



Scottish Antimicrobial Prescribing Group

Surveillance of Antimicrobial Use and Resistance: Guidance for Antimicrobial Management Teams

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1. Timelines for implementation of recommendations

A key objective of this guidance is to align the surveillance of antimicrobial use and resistance at local and national level to support Antimicrobial Management Teams (AMTs) and front line staff to allow access to standardised information that is relevant to their own practice, ward or clinical area.

Timely and coordinated efforts to implement the required surveillance systems are essential to underpin the antimicrobial stewardship programme that currently is being implemented in all NHS boards.

SAPG **recommends** that the systems described in this guidance are **implemented no later than 31 March 2011**. For NHS boards that experience delays in the implementation of VITEK 2 interface (Observa 3 software) and HMUD, the required surveillance systems should be in place **no later than 6 months after successful implementation of VITEK 2 interface and/or HMUD**. In NHS Boards that are out with the scope of HMUD, plans should be developed to produce the required information on hospital use of antimicrobials.

Antimicrobial Management Teams should in conjunction with Infection Control Teams develop action plans for implementation of local surveillance systems, containing as a minimum the recommended systems described in this guidance and a communication strategy for dissemination of surveillance information to front line staff. **It is recommended that Action plans for local surveillance should be finalised by 31 December 2010.**

The guidance on surveillance of antimicrobial use and resistance will be issued in June 2010 and reviewed in April 2012.

2. Purpose

The purpose of this document is to support Antimicrobial Management Teams by describing the national surveillance programme for antimicrobial use and resistance and to provide guidance on the components of local surveillance that should be developed.

3. Background

Resistance to antimicrobial drugs is a recognised threat to public health and patient safety – it reduces the available treatment options and causes increased morbidity and mortality as well as increased costs due to failure of empirical antimicrobial therapy (¹Molstad, 2008). It is accepted that the way in which antimicrobials are used, sometimes inappropriately, will increase the selection pressure for antimicrobial resistance.

Implementation of national programmes which monitor antimicrobial use and resistance and which coordinate efforts to promote rational use of antimicrobials have been shown to be an efficient approach to preserving the effectiveness of antimicrobial agents. In Sweden, where a national programme was introduced in 1995, sustained reduction of antimicrobial use and low resistance rates have been observed over a decade (²Molstad, 2008). Rational use of antimicrobials also plays a key role in preventing and controlling *Clostridium difficile* infection (CDI).

The information workstream of Scottish Antimicrobial Prescribing Group (SAPG) is led by Health Protection Scotland (HPS) and Information Services Division (ISD) and supports the implementation of the 'Scottish Management of Antimicrobial Resistance Action Plan' (ScotMARAP). It is responsible for national surveillance relating to use and resistance of antimicrobials by collection, analysis and reporting of information. This is currently under development. A key objective is to align the surveillance of antimicrobial use and resistance at local and national level to support AMTs and front line staff to allow access to standardised information that is relevant to their own practice, ward or clinical area across the NHS in Scotland. The aims are to contain antimicrobial resistance, preserve the effectiveness of antimicrobial drugs, and preventing and controlling CDI.

This paper describes the national surveillance programme for antimicrobial use and resistance and provides guidance for AMTs and diagnostic microbiology laboratories on the key components of local surveillance programmes. National surveillance is not intended to replace local surveillance which is necessary to identify and act on unusual patterns of resistance and/or unexplained rises in antimicrobial resistance rates. Both national and local surveillance programmes are essential for the development of

effective antimicrobial stewardship programmes and should be complementary in the information gathered.

4. Feedback to prescribers and other clinical staff

An essential component of any surveillance system for antimicrobial use and resistance is the way in which information is made available to prescribers and other clinical staff. There must be an ethos of quality improvement in antimicrobial stewardship to inform clinical management of patients, prescribing policies and infection control interventions.

Information collected as part of national and local surveillance of antimicrobial use and resistance should be fed back to prescribers and other clinical staff in hospital and primary care by AMTs and others where appropriate. This will guide empirical therapy and interventions and help formulate local antimicrobial policies that can minimise the evolution, spread and persistence of resistant organisms (Fluit, 2006).

