From: Ian Scragg
To: paula.stam@hse.gsi.gov.uk
CC: Lisa Grayson
Date: 27/4/2009 15:42
Subject: Connected programme of work

Dear Paula,

apologies for taking a few days to respond- last week I was involved in a five day external audit of the University's H&S management system.

Further to your letter of 2 April and my e-mail reply on 3 April I write to outline my current thoughts on how to ensure compliance with Regulations for your comment. My thoughts are based upon ensuring that you as the Competent Authority have an understanding of how we are managing the risks associated with our current and future research involving the genetic modification of micro-organisms. Our research involves three types of risk:

1. Investigation of gene function using well characterised, commercially available viral vector systems with a history of safe use. I have reviewed our existing CU2 notifications and I consider that these risks have been adequately addressed in GM6 07.1, GM6 05.1, GM197/00.1 transferred to GM6, GM317/trans B to GM6, GM6 02.1, 02.2, and 02.3, and GM6/97.2.

Therefore, this research does not need to be included in the recently submitted connected programme or work.

2. Investigation of gene function using replication competent viruses such as adenovirus (GM 317 transA transferrecd to GM6) and vaccinia virus (GM6.98.1). Proposed work is to start research with vaccinia virus again to express defined immuno-dominant epitopes. The genetic modification of these replication competent viruses will not alter the tissue tropism or host range, and are unlikely to increase pathogenicity. These risks have been documented in previous notifications- although I wrote to inform you that work with vaccinia virus (GM6.98.1) had stopped in 2006.

Therefore, is it possible to re-activate the vaccinia notification? and to expand the notification to include in vivo work? or would you prefer a new connected programme of work be submitted?

3. Investigation *in vitro* and *in vivo* of cellular processes of Hazard Group 2 bacterial pathogens clinically relevant in the UK. Current notification covers work with E. coli K1 (GM101/04.1 transferred to GM6). Proposed work includes enteric pathogens Campylobacter jejuni and Salmonella enetrica. It is likely that cellular processes of other pathogens such as Staphylococcus aureus may also be investigated. If the work with Salmonella proceeds as planned then a collaborator in Switzerland will provide a strain that is likely to be more pathogenic than wild type. However, the building of a CL3 facility is not warranted for the reduction in risk it would bring so it has been agreed by the GM6 GMSC that *in vitro* elements of this work can proceed in a dedicated lab to CL2 standard, with tight control on waste management, and *in vivo* elements to the very high standard required by veterinary inspector under animal welfare legislation.

Therefore, would you accept a connected programme of work to cover work with Hazard Group 2 bacterial pathogens to the level of risk of the work with Salmonella? In terms of boundaries this research would not include work with micro-organisms previously documented as requiring Containment Level 2+ in ACDP Guidance 'Categorisation of biological agents according to hazard and categories of containment' 4th Edition 1995.

I look forward to your comments on this suggested approach.

Kind regards, Ian

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