

COMMITTEE ON POSTAL, QUARANTINE AND SAFETY REGULATIONS REPORT 1994-1996

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Summary

The World Federation for Culture Collections expanded its Committee on Postal, Quarantine, and Safety Regulations at the Seventh International Congress for Culture Collections (ICCC-7) to attempt to follow changes in regulations in more regions of the world. The Committee members undertook to monitor changes in regulations and guidelines, not only in their own country but also in their region of the world.

The object was not to duplicate information published by other organisations but to draw together information to be presented to members of the WFCC to keep them informed of changes and developments. This report is produced with that aim in mind.

The report summarises changes in legislation in quarantine, transport and packaging regulations and safety in the handling of biological agents. It provides information on some new and useful sources of information and lists some relevant publications that can also provide useful data. The report begins with a series of issues that, in the opinion of this committee, require further consideration and development.

Four publications, in particular, cover most of the ground that falls within the remit of this committee. The restrictions imposed on the transport of biological materials, their import, export and movement within the USA is covered by the *Packaging and shipping of biological materials at ATCC*. Rockville, Maryland: American Type Culture Collection. The booklet provided by the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ), Braunschweig, Germany, *Shipping of infectious, non-infectious and genetically modified biological materials. International Regulations* covers shipping regulations world-wide and is particularly informative on procedures for Europe. A useful feature of the latter is that it lists the countries that do and do not allow the transport of infectious and non-infectious biological materials. Two further publications cover the movement of quarantine organisms for Europe. *Quarantine Pests for Europe* edited by Smith, McNamara, Scott & Harris (1992) and the *Phytosanitary Regulations of EPPO Member Countries* (1990) produced by the European Plant Protection Organisation.

In this report the contributions of the committee members are compiled and therefore coverage may not be exhaustive, if any reader has further information or would like to comment on omissions please do not hesitate to contact the chair of this committee. The information provided is intended to ensure those who import or export biological agents are aware of legislation and can comply with it.

There have been major developments in legislation on health and safety issues that concern the handling of microorganisms. The major development in Europe being the EU Directives on the classification of biological agents, their safe handling and containment. The information given and the references listed will enable the reader to obtain information to enable the safe handling of biological agents and help prevent exposure to the hazards associated with biological agents.

The appendices at the end of this report list some of the organisms with restricted distribution. These lists are not intended to be exhaustive but reflect some recent changes and are offered as examples from different regions. The classification of biological agents in Europe is laid down in the European Council Directive 93/88/EEC and is based on the organisms ability to cause human infection and the degree of harm caused. Each European country must accept this classification system and the containment and procedures associated with it as their minimum standard but can implement tighter control and an example of the latter is given for the UK. Also listed in the appendices is the list of animal and human pathogens as classified in Japan and the recommended list of select infectious organisms which have the potential of causing severe harm.

AREAS OF CONCERN THAT MAY REQUIRE FURTHER DEVELOPMENT

There are several areas that require further attention under the auspices of the WFCC Postal, Quarantine and Safety Committee. The list of issues that follows provides some points for discussion and items that may need further development.

