Chapter 12

Legal matters : safety and quality

Summary

Increased awareness of the risk of the transmission of infectious disease has highlighted the importance of ensuring the safety of human tissue. There is a large body of regulation relevant to the safety and quality of human tissue. Legislation originates both in the UK and in Europe. Professional regulation is also important.

Much general regulation, on health and safety at work, or on environmental protection, will apply to human tissue insofar as it presents a hazard to health or to the environment. Where human tissue is used for the production of medicinal products, its use will come under the provisions of the Medicines Act 1968. The regulation of medical devices, and in particular devices incorporating human tissue, such as heart valves, is less comprehensive. Other regulation applies to the use of different types of human tissue for medical treatment or for research. The Medicines Control Agency, for example, licenses and monitors centres handling or processing blood. It is equally important that effective standardised procedures are in place for institutions handling other types of human tissue, both to protect recipients of transplants and those handling the tissue.

There are a number of different legal channels open to those who consider that the protection offered by procedures regulating the safety and quality of human tissue has been unsatisfactory. Failure to comply with laws designed to promote safety can result in criminal sanctions. Civil claims for damages may be made in respect of harm caused by defective tissue. Nevertheless, an injured person faces considerable difficulties before liability can be established. There are many, in both medical and legal circles, who feel that the law is at present inadequate and requires change.

Introduction

12.1 There is heightened public awareness today of the need to ensure the safety and quality of human tissue, for whatever purpose it is used. Increased use of tissue as a result of technological developments has led to a greater appreciation of the problems which can arise from the use of contaminated tissue and to greater attention being focused on the claims of those who suffer damage resulting from such use. All those concerned with the donation, acquisition and use of blood and all other tissue, and the public in general, must be satisfied that proper care is taken to eliminate, or reduce to an acceptable level, all risks.

12.2 There are many rules of general application, for example, those regulating health and safety at work, which are of relevance to those concerned with human tissue. There are also many more specific rules which regulate the use of human tissue in medicines, and for medical treatment and research activities. Taken together, the variety of laws, professional regulations and other codes concerned with ensuring the quality and safety of human tissue can be overwhelming.

12.3 In this chapter, we offer a survey of the existing regulation relating to the safety and quality of human tissue. We have indicated areas where there is concern that the regulatory framework may not be adequate. At the end of the chapter, we discuss the legal channels open to those who consider that the protection offered by the procedures regulating safety and quality of human tissue has been unsatisfactory. This chapter has drawn on several sources.[1]

The regulatory framework

12.4 At the international level, there are advisory bodies, such as the World Health Organisation, which provide valuable information and advice. Initiatives in some countries, in particular the USA, can be influential elsewhere. Within Europe, there are also many bodies providing information and advice.

12.5 At the legislative level, the UK is now controlled from two directions. First, there is UK legislation. Secondly, laws are made by the European Community: the European Commission has been responsible for formulating a stream of relevant Directives[2], which are then incorporated into UK law. In addition to legislation,

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[1] Barton: (1992) "Criminal Liability under the Medicines Act 1968: Private Prosecution and Personal Liability" **Pharmaceutical Medicine 6**: 121-126.
Cash: (1993) "Quality Assurance in the Blood Transfusion Services". **Proceedings of the Royal Society of Edinburgh 101B:** 241-249
Charlesworth: (1993) "Approving Medicines for Marketing in the European Community - Now and in the Future" in **Textbook of Pharmaceutical Medicine** eds Griffin, O'Grady and Wells Queen's University of Belfast.
Cook, Doyle & Jabbari: (1991) **Pharmaceuticals Biotechnology and the Law,** Macmillan
Dodds-Smith and Spencer: (1994) "Product Liability for Medicinal Products" in Powers and Harris (eds), **Medical Negligence**, 2nd ed p 502
Goldberg: (1991) "The Development Risk Defence and Medicinal Products" **36 Jo.Law Soc.Scotland** 376
Hodges: (1993) "Legal and Ethical Issues Concerning Pharmaceutical Products" in **Textbook of Pharmaceutical Medicine** eds Griffin, O'Grady and Wells Queen's University of Belfast
Jones & Jeffreys: (1994) "EMEA and the New Pharmaceutical Procedures for Europe" **Health Trends 26**:10-13.
Snell and Hurley: (1993) "Quality Assurance in Medical Microbiology" **Proceedings of the Royal Society of Edinburgh, 101B**: 311-320

[2] For example: 89/381/EEC extending the scope of Directives of 65/65/EEC and 75/319/EEC on the approximation of provisions laid down by law, regulations or administrative action relating to proprietary medicinal products derived from human blood or human plasma; 89/342/EEC extending the scope of Directives 65/65/EEC and 75/319/EEC and laying down additional provisions for immunological medicinal products consisting of vaccines, toxins or serums and allergens; 90/219/EEC on the contained use of genetically modified

there are professional and industrial bodies, European, national and local, laying down and monitoring standards in respect of virtually every aspect of relevant activity. All that can be done here is to give a very general picture, with some examples, of this complex area.

Examples of general regulation that covers human tissue

Health and safety at work

12.6 The Health and Safety at Work Act 1974 imposes duties upon employers to ensure, as far as practicable, *"the health, safety and welfare at work of all their employees"* and *"to conduct their undertakings in such a way .. that persons not in their employment who may be affected thereby are not exposed to risks to their health and safety."* The Act is operated through the Health and Safety Commission and the Health and Safety Executive which monitors and enforces the detailed health and safety regulations (many of which now originate in European Community Directives).

