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Legislation Affecting the Collection, Use and Safe Handling of Entomopathogenic Microbes and Nematodes

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Introduction

Collection, isolation, handling and maintenance of organisms are subject to safety regulations and legal obligations. Legislation continues to develop and change (Smith, 1996), which undoubtedly affects biologists who collect and characterize organisms in their goal to further scientific knowledge. In particular, the Convention on Biological Diversity (CBD), which was signed at Rio de Janeiro in 1992 and came into force in December 1993 (CBD, 1992) and has now been ratified by more than 140 countries, controls access to *in situ* organisms. The CBD gives sovereign rights over genetic resources to the country of origin. In the simplest of terms, the CBD requires a biologist who wishes to collect genetic resources to seek prior informed consent from relevant authorities and negotiate fair and equitable sharing of benefits that may arise from their use before access can be granted. The Convention and national legislation on access to genetic resources place an enormous duty on the shoulders of the collector, but are not intended to prevent the advancement of science.

Organisms of hazard groups 2, 3 and 4 (see p. 306 for definitions of hazard groups) are hazardous substances under the UK Control of Substances Hazardous to Health (COSHH) legislation. They fall under the EU Biological Agents Directives and are dangerous goods as defined by the International Air Transport Association (IATA) Dangerous Goods Regulations (IATA, 1998), where requirements for their packaging are defined. Further, there are restrictions on distribution imposed by National Postal Authorities, according to which more and more countries prohibit receipt of Infectious, Perishable Biological Substances (IPBS) and, in some cases, Non-infectious

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Perishable Biological Substances (NPBS), including hazard group 1 organisms. Whether organisms are shipped by mail, courier or by hand and whether between or within countries, thought must be given to the regulations that control these matters. The EC Directives 93/88/EEC and 90/679/EEC on Biological Agents set mandatory control measures for laboratories requiring that risk assessments are carried out on all organisms handled. This necessitates the assignment of each strain to a hazard group following a thorough risk assessment including a positive inclusion into hazard group 1 when they are not categorized in hazard groups 2, 3 or 4. The risk assessment should include an assessment of all hazards involved, including the production of toxic metabolites and the ability to cause allergic reactions. Most entomopathogens, in particular those currently used for pest control, are classified as hazard group 1, but care must be taken as they may produce toxic metabolites.

The implications of a laboratory's health and safety procedures stretch beyond the laboratory to all those who may come in contact with substances and products from that laboratory. An organism in transit will potentially put carriers, postal staff, freight operators and recipients at risk. It is essential that safety and shipping regulations be followed to ensure safe transit. More stringent shipping regulations have evolved because of increasing cases of careless and negligent handling. Sound packaging and correct labelling and information must be used to minimize risk.

This chapter draws attention to legislation and requirements relevant to collecting and handling biological specimens. Many countries do not have health and safety or access to genetic resources legislation and in such cases it is recommended that as a guide the regulations of other countries can be followed. Attention is drawn to legislation that could be followed. Ownership of intellectual property rights is discussed, in particular, how this relates to patenting living organisms and the CBD. The importance of health and safety legislation in handling, storage and supply of organisms is raised and their classification on the basis of hazard and associated risk are discussed. Regulations affecting the distribution of organisms covered here concern postal, shipping, packaging, quarantine and control of dangerous pathogens and safety information provision. Sources for further information are provided and some suggestions on sound practices are offered.

Ownership of Intellectual Property Rights

Organisms can be collected from different habitats all over the world. This begs the question: Who owns these organisms and the intellectual property rights associated with them? The CBD bestows sovereign rights over genetic resources to the country where they arise. The landowner and the national government are the first stakeholders, followed by the collector, those involved in purification and growing the organism, the discoverer of intel-

lectual property, depositor, collection owner and the developer of any process. It is clear that they do not all have an equal stake and this will depend upon their input to discovery or process. This has implications for the sharing of benefits arising from exploitation of the genetic resource. These are amongst the issues that are being discussed by delegates from the countries signatory to the CBD who meet at the Conference of the Parties and their workgroups. Information on the progress of these discussions can be found on the CBD web site (http://www.biodiv.org/).

