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ADVISORY COMMITTEE ON DANGEROUS PATHOGENS

Secretariat Report for the 89th meeting of the ACDP, and matters arising from the 88th meeting

1. This paper includes reports on progress made with matters arising from the last meeting, reports from ACDP Working Groups and other relevant advisory committees as well as other items of interest to members.

Matters arising from the 88th meeting

Status of vaccination against Q fever

2. HSE had written to the Chairman of JCVI last year requesting advice on the efficacy and safety of the Q fever vaccine (Q-vax) currently used in Australia for vaccination of high risk exposure groups. This matter was raised at the JCVI meeting on the 13th February.

3. Based on the experiences of outbreaks in Scotland, the view of the committee was that there would be no window of opportunity to vaccinate workers in an outbreak. There is a long lag period between exposure to, and diagnosis of, Q fever, so many people would already have been exposed before the outbreak was identified. It was noted that there were also operational issues in delivering the vaccination programme, for example, GP practices do not routinely administer intradermal injections.

4. The committee asked the Secretariat to obtain more information on how the Q fever vaccination program is delivered in Australia, and to find out whether alternative acellular Q fever vaccines are available. They will revisit this when this information has been gathered.

Seasonal influenza vaccination programme for poultry workers

5. DH will report verbally on the 2007/2008 programme at the meeting.

PETS Travel Scheme Update

6. Since the last ACDP meeting (February 2008), a significant development for the UK rabies policy has been the granting of an extension to the period for transitional arrangements to those countries originally granted them for additional pet import controls. In the case of the UK these extra controls are for rabies: post vaccination blood testing, followed by a pre-entry waiting period, and certified pre-entry tick and tapeworm treatments within the time periods specified. The extension of the period for transitional arrangements also applies to Sweden, Ireland, Malta and Finland who all have additional pet entry controls compared to other Member States.

7. The original transitional period was due to expire on 3 July 2008. However, the Commission's report on whether these extra controls should stay in place was delivered 8 months late, therefore, in October 2007 the Commission submitted a proposal to extend the transitional period until 31 August 2009. To date, the Commission have not submitted proposals for a pet movement regime at the end of the transitional period. In the absence of any new proposals, at the expiry of the transitional arrangements, pet entry requirements would revert to those that apply to all other MSs.

8. The European Parliament's Environment Committee submitted a further amendment so as to further extend the transitional period to 30 June 2010. The Commission has accepted this amendment to its proposal and it has been adopted by the European Parliament. It is expected to be ratified at Agriculture Council at the end of May 2008. Therefore, it is likely that the UK's current Pet Travel Scheme rules will remain unchanged until June 2010. Though this is good news, the need to secure the UK controls beyond 2009/10 remains, and hence the UK will continue to press for permanent arrangements for tick and tapeworm controls and for certain rabies controls to remain unchanged, until such time as the EC reviews the EU Pet travel scheme overall.

9. The HPA has prepared the public health evidence for retention of current tick and tapeworm controls for pets entering the UK and this is presented for Members information as a closed Annex (Annex 1) to this paper.

10. To view the amendment to Article 23 of the Regulation (EC) No 998/2003 on the animal health requirements applicable to the non-commercial movement of pet animals as regards the extension of the transitional period, click on the following link:
http://www.europarl.europa.eu/sides/getDoc.do;jsessionid=F065FE660979E740BC7B850A1AE4735F.node2?pubRef=-//EP//TEXT+TA+P6-TA-2008-0109+0+DOC+XML+V0//EN#top

Reports from ACDP Working Groups

TSE Working Group

11. The TSE Working Group has met once since the February ACDP meeting, on the 21st February 2008. Many of the issues discussed by the Working Group in recent meetings will be covered under agenda item 8 of this meeting.

Annex J

12. The updates to Annex J were approved for publication by the Working Group at their February meeting, subject to some minor adjustments. The Annex was then signed off by the ACDP Chairman. It was published on 1st May 2008 at:
http://www.advisorybodies.doh.gov.uk/acdp/tseguidance/tseguidance_annexj.pdf

Annex F

13. Annex F and the consensus statement have been updated by the Working Group with significant input from Dr Miles Allison, a gastroenterologist on the CJD Incidents Panel. The changes largely relate to the inclusion of new information on invasive endoscopic procedures, including advice on how to reduce the contamination of the scope via the use of a disposable sheath. In

addition, endoscopes used on at risk individuals may now be eligible for refurbishment, rather than indefinite quarantining, and this information has been included. References to new decontamination guidelines have also been updated.

14. The changes were discussed in depth at a TSE Working Group meeting last year, which was attended by a number of clinicians who carry out endoscopy on at risk individuals.

15. The updates to this Annex have been approved by the ACDP Chairman, and it will shortly be published at: http://www.advisorybodies.doh.gov.uk/acdp/tseguidance

Annex C

16. This Annex has needed a complete update for some time, and efforts to complete this via email have floundered. The Secretariat has thus agreed to set up a meeting to discuss this update with a number of TSE Working Group members.