12.7 For example, the Control of Substances Hazardous to Health Regulations 1994 (COSHH) impose rules and procedures in relation to employees who are exposed to hazardous substances. COSHH regulations require employers to assess the risks to health created by the use of substances such as toxic chemicals and biological agents. COSHH provisions would, therefore, cover human tissue insofar as it may be hazardous to health. It should be noted that no substance administered in the course of medical treatment is considered a substance hazardous to the health of the patient. These are subject to a separate regulatory regime outlined below (paragraphs 12.11 - 12.26).

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microorganisms; 90/220/EEC on the deliberate release into the environment of genetically modified organisms; 90/679/EEC on the protection of workers from risks related to exposure to biological agents at work; 92/59/EEC on the safety of products; 93/39/EEC in respect of medicinal products; 93/41/EEC repealing Directive 87/22/EEC on the approximation of national measures relating to the placing on the market of high technology medicinal products, particularly those derived from biotechnology. There are also Council Regulations which have immediate effect as law in each Member state, for example, Council Regulation 2309/93 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Agency for the Evaluation of Medicinal Products.

Pursuant to an EC Directive on General Product Safety (92/59/EEC) there are broad framework provisions dealing with the supply of any unsafe products and giving the Commission power to take Community-wide action if necessary. However, to the extent that there are product safety provisions applicable to specific products as outlined above, they supplant the requirements of the General Directive.

Environmental protection

12.8 There are many rules concerned with environmental matters. For example, when research work is completed, any waste materials, particularly if hazardous, must be disposed of in compliance with the terms of the Control of Pollution Act 1974 and the Environmental Protection Act 1990. Waste human tissue, body fluids, drugs, swabs or dressings, and syringes or needles are defined as clinical waste. Such waste must be appropriately contained, stored, transported and disposed of, for example by incineration by specialist commercial waste disposal contractors.

Genetically modified organisms

12.9 Particular attention has been paid to the deliberate release of genetically engineered organisms into the environment. These are defined as micro-organisms *"in which the genetic material has been altered in a way that does not occur naturally by mating and/or recombination"*. This could therefore cover micro-injection of human or other DNA into cells, and genetic manipulation of DNA sequences in viruses. The Contained Use Directive[3] and the Deliberate Release Directive[4] and, in the UK, the UK Genetically Modified Organisms (Contained Uses) Regulations 1992, regulate all aspects of the deliberate release of genetically modified organisms.

12.10 These laws and procedures are thought to be effective, but are criticised by some as being too rigid and putting European industry to much greater expense than its competitors elsewhere. The European Commission is aware of this concern and is anxious to ensure that, without prejudicing public confidence in biotechnology, regulatory control is sufficiently flexible to enable some rules to be relaxed where, in the light of improved knowledge, the risks are seen to be lower than previously thought.

[3] The **Contained Use Directive** (90/219) imposes minimum standards (which can be increased by Member States if they so wish) for all aspects of the production, development and use of genetically modified organisms under containment. Commercial use is treated slightly differently to basic research: the former requires prior approval, even though the same genetic manipulation for academic purposes does not. All work involving human pathogens must be notified to a national Competent Authority before it can proceed.

[4] The **Deliberate Release Directive (90/220**) deals with the regulation of releases in the European Union. In the main it applies to new plants.

Use of human tissue in medicines and medical devices

12.11 Much research, especially industrial research, on human tissues or their naturally occurring products has as its purpose the development of therapeutic medicines, implantable devices or diagnostic agents intended after development to be manufactured on a commercial scale and sold.

The Medicines Act

12.12 The main catalyst for strengthening controls over the production and use of medicines was the Thalidomide tragedy. The first response in the UK was the setting up in 1964 of a voluntary system for monitoring the results of clinical trials and adverse drug reactions. This Committee on the Safety of Drugs (the Dunlop Committee) was replaced by a much more detailed statutory regime under the umbrella of the Medicines Act 1968. The parallel European response, starting with Directive 65/65, was to develop a comprehensive and harmonised Community regulatory system, which has been incorporated into UK law.[5]

12.13 Thus, in the UK, it is the Medicines Act 1968 and its accompanying Regulations, which provide the legislative control over virtually all aspects of the manufacture, sale, supply and use of medicines for human and veterinary purposes. Both the Medicines Act and its European counterpart, Directive 65/65, are concerned with *"medicinal products"*. These comprise, very broadly, any substance or combination of substances used for treating or for preventing disease in human beings and animals.

12.14 The Medicines Act is administered and enforced by the Medicines Control Agency acting on behalf of the Licensing Authority who are the Ministers of Health and Agriculture of the United Kingdom. Guidance documents relevant to the assurance of safety and quality are regularly issued and updated by the Medicines Control Agency. There is also a global move towards international harmonisation of safety and quality requirements and inspection procedures.

[5] The most recent regulations implementing Community provisions concerning the marketing of medicinal products are The Medicines for Human Use (Marketing Authorisation etc) Regulations 1994, SI 1994/3144. For a commentary on this see Medicines Control Agency (1995) **The Medicines for Human Use (Marketing Authorisations etc) Regulations 1994** Medicines Act Leaflet MAL 81

12.15 Licences are of three sorts: **product**, **manufacturing** and **wholesale**. Thus the Medicines Act regulates not only the granting of product licences, but also all those in the chain of supply, from manufacturer to ultimate user. The granting or denial of **product licences** is based on expert assessments of safety (of each description to which the licence relates), efficacy (for the purposes of which the medicines are to be administered) and quality (according to the specification and proposed method of manufacture of the products and the provisions proposed for securing that the product as sold or supplied will be of that quality). The granting of **manufacturing** and **wholesale licences** turn on assessments of the operations proposed to be carried out in pursuance of the licence, the premises, the equipment, the qualifications of those under whose supervision the operations will be carried out and the arrangements for securing the safekeeping and maintenance of adequate records. Premises and processes are subject to regular inspections and reports.[6]

12.16 Although trials of medicinal products in patients are generally subject to the provisions of the Medicines Act, trials on healthy volunteers are not. Substances used in tests on volunteers are not normally considered *"medicinal products"* for the purposes of the Medicines Act. However, all proposals involving human subjects are reviewed by research ethics committees.

