Inquiry into the progress in the implementation of the recommendations of the 1999 Joint Expert Technical Advisory Committee on Antibiotic Resistance

Department of Health and Ageing responses to Questions on Notice

1. In his submission Professor Grayson (sub 19) addressed improved hygiene through use of alcohol-based hand rub and bleach-based cleaning.
    a. Do microbes develop resistance to the broad range of things we do to try to defeat them, or are there particular things that are more susceptible?
    b. For example, will microbes become resistant to hand washing, cleaning with bleach and cooking food, in the same way they are becoming resistant to antimicrobial drugs?

Response:
Microorganisms can become resistant to certain disinfectants (e.g. triclosan-containing products) however, resistance has not been reported to alcohol or bleach. Alcohol-based hand-rub remains effective against bacteria carried on the skin.

Some viruses (e.g. norovirus) and some bacterial spores (e.g. those associated with *C. difficile*) are inherently resistant to alcohol, and it is for this reason that alcohol-rub is not recommended in such outbreaks. The resistance displayed by these microorganisms is inherent rather than developing due to resistance mutation.

Bleach is an ideal disinfectant because it is highly effective against all bacteria (including those that produce spores), viruses (including HIV) and fungi, if used in the correct concentrations.

Heat (e.g. as used in cooking) is effective for killing bacteria, but its efficacy is dependent on the temperature attained and the duration of heat exposure (i.e. high heat for long periods is more effective than lower temperatures or short-duration cooking).

2. In his submission Professor Grayson highlighted the importance of single rooms in hospitals.
    a. Are you able to provide the committee with any studies that have addressed this issue and provide evidence of reduced infection rates or reduced resistance?
    b. What is the current proportion of beds in hospitals that are in single rooms and what is the trend over the past decade?
    c. What are current policy and guidance settings in relation to single rooms in hospitals?

Response:
a) The importance of spatially separating infected patients has been well-known since the days of Florence Nightingale and was the basis for the design of communicable disease hospitals prior to the discovery of antibiotics. However, since the development of antibiotics many of these basic principles have been changed in hospital design, as the use of antibiotics often "compensated" for any patient-to-patient-transmission of infections.

Dr Roger Ulrich is a recognised leader in evidence-based healthcare design and has produced many publications on this issue. His research indicates that improved design of NHS buildings can have a significant impact on the control of infection in clinical areas and help to reduce the more than £1bn annual cost burden of HCAIs (Ulrich and Wilson 2006).

The following article provides a useful synthesis of the literature:

- Ulrich, R., & Zimring, C., & Zhu, X., & DuBose, J., & Hyun-Bo, S., & Choi, Y.-S., & Quan, X., & Joseph, A. (2008). A review of the research literature on evidence-based healthcare design. *Health Environments Research & Design Journal,1*(3), 61-125.

A number of recently designed Australian hospitals (e.g. the new Royal Perth Hospital and the Royal Adelaide Hospital) have incorporated these key principles in their designs such that they each have about 80% single rooms, each with their own bathroom, to avoid sharing of toilet facilities.

There are many publications on this topic, including the following articles on various bacterial infections:

- Bracco D, Dubois MJ, Bouali R, Eggimann P. Single rooms may help to prevent nosocomial bloodstream infection and cross-transmission of methicillin-resistant Staphylococcus aureus in intensive care units. Intensive Care Med. 2007; 33(5):836-40.
- Vandenbroucke-Grauls CM. Methicillin-resistant Staphylococcus aureus control in hospitals: the Dutch experience. Infect Control Hosp Epidemiol. 1996; 17(8):512-3
- Heddema ER, van Benthem BH. Decline in incidence of Clostridium difficile infection after relocation to a new hospital building with single rooms. J Hosp Infect. 2011; 79(1):93-4

b and c) While the Australian Government makes a significant financial contribution to the delivery of public hospital services, state and territory governments are the public hospital system managers. This includes responsibility for setting policies relating to the number and allocation of single rooms. As a result, the Australian Government does not have visibility of the number of single rooms in hospitals. This question should be directed to state and territory governments.

3. Is the Department able to provide any examples from other countries which have been successful in reducing AMR or halting the growth rate?

Response:
AMR is recognised as a significant global public health issue, and although many countries are taking action to address this growing threat, local responses by individual countries in trying to prevent and contain AMR do vary. Furthermore, given the diversity in how different countries' health systems operate and are funded, it is very difficult to directly compare efforts.