Review and revision of TSE Working Group guidance

17. A review of the Working Group's guidance was undertaken by Dr Isobel Rosenstein of the Health Protection Agency's Expert Advice Support Office. She put forward a number of suggestions for a revision of the guidance, including a complete reformatting, and update of various sections. The Working Group agreed that the guidance needed reviewing, particularly to increase its usability in the healthcare sector, and will be taking this forward with help from the Department of Health.

New Pathology Annex (K)

18. The Working Group are currently drafting guidelines for pathologists and pathology laboratories for the handling of tissues from patients with, or at risk of, CJD. This guidance is aimed at pathologists and individuals working in pathology laboratories who handle tissues from patients. It aims to ensure that laboratory staff are aware of risk factors for CJD prior to carrying out procedures on tissues.

19. The first draft of the new Annex was presented to the Working Group, and various suggestions were made for improvement of the document. The Secretariat will be moving forward with these revisions over the summer, and the document will be sent to various professional bodies for comment.

Revision of the 1996 ACDP Guidance Management & Control of Viral Haemorrhagic Fevers

20. At the last ACDP meeting, it was agreed that DH and HSE would draft an action plan for completion of the updated guidance, and bring it back to the committee. An action plan meeting was duly held on the 9th April 2008, and a revised timeline for completion of the guidance was produced. The updated proposed publication date of the guidance is June 2009.

Updated proposed timeline for completio

21. On the 27th May 2008 HSE organised a meeting between representatives from the two High Security Infectious Disease Units in the country (Newcastle and Royal Free, London) at HSE offices in Birmingham. Both of these centres are currently undergoing change, with a new Unit built at the Royal Free, and a new unit planned in Newcastle. The meeting was arranged to discuss facility design, operation and laboratory diagnostics in the proposed facilities to ensure that key issues are covered by the new ACDP guidance in sufficient details. The meeting was also an opportunity for the representatives to meet and exchange information. The meeting was extremely useful, and it was agreed that the meetings should continue at quarterly intervals alternatively at the two sites.

22. Due to the advanced stages of the two new units, it was agreed that the new ACDP guidance would need to be thorough in its advice to allow flexibility, particularly with regards to the use of primary control methods such as Trexler isolators, protective suits or specialised room ventilation in the protection of the healthcare workers and the patient.

Steering Group for revision of the ACDP guidance on blood-borne viruses

23. Following comments made at the last ACDP meeting, a revised draft of the blood-borne virus guidance will be considered at this meeting.

Other Matters

Re-categorisation of *Bacillus anthracis* Pasteur Strain

24. At 87th ACDP meeting, members advised that, given the level of attenuation, work with *Bacillus anthracis* 'Sterne' strain could be undertaken at COSHH containment level 2, supported by a suitable and sufficient risk assessment. Members asked for further evidence on the level of attenuation of *B. anthracis* 'Pasteur' strain before providing advice on appropriate containment.

25. *B.anthracis* has a number of known virulence factors, including both chromosomal and plasmid located, the two major ones being, the anthrax toxin complex and the capsule. The anthrax toxin complex is comprised of three different proteins: protective antigen (PA), edema factor (EF), and lethal factor (LF), encoded on virulence plasmid pOX1. The second virulence factor, the poly-D-glutamic acid capsule, is synthesised from an operon (*capBCAD*) encoded on the virulence plasmid pOX2, which acts to prevent the host's phagocytes from destroying the vegetative bacterium. Both plasmids are required for full pathogenicity. Absence of the virulence plasmids has been exploited in the manufacture of vaccines *e.g.* Sterne strain is used effectively as a live veterinary vaccine.

26. Unlike the Sterne strain, ($pXO1^+/pXO2^-$), the Pasteur strain retains $pXO2^+$ but lacks $pXO1^-$ plasmid, thus endowing a phenotype that retains the bacterial capsule but lacks the anthrax toxin complex. The Pasteur strain was derived through heat attenuation (growth 42-43^oC) resulting in selective loss of pXO^- plasmid. Early versions of the Pasteur strain varied in there level of attenuation, when used as animal vaccines, due to residual bacteria retaining $pXO1^+$. However, the Pasteur strain became a widely used vaccine for sheep and cattle in Europe and South America for over 50 years. The strain retains virulence in mice and guinea pigs in a strain-dependent manner; and retains greater virulence than Sterne strain in these animal models. The extent of

attenuation appears related to level of capsule expression with some strains exhibiting 100-fold attenuation compared to wild type strains (Welkos 1993).