Medical devices

12.17 Until recently most medical devices fell outside the ambit of the Medicines Act.[7] Medical devices, broadly speaking, are appliances or products used for diagnosis or medical treatment that, in contrast to medicinal products, do not act principally by pharmacological means. Examples are diagnostic kits and heart pacemakers.[8] In borderline cases, where it is not clear whether or not something should be submitted for licensing as a medicinal product, guidance is provided.[9] Also, Orders have been made under s.104 of the Medicines Act extending the provisions of the Act to cover a range of devices which are not medicinal products, but are made wholly or partly for medicinal purposes.

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6 There are also provisions under subordinate legislation for granting licences for the parallel importation of medicines.

7 Although evaluation of some has been effected by the Medicines Device Agency of the Department of Health and of others by medical professional organisations.

8 A more detailed definition of a medical device can be found in EC Directive 93/42/EEC.

9 Medicines Control Agency (1990) **A Guide to the Status Under the Medicines Act of Borderline Products for Human Use** Medicines Act Leaflet MAL 8

12.18 The exclusion of many medical devices from the strict controls of the Medicines Act has called into question whether their safety, quality and efficacy are adequately safeguarded. Whereas strict quality control laws apply to diagnostic laboratory reagents in the USA, this has not been the case in Europe. Guidelines are in place in respect of some devices, for example, bone chips, corneas and heart valves, but there does not appear to be comprehensive coverage.[10] The European Commission has now become more active in this matter. Two harmonisation Directives, the Active Implantable Medical Device Directive (90/385/EEC) and the Medical Devices Directive (93/42/EEC) have been adopted. However, because there appears to be considerable diversity in practice in Member states, human tissue and devices which incorporate such tissue were deliberately excluded from the provisions of the Directives.

12.19 The Commission's advisory European Committee for Standards is currently considering standards for *"Tissues for use in medical devices"*. The extent to which a third Directive, proposed for In Vitro Diagnostic Medical Devices, will apply to devices involving the use of human tissue is not yet clear. In any event, there appears to be no intention to include devices used for medical or pharmaceutical research. Research ethics committees, however, are requested to take these matters into account when formulating opinions on research proposals.

12.20 In our view, it would be undesirable to allow human tissue related devices to fall through a gap in the regulatory coverage, and we support those who believe that not only should there be comprehensive guidelines laid down in respect of the manufacture and use of all human tissue related medical devices but also that the proposed Directive concerned with In-Vitro Diagnostic Medical Devices should extend coverage to all such devices.

[10] The Medical Devices Agency (formerly the Medical Devices Directorate) is the competent UK authority for introducing and enforcing statutory controls on medical devices under European Directives and is also responsible for auditing the quality assurance systems of medical devices manufacturers supplying the NHS from overseas, for investigating adverse incidents involving medical devices and for managing a programme to evaluate medical devices and publish reports. It has also adopted a Code of Practice on enforcement.

Examples of other regulations applying to medicinal products and medical devices

European Medicines Evaluation Agency[11]

12.21 The European Union is moving towards a single pan-European system to regulate all procedures including safety, quality, efficacy, and information handling that affect medicinal products. A major step towards this objective has been the recent establishment of the European Medicines Evaluation Agency in London. It will be responsible for the co-ordination of the registration procedures for medicines in the Community. Centralised procedures are now compulsory for the licensing of biotechnological medicines involving recombinant DNA technology, controlled expression of genes coding for biologically active proteins and hybridoma and monoclonal antibody methods. The procedures are optional for other high technology medicines and new active substances.

12.22 The Agency will also be responsible for the coordination of national monitoring and inspection and other controls in order to guarantee the safety of medicinal products available in the Community. A decentralised procedure will enable a marketing authorisation issued by one Member state to be extended to one or more other Member states as a result of the recognition of the original authorisation. There are also moves towards a broad international harmonisation of technical and other aspects of product registration through the International Conference on Harmonisation.

Biological standards

12.23 The National Biological Standards Board, set up under the Biological Standards Act 1975, manages the National Institute for Biological Standards and Control (NIBSC). The NIBSC monitors the safety and quality of biological substances used in medicine such as vaccines, hormones and blood products, whose purity or potency cannot be adequately tested by chemical or physical means.[12]

[11] See, Jones & Jeffreys: **EMEA and the New Pharmaceutical Procedures for Europe" Health Trends** 1994. 26. 10-13.