Examples of successful initiatives internationally are noted below:

<u>European Centre for Disease Prevention and Control - Program impact</u>
The most recent annual report from the European Antimicrobial Resistance Surveillance Network (EARS-Net) states that 'national efforts on infection control and containment of resistance are effective, as illustrated by the trends for methicillin-resistant *Staphylococcus aureus* (MRSA), antimicrobial-resistant *Streptococcus pneumoniae* and antimicrobial-resistant enterococci, for which the situation appears generally stable or even improving in some countries'.

Reference: European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2011. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2012.

The Swedish Strategic Program against Antibiotic Resistance (STRAMA) - Program impact
In 2008, information on STRAMA's activities and achievements during the period 1995–2004 was published, noting the following outcomes:

- Antibiotic use for outpatients decreased by 20% from 157 to 126 defined daily doses per 1000 inhabitants per day.
- Antibiotic prescription presentation fell by 23% from 536 to 410 per 1000 inhabitants per year. In 2010, this figure had fallen even more, to 390 prescriptions per 1000 inhabitants per year.
- There was a 52% reduction in antibiotic use in children aged 5–14 years.
- The antibiotic class showing the greatest decline in use were macrolides (e.g. erythromycin), for which consumption fell by 65%.
- The epidemic spread of penicillin-resistant *Streptococcus pneumoniae* in southern Sweden was curbed.
- The number of hospital admissions for acute mastoiditis, rhinosinusitis and quinsy (peritonsillar abscess) was stable or declining; this was considered as an indication that there was no under prescribing and no measurable negative consequences.

Reference: Mölstad S, Erntell M, Hanberger H, Melander E, Norman C, Skoog G, Lundborg CS, Söderström A, Torell E, Cars O. Sustained reduction of antibiotic use and low bacterial resistance: 10-year follow-up of the Swedish Strama programme. *The Lancet Infectious Diseases.* 2008;8(2):125-132.

4. Friends of the Earth Australia in its submission raised the issue of the use of nano-silver in various medical and commercial forms.
    a. What are current policy and regulatory settings in relation to the use of nano-silver for nonmedical applications?
    b. What actions have been taken by the Government to date to address the problems raised regarding nano-silver?
    c. What have other countries done to address resistance problems arising from the use of nano-silver?
    d. Can you provide examples of whether those approaches have been successful?

Response:

a. As part of Australia's regulatory framework for industrial chemicals, the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) registers introducers of industrial chemicals, assesses industrial chemicals for their risks to human health and the environment, and where relevant, makes recommendations to Australian Government, state and territory regulators regarding risk mitigation.

   NICNAS maintains the Australian Inventory of Chemical Substances (AICS) to identify whether or not a chemical requires assessment as a 'new' chemical. *The Industrial Chemicals (Notification and Assessment) Act 1989* does not define nor specify regulatory requirements for industrial nanomaterials. Therefore, the regulatory settings that apply to conventional industrial chemicals also apply to their nano-forms. New industrial chemicals, including their nano-forms, must be notified and assessed before being manufactured or imported into Australia, whereas a chemical listed on AICS (such as silver), including its nano-forms, may generally be used without further notification or assessment.

b. The Department has not taken any specific actions relating to nano-silver, and notes that there are very limited data to support human toxicological risk assessment. Further studies are needed to understand the many forms of nano-

silver and their effects. Concerns that exposure to nano-silver may potentially lead to AMR are not supported by evidence of any increased bacterial resistance to silver in the medical literature.

c. The Department is unable to advise the Committee regarding actions other countries may have taken in relation to the use of nano-silver.

5. In its submission, the Australian Society for Infectious Diseases (Sub 18) noted that community acquired resistant infections have become more common. Are you able to provide the committee with information demonstrating the increase and reasons for the increase?
6. Please provide the committee with trends in infection rates of common resistant microbes in Australia. Where possible, also indicate the where the infection was acquired, for example in hospitals, in other health care, community acquired.
7. Please provide the committee with trends in resistance rates for common resistant microbes in Australia. Where possible, also indicate the where the infection was acquired, for example in hospitals, in other health care, community acquired.

Response (questions 5-7):
The Australian Group on Antimicrobial Resistance (AGAR) has conducted surveys over a number of years which provide some data on trends in infection rates, resistance patterns and source of infections. These are the best sources of data we have. The most problematic microorganisms from a clinical perspective are *Staphyloccus aureus* (golden Staph), enterococcal species, and a number of Gram-negative bacteria. The resistant infections due to these organisms are discussed below. All specimens from which bacteria were isolated were taken from patients with symptomatic infections.