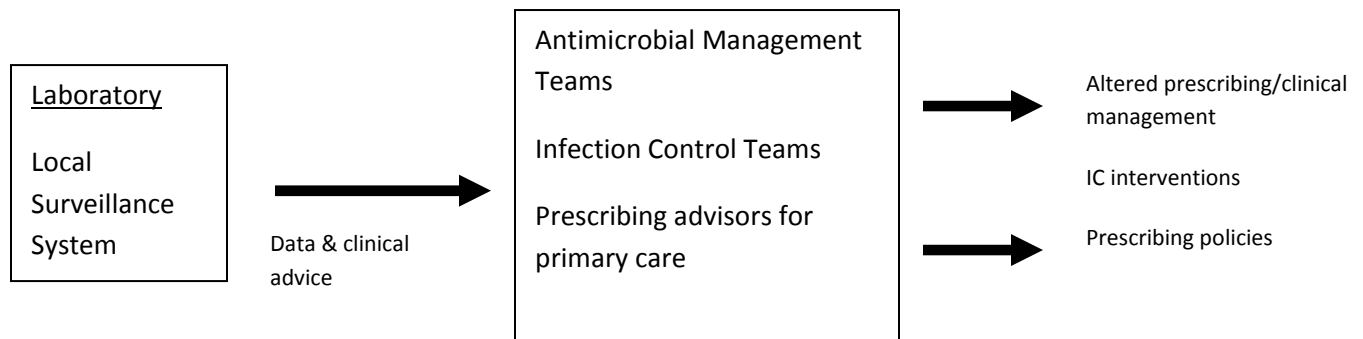


Figure 1. Feedback of surveillance data is an essential part of antimicrobial stewardship and supports and informs clinical management of patients, infection control interventions and prescribing policies.

5. National Surveillance

The aim of the national approach to surveillance of antimicrobial use and resistance is to provide standardised information to AMTs to support NHS Boards in their long-term strategic planning, implementation and evaluation of antimicrobial prescribing and infection control activities to preserve the effectiveness of antimicrobials used.

5.1 Use of antimicrobials

In 2009, SAPG in partnership with AMTs developed a set of national primary care prescribing indicators, which provide a broad overview of quantitative and qualitative information on the use of systemic antibacterials in primary care.

The information on the use of antibacterials in primary care is obtained from a database of all NHS prescriptions dispensed in the community in Scotland. ISD collate and present this information through a system known as Prescribing Information System for Scotland (PRISMS). PRISMS is a web-based system that is centrally updated by ISD on a monthly basis, three months behind real-time and always contains the most recent five years of information. The national prescribing indicators are available as routine standard reports to registered users of PRISMS.

The standard reports for national prescribing indicators present information on antibacterial usage at NHS Board level. PRISMS functionality allows registered users to access this information at Community Health Partnership and GP practice level.

The standard reports of national prescribing indicators present information on;

- Overall use of all antibacterials
- Seasonal variation of quinolones (to support HEAT target)
- Use of antibacterials recommended by SAPG
- Use of antibacterials associated with increased risk of CDI; cephalosporins, quinolones, co-amoxiclav and clindamycin
- Use of antibacterials by class; penicillins, cephalosporins, tetracyclines, macrolides, sulphonamides & trimethoprim and quinolones.

The national prescribing indicators express the use of antibacterials in numbers of Defined Daily Doses (DDD) and items.

The Defined Daily Dose (DDD) is the internationally recognised technical unit of measurement of medicine consumption. DDDs are recommended by the World Health Organisation (WHO) as the standard to allow comparative use of medicines over time and between different locations. The DDD is the assumed average maintenance dose per day for a medicine used in its main indication in adults. In general, the DDDs for antibacterials are based on their use in moderately severe infections. However, some antibacterials are only used in severe infections and their DDDs are assigned accordingly.

The use of number of items to depict activity refers to the number of times an antibacterial appears on prescription.

The national prescribing indicators present information on use of antibacterials expressed as total DDD per 1000 population in Scotland per day (DDD/1000/day) and number of items per 1000 population per day (items/1000/day). This allows comparison of usage over time.