[12] National Institute for Biological Standards and Control (1993/4)4) **Annual Report 1993/94**, Potters Bar

Records

12.24 There are obligations to maintain records relating to medicinal products. Persons responsible for placing medicinal products on the market have a duty to make arrangements for archiving of documentation; the investigator must arrange for the retention of the patient identification codes for at least 15 years after the completion or discontinuation of trials; any changes of ownership of all data must be documented; and all such data and documents must be made available if requested by relevant authorities.[13]

Audit

12.25 Independent audits of organisations or hospital departments handling blood or other human tissue are now often required. For example, Clinical Pathology Accreditation (UK) Ltd, provides an external audit of the quality of service provided by pathology departments.[14] It defines, reviews and monitors standards for the organisation and performance of clinical pathology and it provides accreditation for pathology departments. Detailed standards and guidelines are set out relating to all aspects of pathology work.[15] Thus, when blood and blood products are stored, it is necessary to ensure that facilities are adequate and secure; when they are moved, for example when blood is transferred between hospitals, the recipient must request written confirmation of satisfactory prior storage conditions; there are also written procedures relating to specimen collection, handling and disposal.

Good laboratory practice

12.26 Underpinning all this detail are requirements to comply with *"Good Laboratory Practice"* and to provide evidence of compliance; this must be done, for example, by pharmaceutical companies when applying for marketing authorisation for a medicinal product; and by laboratories which carry out tests on chemical and biological products to determine their safety for man.[16]

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[13] See EC Directive 91/507/EEC (Updated Standards and Protocols for the Testing of Medicines for Human Use).

[14] This is a non-profit making company incorporating as shareholders *inter alia* the Royal College of Pathologists, the Association of Clinical Pathologists and the Association of Clinical Biochemists.

[15] These relate, inter alia, to organisation, administration, staffing, facilities and equipment, policies and procedures, staff development and education and evaluation. All equipment has to be appropriate for service demands and properly checked; and adequate storage facilities must be provided for specimens, reagents and records.

[16] There are two EC Directives (87/18/EEC and 88/320/EEC) which harmonise principles of Good Laboratory Practice (GLP) to ensure that there is compliance with all relevant Regulations. The detailed information requirements are set out in the Annex to Directive 87/21/EEC as amended by Directive 91/507/EEC. Member

Regulations applying to specific tissue

Blood and blood products

12.27 Products derived from human blood and plasma can be considered in two main groups:

1 Whole blood or blood products derived from single donations, or from pools of source material deriving from fewer than 12 donors, collected and distributed by blood centres. Whole blood is unprocessed and blood products such as cell concentrates are subjected to only one or a few separation procedures. Thus safety and quality is largely dependent on careful selection and control of donors, on microbiological screening of donations and on measures taken to minimise contamination during processing.

2 Blood products derived from plasma, produced on an industrial scale from pools of source material, and by various manufacturing procedures. These products are covered by the Medicines Act. Their quality and safety are assured not only by selection and screening of source materials, but also by the choice and control of manufacturing process. The products include albumin, immunoglobulins, plasma protein solutions, coagulation factors and antiproteases or other plasma fractions.

12.28 All national centres concerned with handling or processing blood, and the processing procedures involved, are licensed by the Medicines Control Agency. The Agency issues detailed guidelines: for example, *"Validation of virus vemoval and inactivation procedures"* and *"Medicinal products derived from human blood and plasma"*. The Medicines Control Agency also licenses imported blood products and samples are checked regularly.

12.29 When new risks arise and when knowledge improves, procedures change. The impact of more virulent or newly recognised viral infections has resulted in much higher priority being given to quality assurance programmes. Improved quality systems are being put in place in connection with blood collection programmes, donation testing and processing programmes, and the clinical use of blood and blood components. For example, donated blood is now routinely screened for hepatitis C.

States carry out inspections to verify compliance with GLP. The UK GLP Monitoring Unit is within the remit of the Department of Health. The Guide to Good Pharmaceutical Manufacturing Practice (the Orange Guide) set out general pharmaceutical manufacturing principles to ensure that end products were fit for their intended use. More recently, the European Community has published "Rules Governing Medical Products in the European Community, Vol. IV: Guide to Good Manufacturing Practice for Medicinal Products". Beyond these general guides are more detailed Guidelines for particular areas.

12.30 Nevertheless, there is no room for complacency. Incidents are regularly reported which call into question the effectiveness of particular procedures. When a private Germany company allegedly supplied unchecked and probably contaminated blood to many hospitals in Germany and abroad, it certainly highlighted the difficulties in calculating the risk of the medical use of imported human tissue. Another incident originated in France: it concerned one of the largest producers of blood products in the world which had specialised in collecting placentas from maternity units in some 40 countries for the production of albumin, immunoglobulins, and collagen, which were then sold worldwide. The placentas often came from countries where AIDS is common: it was alleged that the history of disease in the women sources was not sought and that serological tests had not been performed. Some experts maintained that, however thorough the inactivation processing, there was a potential risk of transmission of prion diseases such as Creutzfeldt-Jakob disease (CJD).[17] Clearly, legislative and professional safety and quality procedures must be strictly applied if they are to be effective.

Human milk banking

12.31 The steps to safeguard babies from the accidental transmission of disease in donated human milk are similar to those recommended for donated tissues or organs. There is careful screening of potential milk donors to ensure that those at high risk of infection are excluded (for example, blood tests to exclude HIV, hepatitis B and C), careful testing (and, where appropriate, counselling) of donors, proper treatment of the milk and proper maintenance of records about the donors and recipients.