Patents including living organisms

The general principles of international patent law require that details of an invention must be fully disclosed to the public. Inventions involving the use of organisms present problems of disclosure as a patented process often cannot be tested following the publication of a written description alone. If a process involving an organism has novelty, inventiveness, utility or application and sufficient disclosure, it can be subject to patent (Kelley and Smith, 1997). Organisms are not patentable in their natural state or habitat, new species are discoveries, not inventions. The invention of a product, a process of manufacture or a new use for a known product is an intellectual property owned by the inventor whether it involves an organism or not. It is often difficult to patent organisms as products themselves, although genetically manipulated microorganisms are usually considered as a human invention and are therefore patentable. The situation is less clear in the case of spontaneous or induced mutants of naturally occurring organisms, which fall midway between the natural and the artificial.

In many cases the organism involved must be part of the disclosure. This reasoning has led to an increasing number of countries either requiring by law or recommending to inventors that the written disclosure of an invention involving the use of organisms be supplemented by the deposit of the organism in a recognized culture collection. It is recommended by most patent lawyers that the organism is deposited, regardless of it being a requirement, rather than running the risk of the patent being rejected. To remove the need for inventors to deposit their organisms in a collection in every country in which they intend to seek patent protection, the 'Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purpose of Patent Procedure' was concluded in 1977 and came into force towards the end of 1980. This recognizes named culture collections as 'International Depositary Authorities' (IDA) and a single deposit made in any one is accepted by every country party to the treaty. Any collection can become an IDA providing it has been formally nominated by a contracting state and meets certain criteria. The CABI Genetic Resource Collection is one of 29 IDAs around the world accepting patent deposits of fungi, including yeasts, phytopathogenic bacteria and nematodes. There are six other

IDAs in the UK and many of the others are collections belonging to the European Culture Collection Organization (Anon, 1995). The Budapest Treaty provides an internationally uniform system of deposit and lays down the procedures which depositor and depository must follow, the duration of deposit and the mechanisms for the release of samples. Thirty-six states and the European Patent Office are now party to the Budapest Treaty.

The World Intellectual Property Organization (WIPO) publishes data on the numbers of microorganisms deposited in collections under the terms of the Budapest Treaty (1977). Since the treaty's inception, there were 24,712 deposits up to December 1994 (Anon, 1996a). Patent protection is covered in Article 16 of the CBD under which parties must cooperate, subject to national legislation and international law, to ensure patents and other intellectual property rights are supportive of, and do not contravene, the objectives of the Convention (Fritze, 1994). This remains an area of dispute as the Article leaves open the possibility that the CBD takes priority over national patent law. Patent law and the CBD are generally compatible but can conflict in cases where exploitation may endanger the resource. In many cases where organisms are grown artificially there is no threat to the existence of the species. Details of the requirements for a collection which relate to the deposit of an organism can be obtained directly from IDA collections and are summarized by Kelley and Smith (1997).

It is quite clear that every intermediary in an improvement or development process is entitled to a share of the IPR, which adds another dimension to ownership. It is therefore critical that clear procedures on access, mutually agreed terms on fair and equitable sharing of benefits and sound material transfer agreements are in place to protect interested parties.

The Convention on Biological Diversity

The CBD aims to encourage the conservation and sustainable utilization of the genetic resources of the world and has a number of articles that affect biologists. These cover:

- Development of national strategies for the conservation and sustainable use of biological diversity.
- Identification, sampling, maintenance of species and their habitats and the production of inventories of indigenous species.
- Encouraging *in situ* and in-country *ex situ* conservation programmes.
- Adoption of economically and socially sound measures to encourage conservation and sustainable use of genetic resources.
- Establishment of educational and training programmes and the encouragement of research.
- Commitment to allow access to genetic resources for environmentally sound uses on mutually agreed terms and with prior informed consent.

- Fair and equitable sharing of benefits and transfer of technology resulting from exploitation of genetic resources.
- Exchange of information.
- Promotion of technical and scientific cooperation.

The principles should not affect the development of science, but unfortunately some countries' legislation is placing obstacles in the way. It is essential that biologists continue to lobby their country representatives to ensure that science is not impeded whilst the principles of the CBD are being implemented. For example, Brazil is currently developing a new intellectual property law, which includes an article protecting traditional and ethnic knowledge. However, scientists fear that if the law is too restrictive and, by making it a criminal offence to remove genetic material from the country, it will restrict collaboration with foreign researchers (Neto, 1998). Currently, any foreign scientist wishing to work with biodiversity in Brazil must be accompanied by researchers from Brazil and confer co-authorship on subsequent publication of results.