Significant work is ongoing in ISD to deliver a national web based database of hospital use of medicines. Hospital Medicines Utilisation Database (HMUD) will collect information from individual hospital pharmacy systems and will present standardised information on the use of medicines at hospital and national level for a majority of NHS Boards in Scotland. The first clinical area to benefit from HMUD information will be surveillance of use of antimicrobials in a hospital setting. HMUD will allow registered users access to a range of standard reports on the use of antimicrobials at hospital level and to undertake specific hospital level analysis of antimicrobial use.

5.2 Antimicrobial Resistance

The national surveillance of antimicrobial resistance is still in development. The first step is to achieve the electronic transfer of antimicrobial resistance data from all diagnostic microbiology laboratories in Scotland, as detailed below. Once fully established national surveillance will;

- monitor the occurrence of antimicrobial resistance in organisms associated with infections in humans using standardised susceptibility testing based around a core dataset based on the European Antimicrobial Resistance Surveillance scheme (EARSS) of blood culture isolates :

Streptococcus pneumoniae
Staphylococcus aureus
Enterococci
Escherichia coli
Klebsiella pneumoniae
Pseudomonas aeruginosa
Acinetobacter (not currently part of the EARSS scheme but of concern within the UK)

- monitor the emergence, spread and persistence (i.e. the epidemiology) of the above resistant organisms associated with infections in humans through enhanced surveillance and prevalence studies of infections cause by these organisms at other body sites e.g. urinary tract, respiratory tract.
- monitor the emergence of new and/or unusual resistance profiles that will potentially impact on treatment of patients via a semi-automated alert system based on the original Surveillance of Antimicrobial Resistance In Scotland (SARIS) scheme. Where new or unusual resistance patterns are identified, ensure associated resistance mechanisms are characterised in the appropriate reference laboratory and alerts are issued to the service as required.
- monitor the rate of CDI and antimicrobial resistance in *C. difficile*.
- Allow meaningful comparisons of standardised data within Scotland and with other parts of the UK, European countries and the wider international communities.

To support capture of information on antimicrobial resistance all diagnostic microbiology laboratories in Scotland have now installed and implemented the VITEK 2 bioMérieux systems for automated standardised susceptibility testing. The acquisition of the VITEK 2 systems in all the laboratories was achieved through national procurement. HPS is responsible for setting up and coordinating the automatic electronic transfer of standardised antimicrobial resistance data from the diagnostic microbiology laboratories to HPS via the Electronic Communication of Surveillance in Scotland (ECOSS) system.

Appendix 1 shows a representation of the flow of antimicrobial resistance information from the VITEK 2 systems in diagnostic microbiology departments into ECOSS.

Susceptibility data are collected by the **site of infection** (for example blood infection, urinary tract infection, lower respiratory tract infection).

Episodes of infection are based on international standards when available. In the absence of international standards, a new episode is defined as a second positive culture of the same microorganism from the same person that occurred at least 14 days after the first positive culture. A new episode is recorded if there is a shift from sensitive to resistant for any of the antibiotics monitored in the surveillance programme.

Data will be collected on all antimicrobials tested by the VITEK 2 system for that organism or group of organisms

Resistance rates, determined by the Clinical and Laboratory Standards Institute (CLSI) breakpoints in the first instance, but the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint system once introduced in 2011, will be given as ***percent resistant case episodes over a defined period of time*** (i.e. incidence).

For some infections (microorganism/site of infection combinations) it may be appropriate to calculate resistance rates by acute occupied bed days (AOCBD) or by population size (i.e. per 100,000 inhabitants). This will be reviewed as data becomes available.

Data will be categorised by NHS board and source of specimen/location of patient (hospital or G.P.) if possible. This is dependent on the quality and completeness of data sent to HPS which in turn is dependent on the quality of information included on laboratory request forms.

Prevalence studies of resistance rates of key organism/infection combinations (e.g. urinary tract infections) will be carried out each year, the programme and protocol to be agreed with the Scottish Microbiology Forum and SAPG at the start of each year.

For infections with multiple episodes (such as uncomplicated UTI) it may be useful to determine the percent resistant isolates over a defined period to avoid underestimating the burden of resistant infections.

