Biological Resource Centres Compliance with Law

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Did you know that there is extensive legislation governing the handling, use and distribution of microorganisms?

Microorganisms are isolated, grown, characterised, preserved for the long-term, stored and transported between laboratories. They are shipped by various means, by mail, courier or by hand, from one laboratory to another within countries and often across borders or continents. They are sent for identification, reference, research or for production purposes from colleague to colleague, from and to culture collections. All these actions must be carried out safely and compliant with the various legislation and regulations that control these matters. Not only does the legislation exist but also from time to time it is changed or added to (http://wdcm.nig.ac.jp/wfcc/wfccreports.pdf).

The importance 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. A microorganism in transit might put carriers, postal staff, freight operators and recipients at risk, some organisms being relatively hazard free whilst others quite dangerous. It is essential that safety and shipping regulations are followed to ensure safe transit. There are several other pieces of legislation that restrict the distribution of microorganisms of which a microbiologist must be aware. This paper presents information on how a Biological Resource Centre (BRC) or culture collection should comply with:

Health and Safety requirements
Classification of Micoorganisms on the Basis of Hazard
Quarantine regulations
Ownership of Intellectual Property Rights (IPR)
Convention on Biological Diversity
Safety information provided to the recipient of microorganisms
Regulations governing shipping of cultures
Control of Distribution of Dangerous Organisms

It is critical that biological resource centres operate to high standards and currently there are some guidelines available for adoption and use. One of the goals of the EBRCN project is to establish a European Standard for the operation of biological resource centres. Some examples of guidelines and quality management systems are:
CABRI http://www.cabri.org/guidelines/gl-framed.html
WFCC http://wdcm.nig.ac.jp/wfcc/GuideFinal.html
UKNCC http://www.ukncc.co.uk/html/Information/docs/UKNCCQAP.doc

In the process of isolation, handling, storage and distribution of microorganisms and cell cultures there are many stages where compliance with the law, regulations or voluntary international conventions is required (Table 1).

Health and Safety

The importance 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. A risk assessment of handling and supply of organisms is required and should include an assessment of all hazards involved, not just infection, but also all others amongst which are, the production of toxic metabolites and the ability to cause allergic reactions. Organisms that produce volatile toxins or aerosols of spores or cells present a greater risk. It is the responsibility of the microbiologist to provide such assessment data to a recipient of a culture to ensure its safe handling and containment.
Whether it is compliance with the law, or duties of a caring employer, the basic requirements in order 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

Table 1. Regulatory control of microbiology

Action	Requirement	Law, Regulation, Convention	Further information
Collecting in the field	Prior Informed consent from a recognised authority	Convention on Biological Diversity	http://www.biodiv.org
	Mutually agreed terms on use	Convention on Biological Diversity	http://www.biodiv.org
	Consent from the land owner	Property law	
Import	Non-indigenous plant pathogens require licenses from country authority	Quarantine regulations	
	Human, animal and plant pathogens can often only be imported to specified laboratories	Health and Safety	
Handling: Manipulation; Growth	Containment dependent on hazard	Control of Biological Agents - Health and Safety EC Directive 2000/54/EEC on Biological Agents	http://eur-op.eu.int/opnews/395/en/r3633.html
Genetic manipulation	Containment of manipulated organisms	EEC Directives 90/219/EEC. Contained use of genetically modified microorganisms (GMO's), *L117 Volume 33, 8 May 1990. EEC Directives 90/220/EEC. Release of GMO's, *L117 Volume 33, 8 May 1990. Cartagena Protocol on Biosafety	http://www.biodiv.org/biosafety/protocol.asp http://biosafety.ihe.be/Menu/BiosEur1.html http://biosafety.ihe.be/Menu/BiosEur1.html
Deposit as part of a patent process	Long-term storage and compliance with the Budapest treaty	Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedure	http://www.cnpat.com/worldlaw/treaty/budapest_en.htm
Storage	Appropriate containment	Health and Safety Licence to hold pathogens Security	
Export to another country	Some plant and animal pathogens require export licences	Quarantine regulations	
	Dangerous organisms with potential for dual use	Export Licences for dangerous organisms, Biological and Toxic Weapon Convention (BTWC)	http://binas.unido.org/binas/regs.php3 http://www.opcw.nl/fact/rel_conv.htm http://www.dfat.gov.au/isecurity/pd/pd_4_96/pd9.html
Distribution	Packaging and transport considerations	IATA Dangerous Goods Regulations (DGR), Universal Postal Union (UPU United Nations Expert Committee on the Transport of dangerous goods	http://www.iata.org/cargo/dg/dgr.htm http://www.upu.int/ http://www.unece.org/trans/danger/danger.htm
	Sovereign rights over the strains	Convention on Biological Diversity	http://www.biodiv.org
	Access and benefit sharing	Bonn Guidelines	http://www.biodiv.org
	Intellectual property Right ownership Customer licensed to receive organism?	Copyright	
	Dangerous organisms	EU Council Regulation 3381/94/EEC on the Control of Exports of Dual-Use Goods from the Community	http://eur-op.eu.int/opnews/395/en/r3633.html See national Export Offices

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

A BRC must put in place procedures to manage the health and safety of all who may be put at risk by its activities. This requires 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 to through their work (Anon, 1996a). These assessments must be reviewed regularly, additionally when changes in procedures or regulations demand, and must be recorded. The distribution of microorganisms to others outside the workplace extends these duties to protect others.

