for measles.[8] Mathematical models of Hib transmission may help in deciding whether this option is feasible. Our experience emphasises the importance of continued high quality surveillance for vaccine preventable diseases even long after their apparent control. Such surveillance is increasingly critical after the introduction of new vaccines, vaccine combinations, or new formulations and will help to inform the best future strategy for the control of vaccine preventable diseases.

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We wish to acknowledge the contributions of colleagues to this editorial through a recent meeting held under the auspices of the Royal College of Paediatrics and Child Health Immunisation and Infectious Disease Standing Committee.

Competing interests: PH and MR have received research grants and reimbursements for attending symposiums from vaccine manufacturers including Aventis Pasteur and Glaxo SmithKline. PH has received fees for consulting from Glaxo SmithKline.

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Human tissue engineered products—drugs or devices?

Tackling the regulatory vacuum

The new Medicines and Healthcare products Regulatory Agency (MHRA) came into existence in the United Kingdom on 1 April 2003. The new agency is the result of the merger of the Medicines Control Agency and the Medical Devices Agency, which have statutory responsibility for the regulation of medicines and medical devices. The merged body does not have new powers and leaves the existing statutory basis of regulation unchanged. Systems of licensing medicines and the control of medical devices will continue as before, but the merger is seen in the Department of Health as strengthening public protection in the context of "growing numbers of products that cross the borderline between medicines and devices."[1] The regulatory status of borderline technologies is uncertain, and acknowledgement of this is highly important for the control of regenerative medicine.

Industry, academic science and engineering, and governments are promoting tissue engineered technologies. In the United Kingdom several research councils are supporting a national centre for tissue engineering research, and other research centres are mushrooming. As a form of regenerative medicine, human tissue engineered technologies may offer notable benefits to patients in longevity, biocompatibility, and performance of implants. Expectations and hopes are high.[2] The technologies combine human tissue or cells (viable or non-viable, allogeneic or autologous) with synthetic biomaterials. They constitute a diverse group of products, at different stages of development. The most widespread existing application is skin systems for treatment of various conditions: chronic wound healing in diabetic patients with ulcers; venous leg ulcers; burns; and cancer.[3–5] Repair of knee cartilage by using cultured autologous cells is promoted in some centres, as are various approaches to bone repair. In the pipeline are many other applications, including vascular, pancreatic, and corneal repair.

The future of these technologies is in the balance. There are several concerns relating to their promotion and regulation. What are the implications for public health and for clinical services? How might the medical and surgical professions and patient advocate groups shape future policy? The number of people with the relevant technical expertise is not large, and many of these are based in industry. What will the relation be between a new regulatory regime and industrial expertise? Will the "precautionary principle" have an impact? What standards of preclinical and clinical evidence are appropriate? How might ethical concerns be voiced? Currently no unified regulatory controls exist for these technologies across Europe, so how will this affect the availability of potentially beneficial applications through the European and global medical products industry? Some clinicians have experience of using existing products and are involved in development and clinical trials of new applications. Evidence and views about the technical potential differ. These developments are being investigated in a current research project supported by a joint programme on innovative health technologies, run by the United Kingdom's Economic and Social Research Council and the Medical Research Council.[6]

Human tissue engineered products may carry greater risks than most medical devices, and these risks

BMJ 2003;326:1159–60

are more difficult to assess.[7] Clinical introduction and the vigilance and surveillance systems for human implant technologies generally are of growing concern.[8]

Regulation and guidance for new medical and healthcare technologies have been changing rapidly in recent years. Regulation has become increasingly Europeanised.[9] The evidence based institutions now have a regulatory role, in the United Kingdom most notably the National Institute for Clinical Excellence (NICE), including the interventional procedures advisory committee, which has a remit for "horizon scanning" emerging technologies. These developments have expanded the regulatory environment beyond statutory control over safety and efficacy, to include criteria of clinical and cost effectiveness. Tissue engineered products lie between existing regulatory systems. In the United Kingdom in 2002 a voluntary interim code of practice for manufacturers was published in the absence of Europe-wide controls.[10]

Many European countries including the United Kingdom have no procedure for market approval of these products if they cannot be treated as medicines or devices. It is likely that new European legislation will be produced. A new separate European regulatory authority has been proposed by the European Commission's scientific committee on medicinal products and medical devices, part of the commission's consumer protection directorate. Others support an extension of the European Commission's existing central medicines licensing agency. Two directives from the European Commission are currently under discussion, one focused on sourcing and control of tissues, the other on approval and control of human tissue engineered products for which the commission surveyed stakeholders' views in an open consultation during 2002.[11]

In the United Kingdom the Medicines and Healthcare products Regulatory Agency will have a leading role in regulating these human tissue engineered technologies. The agency faces a number of challenges. It will have to contribute to and implement the European Commission's legislation, creating appropriate systems of control. In the context of increased public scrutiny, governance arrangements for the agency will be crucial. Issues of enforcement will be highlighted, appropriate technical expertise will be required, and strong links will be needed with NICE and health technology assessment related activity. New procedures for demarcation and classification of borderline products are expected. Strong communication between the medical profession and the agency will be needed to provide clinical evidence. Demand will increase for a high level of transparency in decision making about new technologies and surveillance of their effectiveness. Debate about the ownership of body tissue,[12] together with the potential application of stem cells in tissue engineered technologies, will require the new agency to engage with major social and ethical concerns in the future.

For clinicians the full implications of these changes in the regulatory environment are not yet clear. What is clear is that the medical professions will have a key role in providing clinical evidence about the efficacy and effectiveness of human tissue engineered products and in implementing controls over their potential application in regenerative medicine.

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This article draws on a project, "Medical Device Governance: Regulation of Tissue Engineering in the UK and EU," funded by the Economic and Social Research Council (project number L218 25 2058) as part of the innovative health technologies programme.

Competing interests: None declared.

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