Antimicrobial alerts of unusual or unexpected resistance will be generated based on routine resistance data reported through ECOSS from Laboratory information systems as a prompt for more detailed local investigation.

Data on circulating resistance mechanisms will be collected from the appropriate reference laboratory. Criteria for referral to the Antibiotic Resistance Monitoring and Reference Laboratory (ARMRL) Colindale are attached at appendix 2.

A protocol for data collection for national surveillance expanding on that currently available in the ECOSS handbook will be produced for NHS laboratories.

6. Local Surveillance

6.1 Local surveillance of primary care use of antimicrobials

Local surveillance systems for primary care use of antimicrobials should utilise the standard reports on national prescribing indicators in PRISMS. These indicators should be monitored on a **minimum of a 6 monthly basis** (12 monthly for seasonal variation) and should involve as a minimum;

- Overall use of antimicrobials
- Use of agents associated with a higher risk of CDI (cephalosporins, quinolones, co-amoxiclav and clindamycin)
- Use of recommended antibacterial agents
- Seasonal variation of use of quinolones

Surveillance should include analysis of these recommended national prescribing indicators at GP practice level to identify outliers where specific feedback to prescribers is required.

6.2 Local surveillance of hospital use of antimicrobials

Local surveillance of hospital use of antimicrobials should involve **as a minimum** monitoring of the following agents/classes at **hospital level** every **3 months** (using time periods January–March, April–June, July–September and October–December);

- Overall use of antimicrobials
- Use of agents associated with a higher risk of *Clostridium difficile* infection
 - Cephalosporins
 - Co-amoxiclav
 - Quinolones
 - Clindamycin
 - Piperacillin/tazobactam

- Use of agents that may be regarded for use on restricted basis
 - Carbapenems
 - Daptomycin
 - Linezolid
 - Tigecycline

HMUD will provide this level of information at hospital level. NHS Boards where HMUD information is not available will need to develop local arrangements to report this information.

HMUD uses total issues of antimicrobials from the hospital as the basis for generation of defined daily doses. To maximise the synergy between HMUD and local surveillance systems boards should consider using total issues rather than any measure which excludes issues such as outpatient prescriptions or discharge prescriptions as the basis for local surveillance.

Local surveillance of antimicrobial use should be monitored using number of Defined Daily Dose (DDD) per 1000 occupied bed days (OBD).

HMUD will not support the production of reports at directorate or ward level. Local surveillance of hospital use of antimicrobials should include **as a minimum** the surveillance of all antibacterials in the following units;

- Acute Admission Units – medical, surgical, care of elderly
- Intensive Therapy Units (adult and neonatal)
- Oncology/Haematology units
- Renal Units
- Transplant Units

The use of these antimicrobials should also be monitored using number of DDD per 1000 OBD.

Local surveillance of hospital use of antimicrobials will require to be extended to include enhanced surveillance in particular ward/clinical settings when particular clinical problems with resistant organisms or healthcare associated infections are identified.

Point prevalence studies will complement the above quantitative information by providing information on indication for use and compliance with antimicrobial prescribing policy/guidance.

6.3 Local surveillance of antimicrobial resistance

Local surveillance systems should monitor antimicrobial resistance rates at a minimum of a 3-monthly interval at hospital level and primary care level on the following key organisms plus any of local concern (e.g. *Acinetobacter*);

Streptococcus pneumoniae
Staphylococcus aureus
Enterococci
Escherichia coli
Klebsiella pneumoniae
Pseudomonas aeruginosa

Surveillance systems that focus on blood isolates alone are not sensitive enough to detect emerging resistance mechanisms. Local surveillance should therefore as a minimum routinely monitor the following infection types in addition to blood stream infections¹;

- Urinary tract infections from primary care
- Urinary tract infections from hospital in-patients
- Skin and soft tissue infections

Interpretation of local surveillance of data on antimicrobial resistance must be based on local knowledge of the pattern of local submission of samples.