Tissue for transplantation

12.32 Procedures relating to the safety and quality of material taken from donors are under regular review by, among others, the Department of Health which is currently carrying out a review of tissue banking in the UK. Donors who offer their tissue or organs for transplantation must be carefully screened to eliminate, or reduce as far as possible, the risk of transmission of infectious disease. Specific consent is required before a living donor is tested for evidence of HIV infection. In the case of cadaveric donations, careful enquiries of relatives are made to exclude donors at high risk. Testing procedures for tissue have become stricter. Recently, a bone graft recipient in the US developed AIDS from an implant from a donor who had initially tested negative for HIV but was subsequently found to be infected. As a result, recommendations have been strengthened in relation to all human organs, tissue and body fluids from living donors for transplantation and in relation to semen for artificial insemination. When tissue is stored prior to use it should not be

[17] See Nau, J-Y, **Lancet 342:**1290 (1993), and for a reply, Barré-Sinoussi, F *et al.*, **Lancet 343**:178 (1994).

transplanted until a second negative test at least 90 days later is obtained.[18] The British Association of Tissue Banks is developing guidelines for the safe handling of different stored tissues. Clearly there is a need for standardisation and harmonisation so that best standards of practice are maintained throughout different centres in the UK.

12.33 Several factors make it difficult to eliminate completely the risk of transmission of infectious disease. Different tissue requires different treatment: organs must be transplanted very rapidly, whereas skin and bone may be stored before use. Whether the donor is living or dead will affect the screening procedures used. Thus, tissue banks vary in the purpose for which they store human tissue, the nature of the tissue stored, their organisational structure, and their method of operation (paragraph 4.16). This, and the need for rapid use of much tissue, make it impractical and undesirable to centralise tissue banking. There is, however, a need for the coordination and regulation of tissue banks. This would facilitate the standardisation and harmonisation of procedures for ensuring the safety and quality of human tissue. We recommend that the Department of Health establish a central register of tissue banks approved for supplying tissue for medical treatment and for research. The maintenance of such a register would serve to coordinate the activities of different tissue banks and would improve the regulation of safety and quality.

Cadavers

12.34 Safety matters concern not only the ultimate recipients of human tissue. They are also imposed to safeguard those coming into contact with possible contaminated material. For example, advice has recently been given to licensed Anatomy Departments and all those involved with handling dead bodies, whether in post mortems or as part of anatomy teaching or research. The advice was to alert them to the small risk of transmission of disease posed by handling of the brains, spinal cords and eyes removed from the bodies of those who have or may have died from Creutzfeldt-Jakob disease (CJD) or Gerstmann-Straussler-Scheinker Syndrome (GSS), both rare prion diseases.[19] Anatomy Departments are required to make enquiries to establish whether there are such problems.

[18] Chief Medical Officer (1990) **Guidance and Advice Concerning Prevention of HIV Infection by Tissue Transplantation** PL/CMO (90)2

[19] Chief Medical Officer (1993) **Creutzfeldt-Jakob Disease from Treatment with Human Pituitary Gonadotrophins** PL/CMO (93)11

12.35 Cases of this kind point to the desirability of preserving records for longer than the minimum statutory periods: persons may now be at risk as a result of treatment many years earlier and need to be traced. This can be seen from another, similar, example. Between 1956 and 1985, hormones from the pituitaries of cadavers had been used to induce ovulation in the treatment of some infertile women whose ovaries did not produce eggs naturally. Recently, it was discovered that a small number of such women in the UK were at risk of developing CJD as a result of this treatment. Steps were taken to trace the women now known to be at risk to advise and to counsel them.

Wider ethical issues

12.36 It can be seen, therefore, that screening of donors is becoming ever more relevant. This raises issues relating to consent to the questioning of donors and their families and the nature of the obligations to such persons or their families in connection with information obtained as a result of such testing. Record-keeping, confidentiality, counselling and the ability to trace donors are other important ethical issues that have, rightly, attracted much attention. These issues, in addition to those mentioned above (paragraphs 12.32 - 12.33), will also have arisen in the review of tissue banking that is currently being carried out by the Department of Health. We recommend that, when the tissue banking review is completed, the Department of Health, in consultation with the appropriate professional bodies, should seek to take account of these concerns.

12.37 For example, confidentiality in the handling of human tissue and any records of it, is governed both by law and by professional guidelines. There are three statutes that directly touch on the confidentiality of health data. They are the Data Protection Act 1984, the Access to Medical Records Act 1988 and the Health Records Act 1990. There is also voluminous and complicated case law on confidentiality. In addition, healthcare professionals are expected to conform to professional guidelines on confidentiality. For doctors, these are set out by the General Medical Council; for the nursing professions they are set out by the UK Central Council for Nursing, Midwifery and Health Visiting. The Department of Health is currently reviewing confidentiality in the NHS. We recognise that the case law on confidentiality is complex, and that application of the professional guidelines may be difficult in borderline cases. We recommend that the Department of Health, in its current review of confidentiality in the NHS, should take account of the requirements for confidentiality and traceability in the storage and use of human tissue, including biological samples.

Safety and quality : an evaluation

12.38 Anybody attempting to evaluate all the laws and procedures affecting the safety and quality of activities involving the use of human tissue cannot but be overwhelmed by the range of provisions which are involved. It is difficult to assess whether all these mechanisms are appropriate. The European Commission, the UK authorities and the relevant professional bodies have done a great deal to harmonise and strengthen procedures; and, as more information becomes available, increasing standards relating to safety and quality are imposed.

12.39 Some argue that the licensing of products involving the use of human tissue is not all-embracing and that gaps and weaknesses in the Medicines Act should be plugged or at least strengthened to protect the consumer.[20] There is a continuing need to match the rapid technological advances with the development of parallel procedures for assuring the quality of the products which are used.[21] Others maintain that excessive regulation is unnecessarily time-consuming and counter-productive.

