Newsletter 25 - Dec/2010

This Newsletter brings CDS Registrants up to date with some recent changes to the CDS Method. Both the on-line version of the Manual and the downloadable pdf versions have been modified to include all the changes listed below:

1. Quality control

   3.1.4 Measuring and recording reference strains results

   Please note the following statement has been inserted in section 3.1.4: When testing an antibiotic against the reference strains if the annular radii lie outside the acceptable interval on two consecutive testings, retest using a new cartridge from the same batch. If the annular radii from the new cartridge also lie outside the acceptable interval, discontinue the use of this batch. The reason being that with 95% confidence limits, there is a chance of the reading to "occasionally" land outside the acceptable range but is unlikely on two consecutive testings.

2. Change in wording of report of *Streptococcus pneumoniae* susceptibility.

   Streptococcus pneumoniae isolated from sites other than CSF, that have a zone with P 0.5 u or CTX/CRO 0.5 µg of < 6mm in annular radius and a zone with AMP 5 or CTX/CRO 5 µg of > 6 mm are now reported as having a "Decreased Susceptibility" (DS) instead of "Reduced Susceptibility" (RS).

3. Use of 2 disc potencies for *Streptococcus* sp.

   All *Streptococcus* species including group B, *S. mitis, S. sanguis* and the *S. anginosus* group that show resistance to P 0.5 u or CTX 0.5 µg can be tested against AMP 5 µg or CTX/CRO 5 µg. Interpretation of the results is the same as with *S. pneumoniae.*

4. Reporting of Plasmid Mediated AmpC (PM-AmpC)

   Escherichia coli, *Klebsiella pneumoniae* producing a PM-AmpC β-lactamase are usually susceptible to cefepime, a 4th generation cephalosporin but resistant to Augmentin 60 µg, cephalexin 100 µg. Those with high β-lactamase activity are also resistant to cefotaxime 5 µg and ceftazidime 10 µg. For more information, go to section 5.5.3 of the online Manual.

   The results of susceptibility testing are reported according to the standard CDS interpretation.

5. Reporting of *Klebsiella oxytoca*

   The results of susceptibility testing of *K. oxytoca* hyperproducer of K1 enzyme are reported according to the standard CDS interpretation (section 5.5.5).

6. Further studies on the ESCHAPM Group.
   In the CDS laboratory we have been looking more closely at members of the ESCHAPM group *(Enterobacter cloacae, Enterobacter aerogenes*, *Serratia marcescens*, *Citrobacter freundii, Hafnia alvei, Aeromonas hydrophila, Aeromonas caviae, Aeromonas veronii, Providencia stuartii, Providencia rettgeri* and *Morganella morganii*) that are known to produce a chromosomal inducible cephalosporinase, inhibited by aztreonam but not by clavulanic acid (AmpC/Bush group 1). Producers of this cephalosporinase can be detected in the CDS test by a disc approximation test (Plate 11.12.A).

   In addition, some members of this group can give rise, at a high frequency, to derepressed mutants that are AmpC enzyme hyper-producers. This may not always be obvious on disc testing, so that where this enzyme is detected, the strain is reported as resistant to all cephalosporins except the 4^{th} generation irrespective of the zone size. The species that consistently give rise to high frequency mutants (10^{-5} to 10^{-6}) are *E. cloacae, E. aerogenes* and *C. freundii* and we propose that this group be called the EEC group. We recommend that for this group, only the results of 4^{th} generation cephalosporins (cefepime and cefpirome) and carbapenems be reported. We consider it unsafe to attempt to interpret the results of testing with other β-lactams.

   The second group contains only one species, *S. marcescens,* which does not give rise to derepressed mutants when exposed to ceftazidime and aztreonam but does so when exposed to other β-lactams including cefotaxime, Timentin, Tazocin, cefpodoxime, cefotetan, cefoxitin, cefuroxime or cephalexin. With this species, it is considered safe only to report the results of testing of aztreonam and ceftazidime in addition to the 4^{th} generation cephalosporins and the carbapenems.

The third group consists of all members of *Aeromonas* sp. except *A. sobria* which fail to produce the inducible cephalosporinase A1. This group yielded hyper-producing mutants at an extremely variable rate when exposed to cefotaxime, Timentin, Tazocin, cefpodoxime, cefotetan, cefoxitin, cefuroxime or cephalexin. Within each species, the rate varied from 10^{-5} to 10^{-8}. On the other hand, we were unsuccessful in our attempts to obtain any hyper-producing mutants from the same strains by exposure to ceftazidime or aztreonam. Furthermore, when the hyper-producing mutants that were selected by any of the eight β-lactams listed above were tested against ceftazidime or aztreonam, all were susceptible to these two antibiotics. It appears that the substrate specificity of AmpC of *Aeromonas* sp. is different to that of the AmpC of the EEC group. Based on these observations, we recommend that it is only safe to report ceftazidime and aztreonam susceptibility as well that of the 4^{th} generation cephalosporins and carbapenems, the latter only in the case of *A. caviae* (see section 5.2).

The fourth group consists of *H. alvei*, *P. stuartii, P. rettgeri* and *M. morganii.* Wild strains are resistant only to ampicillin, Augmentin and cephalexin (a characteristic pattern of this group) and hyper producers of AmpC are selected only at the very low mutation rate of 10^{-8} when exposed to the β-lactams to which they are susceptible. Members of this group are tested in the usual way by the CDS and reported according to the standard interpretation.

The CDS recommendations on testing and reporting are summarised in Table 10.4. A guide to the reporting of β-lactam antibiotics.