The CBD requires that prior informed consent (PIC) be obtained in the country where organisms are to be collected before access is granted. Terms on which any benefits will be shared must be agreed in advance. The benefit sharing may include monetary elements but may also include information, technology transfer and training. If the organism is passed to a third party it must be under terms agreed by the country of origin. This will entail the use of material transfer agreements between supplier and recipient to ensure benefit sharing with, at least, the country of origin. Many biological resource centres or culture collections have operated benefit sharing agreements since they began, giving organisms in exchange for deposits and re-supplying the depositor with the strain if a replacement is required. However, huge rewards that may accompany the discovery of a new drug are illusory as the hit rate is often reported as less than 1 chance in 250,000. In the meantime, access legislation and the hope for substantial financial returns from isolated strains are restricting the free deposit in public service collections and the legitimate free movement of strains. An EU DG XII project, Micro-organisms Sustainable Use and Access Regulation International Code of Conduct (MOSAICC) is developing mechanisms to allow traceability and enable compliance with the spirit of the CBD and with national and international laws governing the distribution of microorganisms, whilst not restricting scientific goals (Davison *et al.*, 1998).

Perspectives on the Convention

There have been several interpretations on how the Convention affects the microbiologist, but discussions continue to leave unresolved problems. Six years on from the Earth Summit in Rio de Janeiro, yet more problems were

raised at the fourth Conference of the Parties held in Bratislava in 1998. It is difficult for biologists to know what is required of them, particularly where there is often no country law and codes of practice for them to follow. Whilst the debate continues, there is a danger that biologists will ignore their responsibilities under the CBD and thus compound the problems. A few simple steps to allow traceability of organisms can ensure compliance with legislation. Interested parties have expressed their views, some thinking the Convention impractical and impossible to implement, others seeing the opportunity for the protection of biodiversity and its sustainable use. Some of these points of view are expressed below (Kirsop, 1993; Sands, 1994; Kelley, 1995).

- Total opposition to intellectual property rights on life forms including humans, animals, plants, microorganisms or their genes, cells or other parts.
- Organisms are the heritage of humankind and consequently should be available without restriction. This view was expressed by the signatories of the 'Thammasat Resolution', *Building and Strengthening Our sui genesis Rights*, the result of negotiation between 45 representatives of non-government and government agencies, academia and others from 19 countries (Internet communication: 1997; Genetic Resources Action International@igc.org).
- Developing countries see the Convention as a means for financing development.
- Developed countries hoped it would help to preserve threatened environments and biodiversity.
- There is an opportunity for individuals, organizations and countries to profit from equitable sharing of the benefits.
- There is an opportunity to harness the environment as a source of genetic material, rather than of renewable or non-renewable materials, by giving countries a financial interest in its maintenance and preservation and thus allowing the international community as a whole to benefit.
- The Convention impedes the progress of science, and could have an effect on the continuance of some service collections.

It is clear that many concerns exist and these will take time to resolve. In the meantime, countries are developing legislation to control access to their genetic resources and biologists are struggling to comply. The IUCN has produced a guide to designing legal frameworks to determine access to genetic resources (Glowka, 1998) which examines the Convention and national access legislation. In the Philippines, Executive Order 247 puts in place a mechanism to ensure it controls access to and use of its genetic resources. The Andean countries are also developing their own regulations and procedures. The CBD Secretariat offers information on developments to attain workable regulations (http://www.biodiv.org/).

The role of public service collections

Public service culture collections are charged with several tasks, which are influenced by access legislation. They are in a unique position as custodians of *ex situ* genetic resources and therefore have a key role to play in the conservation of genetic resources (Kirsop and Hawksworth, 1994). Biologists who collect organisms for their research and publish information on them should make their most important strains available for confirmation of results and future use by depositing them in public service collections. This will aid collections in their major roles:

- The *ex situ* conservation of organisms.
- Custodians of a national resource.
- Provide a living resource to underpin the science base.
- Receive deposits subject to publication.
- Offer safe, confidential and patent deposit services.

The Convention should not affect these functions and will increase the importance and extent of the collection's role. However, depositors are increasingly concerned about who the customers are, and if their rights as a stakeholder are protected.

Approaches taken by collections to comply with the CBD

To date little guidance has been given to collections to determine actions necessary to comply with the CBD. Collections have therefore developed several approaches independently.