12.40 Whilst we would urge that the monitoring of safety, quality and efficacy should be comprehensive, clearly understood, enforceable and effective, we are conscious that there is continuous activity in this area, at European and national levels, designed to achieve these objectives. The pressures of public opinion, particularly as the result of media publicity, and of litigation, to which we now turn, do much to ensure that standards are adhered to and are continually improved.

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[20] Brahams: "Introduction to the Legal Aspects of Pharmaceutical Medicine: A Brief Overview of Some Emerging Issues" in Griffin, O'Grady and Wells (eds), **The Textbook of Pharmaceutical Medicine** (Belfast, Queen's University of Belfast, 1993).

[21] *"Medicinal products arising from the application of the new biologies (especially recombinant DNA and monoclonal antibody technologies) are being developed for clinical use at an ever increasing rate. Changes in a number of areas have posed unprecedented challenges to the regulatory authorities who are responsible for the licensing and quality control of such products ensuring their quality, safety and efficacy and that they reach the market without delay."* Jeffcoate, Corvel, Minor, Gaines-Das and Schild: (1993) "The Control and Standardisation of Biological Medicines" **Proceedings of the Royal Society of Edinburgh**, **101B**: 221

Criminal sanctions and compensation for injury

Penalties and compensation

12.41 Failure to comply with laws designed to promote safety can result in criminal sanctions. Thus, breach of many of the obligations under health and safety regulations are criminal offences. Similarly, the Medicines Act 1968 creates offences relevant to such matters as licensing, clinical trials, sales, prescriptions, quality, registration, leaflets, labelling and advertising.

12.42 Staff members of medical or research establishments (a medical director or clinical research officer, for example) may be personally criminally liable for offences under the Medicines Act, such as for failure to report adverse drug reactions. Prosecutions of this kind are a matter for the police and other public prosecution authorities. It has been suggested that private individuals or professional bodies might seek to use the criminal process to obtain compliance with, say, the Medicines Act (for example, with regard to false drug claims), but this is likely to be rare.

Civil liability

12.43 Defective human tissue which causes loss or damage, can give rise to claims for compensation. Actions may be brought by victims, including those who suffer injuries before birth, against different persons or organisations: the donor; those who use or sell the tissue itself or who manufacture or import human tissue based products; and institutions or authorities, such as the Committee on the Safety of Medicines and the Department of Health, who may be responsible for the proper regulation of activities involving human tissue. Thus, in recent litigation, several of such parties have been joined as defendants. Claims may arise either in contract or, more commonly, in tort law. These will be looked at briefly in turn.

Contract

12.44 Standard law applicable to the sale of all goods or supply of all services in the course of business is that a purchaser may have a claim against the seller should the product prove to be defective.[22] This would also apply where the contract is for the sale of human tissue, whether in its original form, or after treatment, or as a component of another product. We have discussed elsewhere, whether transactions involving

[22] See the Sale of Goods Act 1979, the Supply of Goods and Services Act 1982 and the Sale and Supply of Goods Act 1994. At one time different consequences could have flowed depending upon whether the sale of human tissue was the sale of goods or of services, but this is no longer an issue as far as a claim in contract is concerned.

human tissue should be commercially organised and whether commercial contracts dealing with the sale of blood and other human tissue are currently entered into. It seems clear that the activities of any institution which sells human tissue, whether at cost-recovery or for profit, would be *"in the course of business"*: this would include the National Blood Service, a tissue bank, a private hospital or, indeed, an NHS institution which entered into such contracts.[23]

12.45 Such tissue must be of merchantable quality and suitable for *"all the purposes for which goods of the kind in question are commonly supplied"*. It is not necessary for the purchaser to show that the supplier has been negligent in any way; it is only necessary to show that the product which has been sold does not satisfy the terms, express or implied, of that contract. So, where a research organisation buys human tissue from a foreign supplier, that supplier (if it can be sued in the UK) may be liable for the poor quality of the product, because it would not meet the statutory requirement that it be of *"satisfactory quality"* or *"appropriate for its contemplated use."* Even if the purchaser does not bother to test the quality of the tissue, this will not count against it in an action for breach of contract. If the tissue is bought by one person and then sold on, the parties to each contract have similar obligations, but only to the other party to their contract.

12.46 The donor of defective human tissue would not ordinarily be liable **in contract** for any defects, since there would no contract relating to the supply of that tissue. Nor would most medicinal products prescribed under the National Health Service: the courts have held that there is no contract between a patient and a pharmacist in connection with the drugs since a pharmacist has a statutory duty to supply the patient on presentation of a prescription.

12.47 In most cases, in any event, actions in respect of defective human tissue are likely to be brought under tort law, that is, where independently of any contract, a claim for damages may be brought for harm suffered.

[23] The contractual situation can be quite complex. For example, in the case of the supply of blood: the National Blood Service (NBS) sells whole blood and blood components to National Health Service authorities and non-NHS, private sector, bodies. The NBS also sells plasma to the Bio Products Laboratory (BPL) for production of plasma products. BPL, in turn, charges NHS and private sector bodies for supplies of plasma products. In all these transactions, there is no charge for the whole blood, blood component or plasma itself, since it is derived from freely donated blood. The charges are intended to reflect the costs to the National Blood Service, and Bio Products Laboratory, of producing and supplying blood products.

Actions for breach of statutory duty

12.48 We have already noticed that failure to comply with health and safety regulations often gives rise to criminal liability. In some cases, those injured as a result of such breaches may also use the offence as the basis of a civil action for breach of statutory duty. The courts will allow such actions where it is expressly provided in the relevant law or where they believe that it was the intention of Parliament to allow such a civil action. It is widely applicable for breach of health and safety at work regulations; it is less commonly available in other legislation, including the Medicines Act 1968.