1. An improved more efficient way of gathering and distributing quarantine, safety and shipping data world-wide.
2. Increased vigilance on the shipping of dangerous biological agents that could be used in biological or chemical warfare and keeping abreast of new initiatives such as the USA rule on stricter control of the use and distribution of select infectious agents. Some developments in this area are covered in this report see Changes in guidelines and regulations under the sub headings Japan: Biological Weapons and USA: Regulatory alert. Also see the publications section under transport of biological materials: Conference paper (1993). Appendix 5 lists select infectious agents identified for the USA.
3. The WFCC needs to take a more active role in the development stages of new relevant legislation.
4. A restatement of the remit for the WFCC Committee on Postal, Quarantine and Biosafety and procedures is required that will give most benefit to WFCC members.
5. The production of Safety Standards for Microbial Resource Collections would be useful step to take. It would be in keeping with other guidelines produced by the WFCC and would help set acceptable standards to be attained by collections worldwide.
6. Compilation of information on microbial toxins, their production, containment, safe handling and hazard status.
7. It seems that the tendency for organisms to be listed in higher level hazard groups sometimes on the basis of uncritical determinations and sometimes with very little supporting data, should be a matter of concern for researchers. For instance, the blanket inclusion of plant pathogenic *Burkholderia* spp. and *Enterobacter* spp. in Hazard Group 2 lists is difficult to justify. Further, the uncritical application of *Bacillus cereus* as a label for some toxigenic and therefore hazardous strains is also questionable. This listing will stand in the way of the rationalization of the nomenclature of this taxon, which should include strains labelled as *B. thuringiensis*, the benign and positively beneficial component of this taxon. Concern is that the tendency is for such lists to form the basis of compilations by interested nations without critical scrutiny and to result in circular reinforcement gives cause for concern. The WFCC Postal, Quarantine and Safety Committee could provide more accurate data for future revisions of hazard lists.

CHANGES IN GUIDELINES OR REGULATIONS

QUARANTINE, TRANSPORT AND PACKAGING

General

The major development affecting the collecting and supply of cultures is no doubt the Convention on Biological Diversity, agreed at the UNCED *Earth Summit* at Rio de Janeiro in 1992. Its main aim is to protect the world's biodiversity. However, it also attempts to protect a country's right over genetic material that originates in that country. Permission to collect material in another country must be sought and agreement made for fair and equitable sharing of benefits from the exploitation or sustainable use of that material. Collections maintain organisms for use by the scientific community and will often supply strains that originated in a country other than that where the material is to be used. In such cases the collection is acting on behalf of the depositor and must seek assurances that the recipient will comply with the spirit of the Convention. A World Federation for Culture Collections publication summarises the position of collections and describes the Convention and its aims: *The role of microbial resource collections in the conservation of biodiversity*, this is available from the WFCC secretariat currently at DSMZ, Mascheroder Weg 1b, D-38124, Germany.

The International Air Transport Association (IATA) rules for the transport of etiologic agents (infectious perishable biological substances) are available from IATA, 33 route de l'Aéroport, PO Box 672, CH-1216 Geneva 15 Airport, Switzerland.

Australia

The Australian Society for Microbiology Safety Committee began revision of their guidelines in 1994. Australia follows IATA regulations for all air transport of biological materials.

Canada

Transport of biological agents is regulated by Transportation of Dangerous Goods Act and Regulations, 1992, Registration SOR 85-77 as amended in 1994 (SOR 94-264).

The following amendments were published in 6/4/94 Canada Gazette Part II, Vol. 128, No. 7 (SOR/94-264 24 March, 1994) (Original document SOR/85-77, 1985 Canada Gazette Part II):

Schedule No. 16

(1) The definition for "infectious substances" was revoked and the following substituted:

"infectious substances" means substances containing viable micro-organisms, including, but not limited to, a bacterium, virus, rickettsia, parasite or fungus, or a recombinant, hybrid, or mutant thereof, that are known or reasonably believed to cause disease in humans or animals, and that are included in risk group II, III or IV of Division 2 of Class 6, in accordance with the classification for risk groups set out in Part II I or in the tables set out in Schedule VII;

(2) Section 1.2 was amended by addition of the following:

"diagnostic specimen" means any human or animal material, including, but not limited to, excreta, secretions, blood and its components, tissue and tissue fluids, that is handled, offered for transport or transported for the purposes of diagnosis; this covers specimens from which microorganisms may be expected to be recovered.

"risk group" means a level of risk of disease of individuals and communities inherent in infectious substances, based on their ability to cause a disease, their ability to spread that disease and the severity of that disease;

Section 2.3.3

(1) These Regulations do not apply to the handling, offering for transport or transporting, by road or railway or by ship, of diagnostic specimens or cultures that are reasonably believed not to contain infectious substances that

are included in risk group II, III or IV of Division 2 of Class 6, in accordance with risk groups set out in Part III or in the tables set out in Schedule VII, if

(a) the diagnostic specimens or cultures are contained in packaging type 1B that meets the requirements of National Standard of Canada CAN/CGSP-43, 125-M90, Packaging of Infectious Substances and Diagnostic Specimens, dated November 1990;

or

(b) the diagnostic specimens are contained in a package that is designed, constructed, filled and closed so that under normal conditions of handling and transporting, there will be no discharge, emission or escape of the diagnostic specimens from the package.