- Statements are prominently displayed on accession forms and on information accompanying delivery of strains explaining the implications of, and requesting compliance with, the Convention. This draws attention to the requirements but does not protect the sovereign rights of the country of origin nor any other stakeholder.
- A requirement for depositors to declare in writing that PIC has been obtained and that this includes unrestricted distribution of the materials to third parties or has clearly defined conditions on distribution.
- A requirement for a signed material transfer agreement on supply of material including mutually agreed terms.

These are minimum requirements and should be followed by all. The difficulty lies in defining the beneficiaries and what is a fair and equitable sharing of benefits.

Development of policies on intellectual property rights (IPR) and compliance with the CBD

Several organizations have addressed these issues and have developed and published their policies. These organizations include large national collections, international organizations and industrial companies. CAB International (CABI) is an intergovernmental organization established by treaty, dedicated to improving human welfare through the application of scientific knowledge in support of sustainable development worldwide, with emphasis on agriculture, forestry, human health and conservation of natural resources, and with particular attention to the needs of developing countries (http://www.cabi.org). The CABI Genetic Resources Collection (GRC) is based at the CABI Bioscience UK Centre (Egham) and is tasked with the collection of organisms to provide a resource for the scientific programmes of CABI and to underpin biotechnology, conservation and science in its member countries. CABI maintains extensive collections that originate from many different countries and has introduced policy and procedures to ensure compliance with the requirements of the CBD. This policy was agreed by member country representatives and published in the 13th Review Conference Proceedings (Anon, 1996b).

The CABI policy offers an example of a mechanism to enable compliance with the CBD. CABI keeps the rapidly changing situation under review and will adopt procedures required to keep its operations within the spirit of the Convention. CABI complies with national legislation of member country governments concerning rights over natural resources and access to genetic material, and interprets its policies in a manner consistent with the CBD. CABI treats all its living material holdings as subject to the sovereign rights of the country of origin. In considering any activity relating to the possible exploitation of biodiversity, CABI will seek to protect the interests of the source country of each element of biodiversity. CABI adds value to living or dead material it receives and collects particularly by ensuring authoritative identifications. It makes its reference collections and the information on them available to institutions in the countries of origin and the scientific community in general.

Supply of living strains from the CABI Collection requires a signed declaration from the recipient undertaking not to exploit the organism or related information. Recipients who wish to exploit materials are requested to negotiate terms through CABI. New deposits are equally controlled. Before CABI can consider the acceptance of strains into its collections confirmation is required from the depositor that the collector has made reasonable efforts to obtain PIC to collect the organisms and also has permission to deposit the strains in a public service culture collection. CABI also needs to know if there is any restriction on further distribution and if there are conditions that must be included in any material transfer agreement that may accompany the samples when they are passed to a third person.

CABI needs to have such information from all depositors regardless of the country of origin of the material or the collector. This is often difficult to enforce, as in most countries a PIC authority has not been appointed. In such cases, proof is required that a depositor has made reasonable efforts to get permission to collect from landowners and a government office.

Biological resource collections, such as public service collections, like the CABI Collection, often add value to received and collected biological material. This is done through purification, expert preparation, authoritative identification, description, determination of biochemical and other characteristics, comparison with related material, safe and effective storage/preservation, evaluation of value for specified uses, and indication of importance of beneficial and detrimental attributes. They often provide samples of deposited organisms free of charge to the depositor and participate in capacity building projects to help establish facilities and expertise in-country to maintain *ex situ* collections. This plays a role in the utilization of genetic resources and defines a collection as a stakeholder.

Suggested code of conduct for collection of biodiversity

Biologists collect entomopathogenic nematodes and microorganisms all over the world, not just in their own country. No matter where they collect they must do so legally, following national and international law. The following principles should be borne in mind:

- Do not collect material from any country without prior informed consent (PIC).
- Routinely seek documentation through standard identification or submission forms to clarify the status of the material received. Do not make the assumption that a sender of material has the authority to allow you to use and dispose of material as you deem fit.
- Do not make material available to third parties for the development of commercial products unless you have been given the authority to do so by the source country, or the recipient agrees in writing not to exploit such material without negotiating an agreement to do so with the source country and stakeholders.
- All material can be used for scientific research but the country of origin should benefit from receipt of published information.
- Collections should be prepared to loan dead material to scientists at government, university and research institutes in all countries of the world for research and identification purposes.
- The depositor of a culture into a collection should be given the right to the return of a replicate of their deposit on request at reasonable intervals without any charge.
- As far as practical, ensure that type material based on specimens submit-

ted is deposited in a recognized reference collection in accordance with any legislation of the country of origin. Where such legislation is not in existence, the material should be deposited in accordance with internationally accepted principles for stewardship of such material and the interests of the international scientific community as a whole.