Negligence actions

12.49 There are three prerequisites to a negligence action. First, the defendant must owe a legal duty to the plaintiff to take care. Those supplying human tissue, or a product containing human tissue, would usually owe such a duty to the injured party to take reasonable care in connection with the acquisition, preparation and use of that tissue.

12.50 Secondly, the defendant must be shown to have been in breach of that duty. It is not sufficient for the plaintiff simply to demonstrate that injury has occurred. It must be shown that the defendant did not exercise the degree of care which would have been expected of a reasonable person in those circumstances. For example, a donor of tissue might be negligent if he knew or should have known that the tissue could be contaminated and fails to disclose this information; other suppliers of tissue who do not take care in handling or treating the tissue might be liable; tissue banks for failing to take care in screening or treating tissue or, indeed, in some cases, the licensing or monitoring authorities for failure to lay down, monitor or enforce appropriate standards.

12.51 Proving negligence is often difficult. Where the defendant did not carry out its statutory or, indeed, its professional obligations or did not otherwise conform with relevant standards or guidelines a presumption of negligence will normally arise, for these standards reflect what experts regard as good practice. It is worth noting, however, that the Medicine Act s.133(2) expressly declares that breach of the provisions of the Act, or Regulations made thereunder, does not amount to negligence *per se.* Nevertheless, unless some good reason can be offered for failing to comply with common practice and guidelines aimed at promoting safety a breach of duty is likely to be established.

12.52 Although **failure** to comply with established standards may be evidence of negligence, it does not always follow that **compliance** with standards and practice is conclusive evidence that the defendant had taken reasonable care. For example, new events may have occurred necessitating a change of practice, even though statutory standards may not have yet been amended accordingly. Nor is the fact that a product has obtained licensing approval necessarily a defence to any particular negligence action. For example, Article 9 of Directive 65/65/EEC provides that a marketing authorisation under European law *"shall not affect the civil and criminal liability of the manufacturer and where applicable, of the person responsible for placing the proprietary medicinal product on the market."* Nevertheless, the fact that a defendant has complied with the appropriate requirements does cast a heavier burden on the plaintiff to establish that there has been a breach of the duty of care.

12.53 Standards of care change from time to time: what was not negligence in 1990 may well be negligence in 1995. As knowledge, and the perception of risks and their avoidance, improve, so too do the obligations imposed upon those who work in these areas. For example, at one time far less was known than today about the various contaminants in blood products: HIV, hepatitis, syphilis, malaria and toxoplasmosis; and methods of screening or heat-treating blood products were not so prevalent. There may have been no negligence liability on the supplier of defective blood had a person then been contaminated with an HIV virus. The situation would be different today, when the norm is to test for such viruses. But what of other viruses? Does an obligation to screen for all known viruses arise as soon as the risk of their presence becomes known? The view has been expressed that as *"more and more minor contaminants of recombinant DNA derived human growth hormone are being identified which are biologically active and pose no safety problem .. the effort and expense in identifying them and then measuring them on a batch-to-batch basis may be out of proportion to the public health risk"*.[24] As long as no adverse consequences follow, that argument may appear to be sound. But what happens if a virus which is deliberately neglected turns out to be far more potent than was anticipated? This has been an issue with hepatitis C: could it be said to be negligent to take a professional, and considered, decision not to screen for this virus even when its presence but not its full potency were known? And what of such bodies as the Committee on the Safety of Medicines and the Licensing Authority (paragraph 12.14): should they be liable for failure to act earlier to impose higher standards of care?[25] In the last resort, it will be for the courts to weigh up all the factors and decide whether the balance struck was reasonable.

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[24] Jeffcoate, Corvel, Minor, Gaines-Das and Schild: (1993) "The Control and Standardisation of Biological Medicines" **Proceedings of the Royal Society of Edinburgh**, **101B**: 207-226

[25] Actions have been commenced against regulatory authorities for negligence in failing to implement stronger statutory requirements. For example, in *Re HIV Haemophiliac Litigation* [1990] NLJR 1349 (CA) the Court of Appeal held that there was an arguable claim in negligence against the regulatory authorities, but the matter has not been conclusively determined.

12.54 The third condition that must be satisfied in a negligence action is that the defendant's breach of duty **caused** the damage complained of. This has often turned out to be the most difficult issue of all. In some of the major drug actions in recent years, defendant drug manufacturers have disputed any causal link between the drug and the injuries sustained, or, if a link is established, that it was the particular defendant's drug, as opposed to the same drug from other companies, that caused the plaintiff's injuries.

12.55 This brief outline of the law of negligence demonstrates that those injured in the course of medical or related activities involving the use of human tissue will often find it difficult, or impossible, to establish that the injuries have been caused by negligence. The unfairness of the negligence system was highlighted by the Thalidomide episode and the ensuing campaign for compensation in the 1960s. Many argued for a new system of compensation to replace negligence in which, if a person is injured by a defective product supplied directly or indirectly by the defendant, compensation should be paid.

Strict liability[26]

12.56 These pressures eventually led to a European Community Directive on Product Liability in 1985 for compensation for injuries resulting from defective products; and this was implemented in the UK by Part I of the Consumer Protection Act 1987. The need to prove fault was abandoned. If a person can show that he or she was injured by a *"defective product"*, then compensation is payable.