Classification of Micoorganisms on the Basis of Hazard

Various classification systems exist which include the definitions for classification by the World Health Organisation (WHO); United States Public Health Service (USPHS); Advisory Group on Dangerous Pathogens (ACDP); European Federation of Biotechnology (EFB) and European Community (EC). In Europe, the EC 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. The definition and minimum handling procedures of pathogenic organisms are set by appropriate authorities in each country and are often the same or similar for all EC countries, in the UK the ACDP list four hazard groups 1-4 with corresponding containment levels. Microorganisms are normally classified on their potential to cause disease, their human pathogenicity, into four groups (Anon, 1995):

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.

A BRC must ensure that all strains are assigned to appropriate risk/hazard groups this includes a positive assignment to risk/hazard group 1 unless otherwise considered hazardous. Hazard information must be recorded and made available to recipients of this material.

Quarantine regulations

Clients who wish to obtain cultures of non-indigenous plant pathogens must first obtain a permit to import, handle and store from the appropriate Government Department. Under the terms of such a licence the shipper is required to see a copy of the Ministry permit before such strains can be supplied.

The BRC must do its best to ensure that non-indigenous pathogens are not distributed unless the recipient has a current licence.

Ownership of Intellectual Property Rights (IPR)

On deposit of a strain BRCs must ascertain ownership and terms and conditions of further distribution for example Intellectual Property rights or from Prior Informed Consent granted under the Convention on Biological Diversity.

The BRC must ensure that information on ownership of IP is passed to third parties recipient to the organism

Convention on Biological Diversity

The Convention on Biological Diversity requires that microbiologists seek prior informed consent from the country in which they wish to collect organisms. They will be required to agree terms on which benefits will be shared should they accrue from the use of the organisms. The benefit sharing may include monetary elements but may also include information, technology transfer and training.

A BRC must ensure transparency retaining the link between country of origin and end user of genetic resources. Biological materials must be received and supplied within the spirit of the CBD ensuring material transfer agreements are in place. A BRC must maintain contact and follow recommendations of its national CBD Contact Point and National Focal Point.

Safety information provided to the recipient of microorganisms

A safety data sheet must be despatched with an organism indicating which hazard group it belongs to and what containment and disposal procedures are necessary. In Europe Code of Practice for Biological Agents 1994 (Anon, 1994). Article 10 of the EU Directive 90/379/EEC regulates 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
- 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 procedure for cultures and ampoules
    - Transport
    - Disposal
    - Procedures in case of spillage

A BRC issues an appropriate safety data sheet with every culture consignment.

Regulations governing shipping of cultures

The IATA Dangerous Goods Regulations (DGR) require that shippers of microorganisms of hazard groups 2, 3 or 4 must be trained by IATA certified and approved instructors (every two years). 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 DGR 2003). IATA DGR also requires that packaging used for the transport of hazard group 2, 3 or 4 must meet defined standards of a UN combination package, IATA packing instruction 602 (class 6.2) (IATA DGR 2003). See IATA homepage http://www.iata.org. Packaging must meet EN 829 triple containment requirements for hazard group 1 organisms (Anon, 1996b).

A BRC must ensure that staff responsible for distribution of cultures have a current IATA Shippers training certificate and ensure organisms are packed and shipped in accordance with IATA requirements, if applicable. Non-infectious microorganisms may be sent by (air) mail, acc. to the UPU requirements.

Control of Distribution of Dangerous Organisms

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' of countries has strict controls for movement outside their group but has lower restrictions within.

A BRC has procedures to check the validity of customers that wish to receive dangerous organisms and if in doubt does not supply.

Useful References

Anon (1994). Approved Code of Practice for Biological Agents 1994. Health and Safety Executive. Sudbury: HSE Books.

Anon (1996b). European Standard EN 829:1996 E: Transport packages for medical and biological specimens, Requirements, tests. Brussels: CEN, European Committee for Standardisation.

Anon (1998) *Shipping of infectious, non-infectious and genetically modified biological materials, International Regulations* DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH, Braunschweig, Germany.

EC Council Directive 77/93/EEC on protective measures against the introduction into the Member States of harmful organisms of plant or plant products. Official Journal of the European Communities **20**, 20-54 (1977)

EEC Directives 2000/54/EEC of the European Parliament and of the Council of 18 September 2000 on the protection of workers from risks related exposure to biological agents at work (seventh individual directive within the meaning of Article 16(1) of Directive 89/391/EEC.