27. More recently *in vivo* studies in murine inhalation models using more precise mutations in pOX1^{+}; pOX2^{+} strains (i.e. deficient in specific toxin or capsule genes) demonstrated residual virulence (mean time to death) reaching levels equivalent to wild type in toxin deficient mutants; whilst capsule deficient mutants were significantly attenuated. However unlike Pasteur strain, these mutants retained regulatory genes sequences and at least one of the toxin genes. The absence of the plasmid rather than specific genes has compounding effects on attenuation by removing regulatory genes that control expression of supplementary virulence factors. For example, *atxA* is a global regulator of virulence factors in B. anthracis and is located on pXO1 plasmid hence is absent from Pasteur strain.

28. Both major virulence determinants are necessary for full pathogenicity. Comparison of plasmid minus strains indicates that residual virulence is greater in capsule-positive non-toxigenic strains (e.g. Pasteur) than converse strains (e.g. Sterne). However, in addition to lacking specific virulence factors, these plasmid minus strains also lack global regulatory genes essential for virulence gene expression.

29. Attenuated live spore vaccines (i.e. Pasteur, Sterne) retain some degree of residual virulence (particularly in murine species) and are not considered suitable for administration to humans. However, both have been widely used to vaccinate ruminant animals and demonstrate significant attenuation in these species.

30. References

Bourgogne, A. et al 2003. Global Effects of Virulence Gene Regulators in a *Bacillus anthracis* Strain with Both Virulence Plasmids, Infection & Immunity, 71, 2736–2743

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Koehler, T. M., 2002. *Bacillus anthracis genetics and virulence gene regulation*. Current Topics in Microbiology and Immunology. 271. p.143-64.

Ivins, B. E. et al 1986. *Immunisation studies with attenuated strains of Bacillus anthracis*, Infection & Immunity, 52, 454-458

Mikesell, P. B. et al 1983. *Evidence for plasmid mediated toxin production in Bacillus anthracis*, Infection & Immunity, 39, 371-376

Uchida, I., Hashimoto, K., and Terakado, N. 1986. *Short communication: Virulence and Immunogenicity in Experimental Animals of Bacillus anthracis Strains Harbouring or Lacking 110 MDa and 60 MDa Plasmids*. Journal of General Microbiology. 132. p.557-559.

Welkos, S. L., N. J. Vietri, and P. H. Gibbs. 1993. Nontoxigenic derivatives of the Ames strain of *Bacillus anthracis* are fully virulent for mice: role of plasmid pX02 and chromosome in strain-dependent virulence. Microb. Pathog. 14:381–388.

Terms of Reference for ACDP

31. The Health and Safety Commission and the Health and Safety Executive were originally established as part of the Health and Safety at Work etc. Act 1974 as two separate non-departmental public bodies. From 1st April 2008 these bodies merged, and HSE became a single national regulatory body responsible for promoting the cause of better health and safety at work. The Commission is now the Board of the new Executive, while members of the old Board have become the Senior Management Team.

32. Due to this merge, the terms of reference for ACDP have been changed to the following:

"To advise the Health and Safety Executive, and Ministers for Department of Health and the Department for Environment, Food and Rural Affairs and their counterparts under devolution in Scotland, Wales and Northern Ireland, as required, on all aspects of hazards and risks to workers and others from exposure to pathogens."

European Commission activities on infections arising from needlestick injuries in healthcare workers

33. The European Commission (EC) has recently conducted both stages of social dialogue on concerns over the potential exposure of European healthcare workers to blood-borne infections from needlestick injuries. The EC has quoted studies estimating the number of needlestick injuries at around one million per year in Europe, and is considering a number of approaches to protect healthcare workers from these risks, including the possibility of an amendment to the Biological Agents Directive (2000/54/EC). Further information on this process to date can be found at: http://www.hse.gov.uk/healthservices/needlesticks/euupdate.htm

34. The EC has commissioned an EU wide impact assessment which should be completed in June. If a draft proposal amending the Biological Agents Directive is taken forward this is likely to appear in October. Most of the recommendations the EC are considering, such as education and training, are already reflected in UK law and good practice. HSE is look at the proposals, and its own impact assessment and will bring a paper to ACDP on this issue shortly.

35. If ACDP members wish to discuss this further then they are asked to contact the HSE Secretariat.

Evaluating the protection afforded by surgical masks against influenza bio-aerosols

36. The Health & Safety Laboratory report entitled "Evaluating the protection afforded by surgical masks against influenza bio-aerosols" has been published on the HSE website.

HSL - evaluating the protection afforded b

Memorandum of Understanding between DH and HPA

37. A Memorandum of Understanding (MoU) has been signed between DH and HPA which sets out an agreement between the two organisations on the support provided by HPA to DH Scientific Advisory Committees (SACs). The roles and responsibilities of key players in the two organisations and the SACs is covered in the document. It is anticipated that this MoU will strengthen the way of working between DH and HPA.


MoU between DH and HPA


MoU Annex A


MoU Annex B


MoU Committee map

Secretariat
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