Most surveillance data has been collected from hospitals, where resistant infections result in prolonged treatment. Data concerning resistance in community settings is limited and the problem is much lower. However from the data that is available, resistant community-acquired infections have also increased.

AGAR [2010 *S. aureus* community survey] reports that community-associated MRSA infections (CA-MRSA) have increased from 11.6% in 2000 to 18% in 2010. The reasons are uncertain, but possibilities being considered by AGAR include infection of individual patients in hospital with their colonising strain of *S. aureus*, or spread of CA-MRSA in the hospital environment with subsequent infection of other patients [AGAR 2011 *S. aureus* susceptibility report].

AGAR [Report on hospital *S.aureus* - June 2012] has also reported that the proportion of MRSA in hospital infections in Australia between 2005 and 2011 has remained relatively constant at about 30-34%. However the proportion of MRSA infections which are resistant to a number of other antibiotics has decreased. AGAR notes that by state and territory, resistance in hospitalised patients with invasive infections ranges from 14% to 44%.

AGAR data shows that since about 1997, resistance in *Enterococcus faecium* infections has been increasing significantly, and that this species now causes about 35% of enterococcal bacteraemia [AGAR 2012 – enterococcal sepsis report]. AGAR does not comment on the possible source of these infections. AGAR does note, however, that 38.5% of *E. faecium* infections are vancomycin resistant, and that by state and territory, resistance ranges from 9% to 46%.

Resistance to enterococcal species has been monitored by AGAR over a number of years [AGAR VRE report 2010]. Overall, *E. faecium* ampicillin resistance has increased from 60% in 1995 to about 85% in 2010, and vancomycin resistance has increased from extremely low levels in 1995 to about 37% in 2010. Similarly, gentamicin resistance in *E. faecium* has increased from 15% to 65% and in *E.faecalis* from 10% to 35% over the same period. In *E. faecium*, streptomycin resistance has remained relatively constant at about 50%, while in *E. faecium*, gentamicin resistance has declined from 18% to 8% over the same period. In summary, resistance in enterococci has increased since 1995, and has risen very markedly since about 2005. AGAR does not express a view as to what proportion of these infections are community and hospital acquired.

[The AGAR 2011 Gram negative survey does not provide trends or comment on CA or HA acquisition].

8. Attachment 3 to the joint submission by the Department of Health and Ageing has a table, listing 15 or so significant actions and outputs between 1998 and 2013. Please provide a revised table that includes a third column that sets out what outcomes have been achieved, focussing on evidence or examples where resistance or infection rates has been reduced, or slowed down.

Response:
An updated table is provided at Attachment A. It is important to note that outcomes achieved in relation to the management of AMR in Australia cannot easily be attributed to any one event, organisation or policy decision.

9. If possible, could the department provide the committee with the current guidelines for hospital staff on practices and procedures to minimise the development and spread of resistant microbes and infections caused by them.

Response:
A number of guidelines and other resources are available to assist hospitals in implementing policies and procedures to minimise the development and spread of resistant microbes, and to promote good infection control and hygiene practices.

National Safety and Quality Health Service (NSQHS) Standards
In September 2011, Health Ministers took a significant step towards improving Australia's health system by endorsing the NSQHS Standards and a national accreditation scheme. The NSQHS Standards are available at: http://www.safetyandquality.gov.au/our-work/accreditation/

The new system will, for the first time, create a national safety and quality accreditation scheme for health service organisations.

The most significant change in relation to antimicrobial stewardship is the Australian Commission on Safety and Quality in Health Care's (ACSQHC) work on the implementation of Standard 3 of the NSQHS Standards "Preventing and Controlling Healthcare Associated Infection".

Standard 3 ensures the appropriate prescribing of antimicrobials and requires that all healthcare services:

- Have an antimicrobial stewardship program in place

- Ensure that the clinical workforce prescribing antimicrobials have access to, and follow, current endorsed therapeutic guidelines on antibiotic usage
- Monitor antimicrobial usage and resistance is undertaken
- Act to improve the effectiveness of antimicrobial stewardship.

From 1 January 2013, the NSQHS Standards were mandated in all Australian public and private hospitals and day procedure services. This means that over 1500 hospitals and other health services will now be taking active steps to address antibiotic resistance.

Australian Guidelines for the Prevention and Control of Infection in Healthcare 2010
The ACSQHC worked with the National Health and Medical Research Council to develop national guidelines that would provide a coordinated approach to the prevention and management of healthcare associated infection.