Resistance rates may vary depending on the nature of clinical services provided within a particular setting, and local surveillance programmes should as a minimum undertake ongoing monitoring of patterns of resistance in the following specific units;

- Acute Admission Units
- Intensive Therapy Units (adult and neonatal)
- Oncology/Haematology units
- Renal Units
- Transplant Units

¹ *Note:* The majority of these data should be achievable through setting up standard queries using the bioMérieux Observa 3 software, which is installed in association with VITEK 2 systems in all diagnostic microbiology laboratories.

EUCAST breakpoints as they become available should be used to categorise isolates into Sensitive (S), Intermediate (I) or Resistant (R). When EUCAST breakpoints are not available then CLSI breakpoints should be used. It is recommended that Minimum Inhibitory Concentration (MIC) distributions are calculated to allow early detection in changes in resistance levels.

Local surveillance systems should monitor unusual resistance profiles that are rare for any organism and specimen type and multidrug-resistant (MDR) organisms in order to;

- a) prompt immediate investigation and further characterisation,
- b) review and revise clinical management of cases.

Local prescribers should be alerted when an unusual resistance profile or multi-resistant organisms are identified.

Recommended local “alert” organisms are;

- Group A *Streptococcus*, penicillin resistant
- Group B *Streptococcus*, penicillin resistant
- Group C *Streptococcus*, penicillin resistant
- Meticillin sensitive *Staphylococcus aureus* (MSSA), flucloxacillin, erythromycin, tetracycline resistant
- Meticillin resistant *Staphylococcus aureus*, (MRSA), vancomycin/teicoplanin resistant
- *Enterococcus faecalis*, vancomycin/teicoplanin resistant
- *Enterococcus faecium*, vancomycin/teicoplanin resistant
- *Klebsiella pneumoniae*, imipenem/meropenem resistant/carbapenemase producer
- *Escherichia coli*, imipenem/meropenem resistant/carbapenemase producer/tigecycline resistant
- *Acinetobacter* spp. imipenem/meropenem resistant
- *Pseudomonas* spp. imipenem/meropenem resistant
- Gram-negative organisms with multi resistance (resistant to three or more antimicrobial classes)
- *Haemophilus influenzae*, amoxicillin/co-amoxiclav/ tetracycline resistant
- *Streptococcus pneumoniae*, penicillin/tetracycline/erythromycin resistant

The referral criteria for characterisation of resistance mechanisms by reference laboratories are available in appendix 2.

Interpretation of antimicrobial resistance information

When interpreting local surveillance data it is important to consider numerous factors that could be responsible for emerging and continuing antimicrobial resistance. Those who interpret local surveillance data should keep track or monitor common risk factors in their area (Monnet, 2000).

Risk factors for developing an infection with a resistant pathogen in hospitals can broadly be classified into four categories;

- Antimicrobial overuse, misuse and co-usage of antimicrobial drugs (note that resistance is often a delayed effect of antimicrobial use)
- Issues with implementation of infection control measures
- Patient risk factors, including severity of disease and use of medical devices
- Issues in the community (e.g. resistant organisms in primary care, animals, food products, water supply).

7. Summary

National surveillance providing standardised information on antimicrobial use and resistance is intended to support NHS boards in their long-term strategic planning of antimicrobial prescribing and allow comparisons within Scotland and with the rest of the UK and other countries.

Local surveillance should be in place to complement national information to feed back to prescribers and other clinical staff in order for them to optimise prescribing and clinical management of patients and for implementation and evaluation of local interventions and local prescribing policies.

8. Bibliography

Fluit A.C. et al. Priorities for antibiotic resistance surveillance in Europe. *Clin Microbiol Infect* 2006; 12: 410-417