Problems to be resolved

There are several problems that can impede the development of procedures for compliance with the CBD and these will need some time to resolve.

- Clarification is required on ownership, intellectual property rights and benefit sharing.
- Identification of country authorities who can grant prior informed consent.
- Identification of stakeholders and assessment of the value of their input.
- Establishing a clear, simple and flexible approach that avoids impractical bureaucracy.
- Monitoring and enforcement of procedures put in place.
- Keeping up to date with country legislation.

The CBD is not an opportunity for all to benefit financially, and prospects of accruing huge profits from exploiting an organism for the country of origin are very slim. Additionally, the process from sampling to market can take from 8–15 years, therefore nothing will be achieved quickly, and is likely to require considerable investment. The CBD was negotiated to protect genetic resources and ensure their sustainable use.

The agreement on Trade-related Aspects of Intellectual Property Rights (TRIPs) is thought to conflict with the CBD where there is concern that developing countries are required to allow companies to take out patents on products and processes of biotechnology. There are several forms of intellectual property rights that are relevant to the Convention in addition to patents, for example copyright, trade secrets and plant breeder's rights. The CBD requires that terms for technologies subject to IPR protection are to recognize and be consistent with adequate and effective protection of IPR (Glowka, 1998). In reality, so long as there is an agreement on mutually agreed terms for benefit sharing with the country of origin, the TRIPs agreement and patenting do not run contrary to the CBD.

Health and Safety

Organisms can present several challenges to health and safety including infection, poisoning and allergies (Anon, 1993; Stricoff and Walters, 1995). Handling, distribution and use of organisms are controlled by regulations.

Whether it is compliance with the law or duties of a caring employer, the basic requirements to establish a safe workplace are:

- Adequate assessment of risks.
- Provision of adequate control measures.
- Provision of health and safety information.
- Provision of appropriate training.
- Establishment of record systems to allow safety audits to be carried out.
- Implementation of good working procedures.

Good working practice requires assurance that correct procedures are being followed and this requires a sound and accountable safety policy.

The UK Management of Health and Safety at Work (MHSW) Regulations 1992 (Anon, 1992) are all encompassing and general in nature but overlap and lead into many specific pieces of legislation. The Control of Substances Hazardous to Health (COSHH) regulations require that every employer makes a suitable and sufficient assessment of the risks to health and safety to which any person, whether employed by them or not, may be exposed through their work (Anon, 1996d). These assessments must be reviewed regularly and must be recorded when the employer has more than five employees. The distribution of microorganisms to others outside the workplace extends these duties to protect others. Such assessments of risk are extended to other biological agents, such as entomopathogenic nematodes, through EC Council Directives on Biological Agents (90/679/EEC; 93/88/EEC).

The effect of some safety regulations on culture storage and supply

The COSHH regulations (1988) require a suitable risk assessment for all work that is liable to expose an employee to any substance that may be hazardous to health. This UK legislation has equivalents in other countries and at the European level. Organisms present different levels and kinds of hazard, evaluation of which represents an enormous, but necessary, task for biologists. A risk assessment, for example, must take into account the production of potentially hazardous toxins. Ultimately, a safe laboratory is the result of applying good techniques, a hallmark of technical excellence. Containment level 2 (Anon, 1996c) is easily achievable and should be standard practice in all laboratories handling organisms that present a risk of infection or of causing other harm. Good aseptic techniques applied by well-trained personnel will ensure pure and clean cultures and will minimize contact with the organism. However, accidents must also be taken into account when assessing risks. The employment of good laboratory practice and good housekeeping, workplace and equipment maintenance, together with ensuring that staff have relevant information and training, will minimize the risk of accidents. The establishment of emergency procedures to reduce potential harm is an additional and sensible precaution.