12.57 A product is *"defective"* when it does not provide the safety which a person is entitled to expect, taking all the circumstances into account. Thus, instructions for use, contraindications and warnings and supplied information in one form or another may in some cases assist in determining whether the product was *"defective"*. Contaminated blood supplied to patients, or a defective organ used for transplantation, are likely to be regarded as "*defective products"* regardless of the information which is given to patients.

[26] In certain cases, where a dangerous activity is being conducted on land and there is an escape from that land causing physical injury, an action for damages will lie without proof of negligence. This action, known as the Rule in *Rylands v Fletcher* is not commonly used today.

12.58 Liability is imposed upon producers, including manufacturers, importers and suppliers of such products. It is likely that human tissue would be regarded as *"products"* for these purposes. This was recommended by the Pearson Royal Commission in 1978.[27] Human tissue used for medical purposes, although not strictly manufactured, would possess the *"essential characteristics attributable to an industrial or other process"*.

12.59 Although these strict liability provisions are an improvement on the negligence action, there are still many difficult hurdles which an injured person has to face before liability can be established. The two most difficult are the so-called *"development-risk"* defence and, once again, causation.

"Development risk" or "state of the art" defence

12.60 When the Product Liability Directive was being drafted, many large manufacturing industries, and in particular the pharmaceutical industry, urged that they should not be made responsible for the unforeseeable consequences of *"state of the art"* drugs. Such vast potential liability would act as a disincentive to industrial research and development.

12.61 The European Commission left it to Member states to decide whether or not it would introduce a *"development risk"* defence. The UK accepted the arguments of industry. Accordingly, s.4(1)(e) of the Consumer Protection Act provides that in any proceedings for liability for a defective product, it shall be a defence to show *"that the state of scientific and technical knowledge at the relevant time was not such that a producer of products of the same description as the product in question might be expected to have discovered the defect if it had existed in his products while they were under his control."* What this means in the context of human tissue, is that if any product involving human tissue causes damage as the result of a risk which the defendant company can show could not have been generally foreseen at the time, there will be no liability: for *"state of the art"* products, negligence has been retained, although the burden of disproving it is for the defendant. In all other cases, however, fault is not a component of this action.

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[27] Royal Commission on Civil Liability and Compensation for Personal Injury (the Pearson Report) (1978. Cmnd. 7054-1):

> "An operation may have unexpected consequences. Blood products may be used which contain viruses the presence of which could not be foreseen. There are now three thousand drugs in common use and ten thousand listed drug interactions, both detrimental and beneficial. More will doubtless be discovered." (Para. 1350)
>
> "We recommend that human blood and organs should be regarded as products and the authorities responsible for distributing them as their "producers" for the purpose of products liability." (Para. 1276).

12.62 The need to prove causation remains, however. Not many cases have come before the courts, but those which have demonstrate what a formidable hurdle this can be. Thus, the issue in *Loveday v Renton*[28] was whether the whooping cough (pertussis) vaccine could cause permanent brain damage in young children. The court held that the plaintiffs had not been able to prove that there was a causal link. The Vaccine Damage Payments Act 1979 provides a scheme for limited payments of compensation for certain types of victim of vaccine damage. Here, too, there can be difficult problems of causation.

Class or group actions

12.63 In recent years, where multiple actions are being contemplated for similar injuries against the same defendant, for example in a drug case, attempts have been made to use procedures which would allow a type of American style class action. This is now, to some extent permitted in English litigation:[29] for example, in connection with Opren (an anti-inflammatory drug prescribed for arthritis); and in respect of claims, which were ultimately settled out of court, by haemophiliacs who had been given HIV infected blood products in the early 1980s when the risks of infection were known, but it was alleged, were not dealt with satisfactorily so as to protect recipients.

Compensation for research injury

12.64 Patients or volunteers who suffer any injury in the course of research in the UK are in no special position as far as compensation law is concerned. Their rights will be determined in accordance with the general law. There are European Guidelines which require the pharmaceutical industry to provide adequate insurance and compensation for subjects in the event of trial related injury or death. In the UK the pharmaceutical industry undertakes to compensate injured non-patient research subjects and also, in more limited circumstances, injured patients; whereas in other areas of research activity, for example, in NHS hospitals, the Medical Research Council and universities, compensation is paid only on an *ex gratia* basis. Fortunately, the number of cases where injuries of this kind occur is low. We would, however, add our voice to those who would prefer to see a fairer and binding obligation upon all researchers to provide adequate compensation.

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[28] *Loveday v Renton* [1990] 1 MLR 117

[29] RSC O.15 Rule 2. provides that where "numerous persons have the same interest in any proceedings [these] may be begun and, unless the court otherwise orders, continued, by or against any one or more of them, as representing all or as representing all but one or more of them."

Conclusions

12.65 Medical malpractice litigation in the UK has increased significantly in the last decade. Claims involving defective medicinal products have been brought, for example, in connection with hormone pregnancy tests, Debendox, Opren, pertussis vaccine, blood products, human insulin and human growth hormone. The deficiencies of the present law, even after the introduction of strict product liability, have been emphasised frequently. Even though procedural changes provide some assistance to those seeking compensation, there are many who feel that the law, as it is at present, is failing us. The cost of litigation is high; the procedures complicated and lengthy; the burdens placed on claimants unfairly weighted against them; and the adversarial nature of litigation procedures socially and professionally damaging. There is dissatisfaction in many quarters. Some would seek to change the present system, for example, to allow liberally applied 'no-fault' or insurance compensation schemes.

12.66 It is beyond the remit of this Working Party to contribute to that particular debate. However, we do agree with those who criticise the present state of the law, and support those who seek a further review of it.