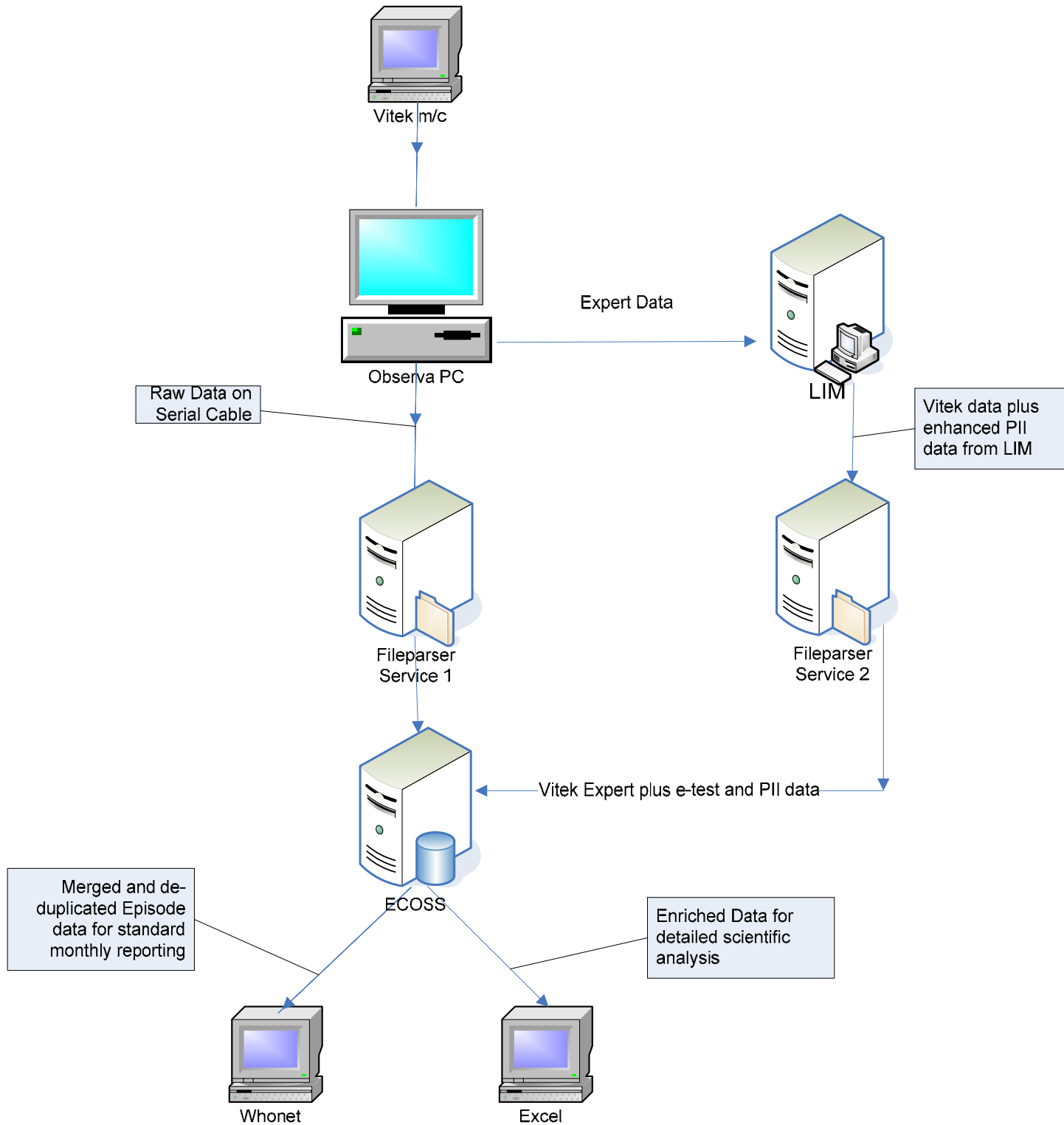
Hammerum et al. Danish Integrated Antimicrobial Resistance Monitoring and research programme. *Emerg Inf Dis* 2007; 13: 1632-1639

¹Molstad, S et al. Sustained reduction of antibiotic use and low bacterial resistance: 10-year follow-up of the Swedish Strama programme. *Lancet* 2008; 8: 125-132

²Molstad et al. Strama – a Swedish working model for containment of antibiotic resistance. *Eurosurveillance* 2008; 46: 1-4

Monnet, D.L. Toward multinational antimicrobial resistance surveillance systems in Europe. *Int J Antimicrob Agents* 2000; 15: 91-101

Appendix 1: Diagram of flow of antimicrobial resistance information flow from the VITEK 2 systems in diagnostic microbiology laboratories into ECOSS