Classification of organisms on the basis of hazard

Various classification systems exist, including those of the World Health Organization (WHO), United States Public Health Service (USPHS), Advisory Committee on Dangerous Pathogens (ACDP), European Forum for Biotechnology (EFB) and the European Commission (EC). In Europe, the EC Council Directive (93/88/EEC) on Biological Agents sets a common base line which has been strengthened and expanded in many of the individual member states. In the UK, the definition and minimum handling procedures for pathogenic organisms are set by the ACDP, who list four hazard groups with corresponding containment levels (Anon, 1996c).

Group 1 A biological agent that is most unlikely to cause human disease.

Group 2 A biological agent that may cause human disease and which might be a hazard to laboratory workers but is unlikely to spread in the community. Laboratory exposure rarely produces infection and effective prophylaxis or treatment is available.

Group 3 A biological agent that may cause severe human disease and present a serious hazard to laboratory workers. It may present a risk of spread in the community but there is usually effective prophylaxis or treatment.

Group 4 A biological agent that causes severe human disease and is a serious hazard to laboratory workers. It may present a high risk of spread in the community and there is usually no effective prophylaxis or treatment.

Risk assessment

The species of bacteria, fungi and parasites falling into hazard groups 2 and 3 have been defined (Anon, 1996c). Similarly, all bacteria from the approved list have been assigned to an appropriate hazard group in Germany (Anon, 1997a, b, 1998). However, species of fungi have not been assigned to hazard group 1 (Anon, 1996c, d). Medically important fungi have been categorized into relevant hazard groups by de Hoog (1996). To meet the UK and European legislation, all microbiologists will have to make a risk assessment on the organisms with which they work or hold in collections. In the case of fungi, it is recognized that many may infect following traumatic inoculation through the skin, or infect a compromised patient, but do not infect healthy individuals. Most fungi from clinical specimens require Containment Level 2 (Anon, 1996c), although a higher degree of containment is specified for a few.

The COSHH regulations work well and can be easily applied in establishments with designed laboratories, but may not work as well in an industrial environment where very large volumes and more hazardous techniques may be used. Total containment is rarely applicable.

Assessment of the risks involved in handling organisms

Compared with chemicals, organisms are more difficult to name, less predictable and more difficult to enumerate or measure. Virulence and toxicity may vary from strain to strain and additional hazards, such as mycotoxin production and allergenicity, must be considered. To meet biological agents legislation, a step by step evaluation of a laboratory procedure or an industrial process must be carried out. The assessment must cover the procedure from the original inoculum or seed culture to the final product or the point where the organism is killed and disposed of. It must be noted that individuals may respond differently to exposure, with some being more sensitive than others. It is therefore critical that the full hazard potential of the organism is considered and that this is related to effects it may have on the particular individual carrying out the work.

Regulations Governing Distribution of Cultures

The distribution of organisms is controlled by numerous regulations. Some are discussed below and include postal and shipping regulations, requirements for packaging aimed at protecting handlers and recipients of organisms, and quarantine legislation to protect plant health. Countries have their own regulations governing the packaging and transport of biological material in their domestic mail. International Postal Regulations regarding the transport of human and animal pathogens are very strict because of the safety hazard they present. There are several organizations that set regulations controlling the international transfer of such material. These include the International Air Transport Association (IATA), International Civil Aviation Organization (ICAO), United Nations Committee of Experts on the Transport of Dangerous Goods, the Universal Postal Union (UPU) and the World Health Organization (WHO).

Postal regulations

It is common to send microorganisms by post, as this is more convenient and less expensive than airfreight (Rohde *et al.*, 1995). However, many countries prohibit the movement of biological substances through their postal services. The International Bureau of the UPU in Berne publishes all import and export restrictions for biological materials by national postal services (UPU, 1998). The UK Post Office leaflet on 'Infectious and non-infectious perishable biological substances in the overseas post' is available from the Post Office (Corporate Headquarters, 30 St James Square, London SW1 4PY. Tel: +44 171 490 2888; Fax: +44 181 681 9387) and provides relevant information. A list, which changes from time to time, of countries that will

not accept human pathogens through the post can also be obtained from the Post Office (also see Anon, 1998; Smith, 1996).