In October 2010 the *Australian Guidelines for the Prevention and Control of Infection in Healthcare* were released to establish a nationally accepted approach to infection prevention and control. The guidelines provide an evidence base on which healthcare workers and healthcare facilities can develop detailed protocols and processes for infection prevention and control that are appropriate for their specific situation. The underpinning risk-management framework ensures the basic principles of infection prevention and control can be applied to a wide range of healthcare settings, including primary care and rural and remote centres.

Standardised Signage for Infection Prevention and Control
Following the release of the *Australian Guidelines for the Prevention and Control in Healthcare 2010*, and a subsequent national series of implementation workshops, the ACSQHC worked with jurisdictions to produce a series of signs for standard and transmission based precautions that can be used by all healthcare facilities.

National Hand Hygiene Initiative
The National Hand Hygiene Initiative has established a national hand hygiene culture-change program to standardise hand hygiene practice and placement of alcohol-based hand rub in every Australian hospital. The purpose of the National Hand Hygiene Initiative is to develop a national approach to hand hygiene.

In 2012, 569 hospitals contributed data to the national initiative, comprising over 90% of public hospitals and over 50% of private hospitals. Since data was first collected in 2009, the national compliance rate for hand hygiene has risen from 64% to 73% in 2012.

10. The dwindling R&D pipeline for developing new antimicrobials was noted by several submitters and witnesses. Even if a good R&D pipeline was in place and new antimicrobials were flowing through, would it just delay the ultimate problem until a time when superbugs would be resistant to an even greater number of antimicrobials? Is there a need to look at this problem in a different way so that an effective solution can be found?

Response:
It is not possible to speculate on the future of yet to be developed antimicrobial drugs. Researchers in Australia and around the world are working on novel alternatives to antibiotics, including antimicrobial vaccines, antimicrobial peptides and bacteriophages (viruses that infect bacteria).

However, even if innovative products are developed to combat antimicrobial resistant microorganisms or that will defeat resistance mechanisms, good stewardship of all antimicrobials will continue to be an important part of a comprehensive strategy to prevent and contain AMR.

11. The submission by the Australian Society for Antimicrobials noted that a future without antibiotics would be grim and highlighted issues for treatments including, but not limited to transplant surgery, haematology, cancer treatment, appendicitis, prostate biopsies, prosthetic joint replacement, and cardio-vascular surgery. What monitoring is currently undertaken on the extent to which the above treatments are being impacted by resistant microbes? Please provide data where possible.

Response:
The Department is not aware of any systematic monitoring of the impact of resistant microbes on these treatments. The AMR Prevention and Containment Steering Committee, jointly chaired by the Secretaries of the Department of Health and Ageing and the Department of Agriculture, Fisheries and Forestry, is reviewing the scope of current AMR surveillance activities in Australia, and considering options for the development of a comprehensive, national surveillance system for AMR.

12. The Committee notes that in an article in *The Age* on 15 March 2013 entitled 'Superbug reports spark concern', it was indicated that there have been cases of superbug infections following prostrate biopsies. Is the department able to provide information on the incidence of these superbug infections following biopsies?

Response:
The Department does not currently collect information on the incidence of infections following prostate biopsies.

13. Noting that antimicrobials include antibiotics, antiviral, antifungals, antiprotozoas and others, which group of antimicrobials has the biggest problem with resistance and why? Does the focus of effort need to be on a particular group, or are there different approaches needed for the different groups?

Response:
Of the groups of microorganisms mentioned, antibiotics cause most concern, followed by antivirals. Fungal, protozoan and other infections are less common, and accordingly drugs to treat these are less frequently used, the consequence of which is that selection pressure for the development of resistance is less. Most viral infections seen in Australia are either self-limiting, i.e. patients recover without specific antiviral treatment (e.g. the common cold), or vaccines are available (e.g. MMR, polio).

Bacteria cause serious or life-threatening infections more frequently than other microorganisms. Antibiotic treatment is often begun before, or instead of, a definitive laboratory diagnosis of the causative organism – known as empirical therapy. A laboratory diagnosis may not be available for a few days. This results in a greater selection pressure for bacterial resistance, particularly as the broad-spectrum antibiotics used in these situations promote resistance more effectively than the narrow-spectrum drugs that would be used if an accurate laboratory diagnosis was available.

This problem is being addressed on several fronts. Patients are being discouraged from requesting antibiotics for viral infections, doctors are prescribing narrow-spectrum antibiotics wherever possible, and rapid tests for bacterial infections, for example using DNA-based technologies, are being developed to reduce the need for empirical therapy. In addition, high dose, short duration therapy is expected to reduce the rate of relapse and emergence of resistant strains.