Appendix 2

Referral criteria for resistant organisms

Antibiotic resistance monitoring and reference laboratory testing services

| Organism | Resistance phenotype | Reference Laboratory |
|--|---|-----------------------|
| <i>S aureus</i> | Any of: vancomycin, teicoplanin, linezolid, quinupristin/dalfopristin | MRSA ref lab, Glasgow |
| Coagulase negative staphylococci | Any of: vancomycin, linezolid, quinupristin/dalfopristin | MRSA ref lab, Glasgow |
| <i>N.meningitidis</i> | Any of: penicillin (high level), ciprofloxacin | SMPRL Glasgow |
| <i>S pneumoniae</i> | Any of: meropenem, vancomycin, teicoplanin, linezolid, quinupristin/dalfopristin | SMPRL , Glasgow |
| <i>N. gonorrhoeae</i> | Any third generation cephalosporin | SNRL Edinburgh |
| <i>Salmonella</i> , <i>Shigella</i> | Wide range of clinically relevant and epidemiologically important antimicrobials. | SSSCDRL, Glasgow |
| Group A B C G b-haemolytic streptococci | Any of: penicillin, vancomycin, teicoplanin, linezolid, quinupristin/dalfopristin | ARMRL Colindale |
| JK coryneforms | Any of: vancomycin, teicoplanin, linezolid, quinupristin/dalfopristin | ARMRL Colindale |
| Enterobacteriaceae including members of genera <i>Enterobacter</i> , <i>Escherichia</i> , <i>Citrobacter</i> , <i>Serratia</i> , <i>Proteus</i> , <i>Providencia</i> , <i>Klebsiella</i> , <i>Morganella</i> | meropenem, imipenem | ARMRL Colindale |
| <i>Acinetobacter</i> spp | Any of: meropenem, Imipenem, colistin | ARMRL Colindale |
| <i>Pseudomonas aeruginosa</i> | colistin | ARMRL Colindale |
| <i>H. influenzae</i> | Any third generation cephalosporin or carbapenem | ARMRL Colindale |

| | | |
|-----------------------|---|---------------------------------|
| <i>M. catarrhalis</i> | ciprofloxacin, any third generation cephalosporin | ARMRL Colindale |
| Anaerobes in general | metronidazole | Anaerobe reference unit Cardiff |
| <i>Bacteroides</i> | Any of: metronidazole, co-amoxiclav, carbapenems | Anaerobe reference unit Cardiff |
| <i>C. difficile</i> | Any of: metronidazole, vancomycin | SSSCDRL, Glasgow |

Exceptional resistances, needing confirmation

| Organism | Resistances to: |
|---|--|
| <i>S. aureus</i> | Any of: vancomycin, teicoplanin, linezolid, quinupristin/dalfopristin |
| Coagulase-negative staphylococci | Any of: vancomycin, linezolid |
| JK coryneforms | Any of: vancomycin, teicoplanin, linezolid |
| <i>S. pneumoniae</i> | Any of: meropenem, vancomycin, teicoplanin, linezolid |
| Group A, B, C, G β -haemolytic streptococci | Any of: penicillin, vancomycin, teicoplanin, linezolid |
| Enterococci | Both Ampicillin and quinupristin/dalfopristin Linezolid. Teicoplanin but not vancomycin |
| Enterobacteriaceae | Meropenem Imipenem (except <i>Proteus</i> spp.) |
| <i>H. influenzae</i> * | Any third-generation cephalosporin, or carbapenem |
| <i>M. catarrhalis</i> | Ciprofloxacin, any third-generation cephalosporin |
| <i>N. meningitidis</i> * | Any of: penicillin (high level), ciprofloxacin |
| <i>N. gonorrhoeae</i> * | Any third-generation cephalosporin |
| <i>Acinetobacter; P. aeruginosa</i> | Colistin |
| Anaerobes in general* | Metronidazole |
| <i>Bacteroides</i> * | Any of: metronidazole, co-amoxiclav, carbapenems |
| <i>C. difficile</i> * | Any of: metronidazole, vancomycin |

* Species outside ARMRL's remit; these should be sent to the appropriate PHLS reference lab.