IATA - International Air Transport Association(2002) Dangerous Goods Regulations. 43rd edition. Montreal; Geneva: IATA.

Websites of interest for information on transport and shipping

Canadian Transport	www.rural-gc.agr.ca/e4.1_canutec.html
Biosafety on the internet Organisation for Economic Co-operation and Development (OECD) United Nations Industrial Development Organisation (UNIDO) Biosafety Information Network and	www.olis.oecd.org/bioprod.nsf

Advisory Service (BINAS) International Service for National Agricultural Research (ISNAR) International Centre for Genetic Engineering and Biotechnology (ICGEB)	www.binas.unido.org/binas/home.html www.cgiar.org/isnar/fora/biotech www.icgeb.trieste.it/biosafety
US Animal and Plant Health Inspection Service (APHIS) Biotechnology Information Centre (BIC) of the US Department of Agriculture (USDA)	www.aphisweb.aphis.usda.gov.biotech www.nal.usda.gov/bic/
US Food and Drug Administration (FDA) Centre for Food Safety and Applied Nutrition (CFSAN) Belgian Biosafety Server The Dutch Genetically Modified Organism Bureau UK Advisory Committee on Releases into the Environment (ACRE)	www.vm.cfsan.fda.gov/ www.biosafety.ihe.be www.rivm.nl/csr/bggo.html www.environment.detr.gov.uk/acre/index.htm
EBIS	www.ivr.nl/ebis.html www.ccohs.ca/products/database/tdg.html
European Commission DGVII – Transport	http://europa.en.int/en/comm/dg07/index.htm
Harmonisation of UN documents etc.	www.hazmat.dot.gov/rules
International Air Transport Association	www.IATA.org/cargo/dg and www.IATA.org/cargo/dg/links.htm
International Civil Aviation Authority	http://hazmat.dot.gov/icao.htm www.volpe.dot.gov/ohm/icao.htm also www.cam.org/~icao/menu3.html
Maritime rules	www.eat.co.uk/ncec/complian/bibliog/bysea.html www.mdnautical.com/imo/cargoes.htm www.imo.org/pubs/pubcats.htm www.info.gov.hk/mardep/notices/mdn98149.htm www.hazmathelp.com/imdg.htm
National Chemical Emergency Response UK	www.eat.co.uk/ncec/complian/bibliog/bibliog.htm
OECD - Harmonisation Documents	
Chemical programme Classification and labelling Chemical testing Currently available test guidelenies	http://www.oecd.org/ehs http://www.oecd.org/class http://www.oecd.org/test http://www.oecd.org/test/testlist
RID/ADR	http://hazmat.dot.gov/RIDADR.htm www.dsidat.com/products/undisk7.htm www.volpe.dot.gov/ohm/ridadr.htm
Transport – general German magazine	www.tci-transport.fr www.hazmathelp.com/dotlink.htm www.cefic.org www.storck-verlag.com/english/gela_e.htm
United Nations meeetings agenda and minutes	www.unece.org/unece/trans/danger/meetdoc.htm
UN Model Regulations	www.ununece.org/unece/trans/main/dgdemo/intro.htm
UN Comittee of Experts	www.tc.gc.ca/tdgoods/consult/unlinks_e.htm
Universal Postal Union	http://ibis.ib.upu.org http://unicc/unece/tra www.de/facil/upustr.htm
USA Dept of Transport's Office of Hazardous Materials Management	http://hazmat.dot.gov
World Health Organisation	www.who.org/emc/biosafe/index.htm

Others:

MIRCEN Scholarships http://www.unesco.org/science/life/life1/rcenform.htm

CBD http://www.biodiv.org/

Biodiversity

Convention on Biological Diversity - http://www.unep.org/biodiv.html

Organisations

World Federation for Culture Collections - http://wdcm.nig.ac.jp/wfcc/wfcc.html

World Data Centre for Micro-organisms - http://wdcm.nig.ac.jp/wdcm/wdcm.html
Microbial Strain Data Network - http://www.bdt.org.br/msdn/msdn.html
The Microbial Underground - http://www.ch.ic.ac.uk/medbact/.index.html
Biodiversity and Biological Collections Web Server - http://muse.bio.cornell.edu/

Patents

Budapest Treaty for the Deposit of Micro-organisms - http://www.wipo.org/eng/iplex/wo_bud0_.htm

Safety and Standards

Advisory Committee on Dangerous Pathogens - http://www.doh.gov.uk/bioinfo.htm
Binas Biosafety Site - http://www.un.org/binas
Control of Substances Hazardous to Health - http://www.open.gov.ac.uk/hse/hthdir/agents.htm

Taxonomy and Nomenclature

Bacterial Nomenclature up-to-date - http://www.bdt.org.br/bdt/bacterianame/
Species 2000 Indexing Project - http://sunrae.uel.ac.uk/species2000/
CABI Bioscience fungal synonomy - http://www.cabi.org