Shipping regulations

The IATA Dangerous Goods Regulations require that shippers of microorganisms of hazard groups 2, 3 or 4 must be trained by IATA certified and approved instructors. They also require shippers' declaration forms, which should accompany the package in duplicate, and specified labels are used for organisms in transit by air (IATA, 1998). There are several other regulations that impose export restrictions on the distribution of microorganisms. These include control of distribution of agents that could be used in biological warfare and EU Council Regulation (3381/94/EEC) on the control of export of dual-use goods. More generally, countries are currently implementing Access Regulations to Genetic Resources under the Convention on Biological Diversity. It is critical that microbiologists are aware of, and follow, such legislation. Details can be found in Alexander and Brandon (1986), *Shipping of Infectious, Non-infectious and Genetically Modified Biological Material, International Regulations* (Anon, 1998) and IATA Dangerous Goods Regulations (IATA, 1998).

In Europe, class 6.2 Dangerous Goods are transported by road, packed according to EN 829 requirements. Transport by road is regulated by the *Accord Européen Relatif au Transport International des Merchandises Dangereuses par Routes* (ADR). This clearly separates class 6.2 into two subclasses: A, highly infectious material (hazard groups 3 and 4), and B, other infectious material. These two groups, A and B, have different packaging requirements. However, currently there are no manufacturers producing these different shipping containers so that the UN specification containers for class 6.2 materials must be used for both subclasses. The EU has made an attempt to coordinate Member State laws on transport of dangerous goods by road with the 'ADR-Directive' (EC Council Directive (94/55/EC) of 21 November 1994) *on the Approximation of the Laws of the Member States on the Transport of Dangerous Goods by Road* and its annexes (EC, 1996).

The basis for all regulations governing the safe transport of goods for all carriers are laid down in the *Orange Book*, *Recommendations on the Transport of Dangerous Goods, Tests and Criteria* (Anon, 1997c).

Packaging

IATA Dangerous Goods Regulations (DGR) require that packaging used for the transport of hazard group 2, 3 or 4 must meet defined standards according to IATA packing instruction 602 (class 6.2) (IATA, 1998). The DSMZ collects all relevant guidelines for the shipping of microorganisms and updates

it on a regular basis (Anon, 1998). It is also available on the DSMZ web site (http://www.gbf.de/dsmz/shipping/shipping.htm). Packaging must meet EN 829 triple-containment requirements for hazard group 1 organisms. However, microorganisms that qualify as dangerous goods (class 6.2) and are sent by air must be in UN-certified packages. These packages must be sent by airfreight if the postal services of the countries through which it passes do not allow the organisms in their postal systems. They can only be sent airmail if the national postal authorities accept them. There are additional costs above the freight charges and package costs if the carrier does not have its own fleet because the package and documentation will need to be checked at the airport DGR centre.

Quarantine regulations

Clients in the UK who wish to obtain cultures of non-indigenous plant pathogens must first obtain a MAFF Plant Health Licence and provide a letter of authority. Such licences can be applied for in England and Wales from the Ministry of Agriculture, Fisheries and Food, Room 340, Foss House, Kings Pool, 1–2 Peace Holme Green, York YO1 2PX, and in Scotland from the Plant Health Section, Agricultural Science Agency, East Craigs, Edinburgh EH12 8NJ. Non-indigenous tree pathogens can only be supplied if the customer holds a current permit issued by The Forestry Commission, Forestry Commission Headquarters, 231 Corsthorphine Road, Edinburgh EH12 7AP.

All shipments to Canada and the USA of plant pathogens must be accompanied by import mailing labels, without which entry of cultures to these countries is refused. Applications for these labels, stating the names of the organisms and the purpose for which they are required, should be made for Canada to the Chief of the Plant Protection Division, Agriculture Canada Science Division, Science Service Building, Ottawa, Ontario, Canada K1AS 0C5, and for the USA to USDA Agricultural Research Service, Plant Protection and Quarantine, Room 764, 6505 Belcrest Road, Hyattsville, MD 20782, USA.

Information on the transport of plant pathogens throughout Europe can be obtained from the European and Mediterranean Plant Protection Organization (EPPO), 1 rue le Nôtre, 75016 Paris, France. EC Council Directive (77/93/EEC), on protective measures against the introduction of harmful organisms and of plant or plant products, also provides useful information.