(2) Subject to subsection (3), these Regulations do not apply to the handling, offering for transport or transporting, by road or railway vehicle or by ship, of diagnostic specimens or cultures that contain infectious substances included in risk group II, in accordance with the classification for risk groups set out in Part III or in the tables set out in Schedule VII, if

(a) the diagnostic specimens or cultures are contained in packaging type 1B that meets the requirements of National Standard of Canada CAN/CGSP-43, 125-M90, Packaging of Infectious Substances and Diagnostic Specimens, dated November 1990;

or

(b) the diagnostic specimens are contained in a package that is designed, constructed, filled and closed so that under normal conditions of handling and transporting, there will be no discharge, emission or escape of the diagnostic specimens from the package.

Subsection 2.9.2(4) was revoked and the following substituted:

(4) These Regulations and the ICAO Technical Instructions do not apply to the handling, offering for transport or transporting by aircraft of diagnostic specimens or cultures that are reasonably believed not to contain infectious substances that are included in risk group II, III or IV of Division 2 of Class 6, or to the handling, offering for transport or transporting by aircraft of a domestic consignment of infectious substances that are included in risk group II, except for the infectious substances set out in paragraphs 2.3.3(3)(a) to (i), in accordance with the classification for risk groups set out in Part III or in the tables set out in Schedule VII, if

(a) the diagnostic specimens or cultures are contained in packaging type 1B that meets the requirements of National Standard of Canada CAN/CGSP-43, 125-M90, Packaging of Infectious Substances and Diagnostic Specimens, dated November 1990; or

(b) the diagnostic specimens are contained in a package that is designed, constructed, filled and closed so that under normal conditions of handling and transporting, there will be no discharge, emission or escape of the diagnostic specimens from the package.

The Regulations were further amended by adding:

Risk Groups Class 6 (Infectious Substances)

3.20.1 Micro-organisms, and recombinants, hybrids or mutants thereof, that affect humans or animals and that are included in Division 2 of Class 6 pursuant to paragraph 3.20(b) shall be included in

(b) risk group III if they are known to present a similar level of risk of disease as that of the infectious substances set out in Table IV, V or VI of Schedule VII or they exhibit similar characteristics, including the following:

(i) the disease they cause seriously affects the health of humans or animals that have contracted the disease,

(ii) they are not readily transmitted from an infected human or animal to an uninfected human or animal by casual contact, thereby representing a high individual risk and a low community risk, and

(iii) one of the following cases applies:

(A) the disease they cause can be treated by antimicrobial or antiparasitic agents, or

(B) exposure to them is likely to lead to the disease they cause;

and

(c) risk group II if they are known to present a similar level of risk of disease as that of the infectious substances set out in Tables VII to X of Schedule VII or they exhibit similar characteristics, including the following:

(i) the disease they cause does not seriously affect the health of humans or animals that have contracted the disease,

(ii) they are rarely transmitted from an infected human or animal to an uninfected human or animal by casual contact, thereby representing a moderate individual risk and a limited community risk, and

(iii) one of the following cases applies:

(A) there exists readily available treatment for humans and animals who have contracted the disease they cause, or

(B) exposure to them rarely leads to the disease they cause.

The legislation lists infectious substances under schedule VII and differentiates between human and animal pathogens. If the infectious substance affects animals only, the shipping name shall be "Infectious substance, affecting animals" and the product identification number shall be "UN 2900". Where the pathogen is able to infect humans, the shipping name shall be "Infectious substance, affecting humans" and the product identification number shall be "UN2814".

