td>
</tr>
<tr>
<td></td>
<td>- formation of a VRE executive group;</td>
</tr>
<tr>
<td></td>
<td>- rapid laboratory identification (30 to 48 hours) using culture and polymerase chain reaction detection of vanA and vanB resistance genes;</td>
</tr>
<tr>
<td></td>
<td>- screening of hospitalised patients with isolation of patients and cohorting of contacts;</td>
</tr>
<tr>
<td></td>
<td>- increased cleaning;</td>
</tr>
<tr>
<td></td>
<td>- electronic flagging of medical records of contacts; and</td>
</tr>
<tr>
<td></td>
<td>- antibiotic restrictions (third-generation cephalosporins and vancomycin).</td>
</tr>
</tbody>
</table>

In the longer term, hospital policies may be changed to restrict antibiotic use, institute targeted screening and increase environmental cleaning efficiency and frequency.

These measures are relevant to a recent outbreak in an area of low endemicity. Some of these approaches may also be relevant in an area of high endemicity.

| Monitoring         | Repeated screening would identify whether the outbreak recurred. |