Control of dangerous pathogens

There is considerable concern over the transfer of selected infectious agents capable of causing substantial harm to human health. There is potential for

such organisms to be passed to parties not equipped to handle them or to persons who may make illegitimate use of them. Of special concern are pathogens and toxins causing anthrax, botulism, brucellosis, plague, Q fever, tularemia and all agents classified for work at Biosafety Level 4 (hazard group 4). The Australia Group Countries have strict controls for movement outside their group of countries but has lower restrictions within. The UK National Culture Collections have implemented a system involving the registration of customers to ensure bona fide supply (see http://www.ukncc.co.uk). The USA have rules that include a comprehensive list of infectious agents, registration of facilities that handle them and requirements for transfer, verification and disposal. Contravention of the rules entails criminal and civil penalties. In the UK, all facilities handling hazard groups 2, 3 or 4 must be registered. Strict control of hazard group 3 and 4 organisms is in place.

Safety Information Provided to the Recipient of Microorganisms

A safety data sheet must be despatched with an organism, indicating to which hazard group it belongs and the containment and disposal procedures required. In the UK, microorganisms are covered by the Control of Substances Hazardous to Health (COSHH) regulations (1988), HSW Act (Anon, 1974) s.6(4)(c) and subject to the Approved Code of Practice Biological Agents (Anon, 1996d). *Substances for Use at Work: the Provision of Information* (1985) provides details of the safety data that must be provided. Article 10 of the EC Council Directive (90/679/EEC) dictates that manufacturers, importers, distributors and suppliers must provide safety data sheets in a prescribed format. A safety data sheet accompanying a microorganism must include:

- The hazard group of the organism being despatched as defined by EC Directive 90/679/EEC *Classification of Biological Agents* and by the national variation of this legislation; for example, in the UK, as defined in the Advisory Committee on Dangerous Pathogens (ACDP) *Categorization of Biological Agents*, 4th edition, and the Approved Code of Practice (ACOP) for Biological Agents (Anon, 1996c).
- A definition of the hazards and assessment of the risks involved in handling the organism.
- Requirements for the safe handling and disposal of the organism:
  containment level,
  opening cultures and ampoules,
  transport,
  disposal,
  procedures in case of spillage.

Such information is absolutely essential to enable the recipient of organisms to handle and dispose of the organisms safely.

Summary

Legislation controls the safe handling and use of organisms, and biologists must ensure they keep abreast of existing, new and changing regulations. Misuse and abuse of rules will inevitably result in even more restrictive legislation that will make the exchange of organisms for legitimate use even more difficult. Health and safety, packaging and shipping, and controlled distribution legislation may be extensive and sometimes cumbersome but it is there to protect us and must be followed. Biologists wishing to collect organisms, characterize them and investigate their roles in nature must remember that many rules and regulations govern their actions. If the organisms or their products are to be exploited, then the country of origin must be taken into account. If agreements are in place, including permission to collect and how the organism may be used, and a suitable risk assessment is completed as soon as practicable, the process of compliance with the law is made much simpler. In the interests of the progress of science, biologists must be able to exchange the organisms upon which their hypotheses and results are based, but they must do this in a way that presents minimum risk to those who come into contact with the organism. Further information can be found in a paper published on the internet on the Society for General Microbiology web site (http://www.socgenmicrobiol.org.uk).

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The EU/EC Directives are available from the Office for Official Publications of the European Communities, 2 rue Mercier, L-2985 Luxembourg.

Appendix 8.1: List of Abbreviations Used

ACDP	Advisory Committee on Dangerous Pathogens
ACOP	Approved Code of Practice
ADR	Accord Européen Relatif au Transport International des Merchandises Dangereuses par Routes
CABI	CAB International
CBD	Convention on Biological Diversity
COSHH	Control of Substances Hazardous to Health
DGR	Dangerous Goods Regulations
DSMZ	Deutsche Sammlung von Mikroorganismen und Zellkulturen
EC	European Commission
EFB	European Forum for Biotechnology
EPPO	European and Mediterranean Plant Protection Organization
GRC	Genetic Resources Collection
IATA	International Air Transport Association
ICAO	International Civil Aviation Organization
IDA	International Depositary Authorities
IPBS	Infectious, Perishable Biological Substances
IPR	Intellectual Property Rights
MHSW	Management of Health and Safety at Work
MOSAICC	Micro-organisms Sustainable Use and Access Regulation International Code of Conduct
NPBS	Non-infectious Perishable Biological Substances
PIC	Prior Informed Consent
UPU	Universal Postal Union
USPHS	United States Public Health Service
WHO	World Health Organization
WIPO	World Intellectual Property Organization