A suitable example of the organisms listed is given in tables V and VII of the schedule and are shown below:

TABLE V. RISK GROUP III - FUNGI

Family	Type
Moniliaceae	Blastomyces dermatitidis
	Coccidioides immitis
	Histoplasma capsulatum including variety duboisii
	Paracoccidioides brasiliensis

TABLE VII. RISK GROUP II - FUNGI

Family	Type
Cryptococcaceae	Candida albicans
	Cryptococcus neoformans
Moniliaceae	Aspergillus flavus
	Aspergillus fumigatus
	Epidermophyton floccosum
	Microsporum all species
	Sporothrix schenckii
	Trichophyton all species

Only substances in risk group IV require an emergency response assistance plan to be filed with Transport Canada. [Note that the risk groups and their assignment are largely based on the Laboratory Biosafety Guidelines - see below under publications.] The Laboratory Biosafety Guidelines identify Risk group I agents as those of low individual or community risk. This group includes those microorganisms, bacteria, fungi, viruses and parasites, which are unlikely to cause disease in healthy workers or animals.

Summary interpretation of above - Any microorganism regulated as risk group II or III must be transported as dangerous goods with appropriate packaging and documentation. These would be shipped by air additionally following IATA regulations or by ground transport. Note that Canada Post does not allow the shipment of "infectious substances".

Handling biological agents - guidelines

The handling of biological agents are governed under "Laboratory Biosafety Guidelines" published by Laboratory Centre for Disease Control, Health Protection Branch, Health Canada, 2nd edition, 1996. The following relevant excerpts are taken from this document:

- The Canada Labour Code requires that each employer provide safe working conditions and that employees be informed about all hazards they will face in the course of their duties. ...
- Other federal legislation such as the Workplace Hazardous Materials Information System (WHMIS) requires that all hazardous substances, including microorganisms, be labelled in a specified manner and that there be a Material Safety Data Sheet (MSDS) to accompany each hazardous substance.

Note that "infectious substances" are regulated by WHMIS under D3 and microorganisms require a Material Safety Data Sheet (MSDS).

Quarantine: Regulations Respecting the Importation of Human Pathogens and their Transfer

Health Canada has introduced regulations to control the importation of human pathogens into Canada and to ensure that adequate facilities exist for proper laboratory handling and containment of these pathogens. The regulations came into effect in 1994. These regulations may be cited as the Human Pathogens Importation Regulations. These regulations do not apply to an animal pathogen, or toxins thereof, incapable of causing human disease.

Previously, Agriculture Canada issued permits for both human and animal pathogens. Now, Agriculture Canada only issues permits for animal pathogens and Health Canada issues for human pathogens. Two permits are required if an organism is both a human and an animal pathogen. Health Canada's Office of Biosafety state that a permit is required to import microorganisms classified in risk groups II and III but not in risk group I. Applications for forms or copies of the Laboratory Biosafety Guidelines can be obtained from: Office of Biosafety, Laboratory Centre for Disease Control, Health Protection Branch, Health Canada, Ottawa, Ontario, K1A 0L2.

Interpretation in these regulations:

"diagnostic specimen" means any human or animal material, including excreta, secreta, blood and its components, tissue and tissue fluids, that is to be used for the purposes of diagnosis, but does not include live infected animals;

"human pathogen" means (a) an infectious substance, (b) the toxin of an infectious substance, or (c) any diagnostic specimen of other material that contains, or that its importer has reasonable grounds to believe contains, an infectious substance or the toxin of an infectious substance;

"infectious substance" means (a) a microorganism or parasite that is capable of causing human disease, (b) an artificially produced hybrid or mutant microorganism that contains genetic components of any microorganisms capable of causing human disease;

"risk group" means a risk group described in the Guidelines.

Some requirements under the regulations are:

4. (1) No person shall import a human pathogen that belongs to Risk group 2, 3 or 4 unless
 - (a) the importation is in accordance with a subsisting importation permit issued to that person under paragraph 7(a);
 - (b) prior to shipment of the human pathogen, that person notifies the supplier that the outer shipping container in which the human pathogen is transported must display clearly, on the outside surface of the container, the importation permit number and the following statement immediately preceding that number:

"Human pathogen - Importation Permit Number: ####"
 - (c) prior to shipment of the human pathogen, that person provides a copy of the importation permit to the supplier and notifies the supplier that a copy of the importation permit must accompany each shipment.
- (2) An importation permit is not valid for more than one entry into Canada
 - (a) in respect of human pathogens that belong to Risk Group 3 or 4; and
 - (b) in respect of human pathogens that belong to more than one risk group.

Importation of Veterinary Biologics, Animal Pathogens and Material of Animal-Microbial Origin

Import permits are required for all veterinary biologics, animal tissues, infectious organisms and related materials which are not indigenous to Canada. Application is made to Agriculture Canada, Food Production and Inspection Branch, Animal Health Division, Ottawa, ON K1A 0Y9.

Importation of Plant Pathogens

Importation of plant pathogens falls under the Plant Protection Act. This is currently interpreted by Agriculture Canada, Food Protection and Inspection Branch, Plant Protection Division, Ottawa K1A 0Y3 as:

permits are required only for plant pathogens. Requirement for an import permit is assessed on an individual basis. If a permit is required, a fee is assessed.

The Plant Protection Fees Regulations published in Canada Gazette Part I, Vol. 129, 9:589-597, state:

1. Import Permits

B. For a permit to import pests such as insects, fungi, viruses, bacteria and weeds, and for a permit to import disease cultures, grapevine material or soil and any thing for which a permit is issued pursuant to section 43 of the Plant Protection Regulations, the fee will be \$34.

Europe

Classification of Biological agents

The lists of biological agents have now been revised and individual countries in Europe are implementing legislation for the handling of these organisms. EU Directive 90/679/EEC Protection of workers from risks related to biological agents and subsequently EU Directive 93/88/EEC classification of biological agents define the hazard status of biological agents and how they should be handled to prevent exposure. The latter sets minimum standards for Europe and allows each country to implement tighter control. The list of fungi and bacteria, part of annexe 1 of the EU Directive 93/88/EEC, is given in Appendix 1.

Implementation of 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 for dangerous chemicals at work. This must be considered with reference to toxigenic fungi, those causing allergies and respiratory sensitisation.

European Standard EN 829 Transport packages for medical and biological specimens. Requirements, tests

This new European Standard will be ratified in 1996 and will replace all national standards on packaging for transport of medical and biological specimens. The purpose of the standard is to lay down standardised definitions, requirements and tests for transport packages in order to minimise risk to man, animals and the environment. It prescribes that the package be leakproof and resistant to mechanical stress, temperature change and decrease in outside pressure. It must also withstand tests including dropping, freezing, reduced pressure and illumination of short wavelength. The packaging must have sufficient absorbent material to absorb any potential leakage and the outer package (bag or box) should be sufficiently strong to withstand the usual stress during transport. Prescribed tests with performance standards are laid down and labelling instructions are given and must conform to existing International Standards. The full Standard is available from European Committee for Standardisation, Central Secretariat, rue de Strassart 36, B-1050 Brussels, Ref. No. EN 829: 1996 E.

GMOs and GMMs

A new annex to Directive 90/219/EEC contains revised classification criteria for Genetically Modified Microorganisms (GMMs) based on the likelihood of harm to health or the environment. This directive is published in L117 Volume 33, 8 May 1990, *EEC Directive 90/219/EEC. Contained use of genetically modified microorganisms (GMO's)* and *EEC Directive 90/220/EEC. Release of GM O's*. The UK Health and Safety Commission (HSC) will implement the Directive by replacing Schedule II to the 1992 regulations (*A guide to the Genetically Modified Organisms (Contained use) Regulations 1992*). Health and Safety Executive. London: HMSO).

New chemical agents legislation

The state of play table of new European Legislation in *Euro safety Issue 12*, Spring 1996 records a proposed directive on chemical agents is being discussed (OJC 191/14.94) which will repeal Directive 90/1107/EEC on chemical, physical and biological agents. The change is in line with the Framework Directive and UK COSHH regulations. The draft goes beyond current legislation by addressing safety aspects of asphyxiants, flammability, temperature and pressure.

France

Only a small number of laboratories in France are authorised to import infectious substances and authorised for international transport of perishable biological materials, these are listed here:

- Institut Pasteur, 25 rue du Dr. Roux, 75724 Paris Cedex 15 (Post Office: Paris Bonvin);
- Institut Pasteur Lille, 1 rue du Professeur Calmette, BP 245, 59019 Lille Cedex (Post Office: Lille Moulins);
- Institut Pasteur Lyon, 77 rue Pasteur, 69635 Lyon Cedex (Post Office: Lyon Guillotiere);
- Laboratoire National de la Sante (National Health Laboratory), 25 bd Saint Jacques, 75680 Paris Cedex 14 (Post Office: Paris Bachelard);
- Laboratoire National de la Sante (National Health Laboratory), 14 rue de l'Ecole de Pharmacie, 34000 Montpellier (Post Office: Montpellier Recette Principale);
- Laboratoire National de la Sante (National Health Laboratory), rue Guillaume Paradin, 69372 Lyon Cedex 2 (Post Office: Lyon Montplaisir Lyon 08);
- Laboratoire National de la Sante (National Health Laboratory), 8 avenue Rockefeller, 69373 Lyon Cedex 2 (Post Office: Lyon Montplaisir Lyon 08).

An announcement of the final listing of the classification of biological agents was made as a result of the EU Directive 93/88/EEC in Dictionnaire Permanent Biologique and Biotechnologies, *Bulletin 11*, 9719. This list adopts the classification as recommended whereas other countries have made minor modifications.

Transport of infectious substances

France follows the international regulations published by IATA and have published their regulations on the transport of infectious substances in the French *Journal Officiel*. *Reglements pour le transport des materials dangereux. Journal Officiel de la Republique Francaise. Edition des Documents Administratives. Annee 1994. No. 113.*

Germany

German Ministry of Transport Round Table, Bohn (1994), held discussions on the EC norm. no. 829 for the transport of medical and biological material. The EC norm evolved from the German DIN 55515. The intention was to have two packaging groups which would include Hazard Groups 2, 3 and 4 which would be transported in the same way. However, the two packing groups should be Hazard Groups 1/2 and 3/4.

The German post accepts roll packages in parcel post only (not in letter post). DSMZ have a new system that meets their regulations.

Japan

There are different mechanisms in place for the classification of hazard status of human, animal and plant pathogenic microorganisms in Japan.

The National Institute of Human Health (NIH), Tokyo is responsible for the Classification of human pathogens (listed here in Appendix 3).

- Class 1 Low individual risk and low community risk.
- Class 2 Moderate individual risk and limited community risk.
- Class 3 High individual risk and low community risk.
- Class 4 High individual risk and high community risk.

The Minister of Agriculture, Forestry and Fisheries designates organisms as animal pathogens based upon the Domestic Animal Infectious Diseases Control Law promulgated by the Animal Health Division, Ministry of Agriculture, Forestry and Fisheries (MAFF), Japan. The classification of animal pathogens on the basis of hazard is governed by the Culture Collection Committee of the Animal Health Experimental Station, MAFF, Japan. A list of organisms designated as animal pathogens is given in *Bulletin of the Japanese Federation for Culture Collections* 2, 19-22 (1986), *inbid* 5, 53 (1989), *inbid* 7, 55-56 (1991), *inbid* 8, 54-55 (1992), *inbid* 9, 159-160, (1993).

- Class 1 Low individual risk: Biological agents that are unlikely to cause animal disease.
- Class 2 Moderate individual risk: Biological agents that cause animal disease of veterinary importance.
- Class 3 High individual risk: Biological agents that cause severe animal disease of veterinary importance.
- Class 4 High individual risk: Biological agents listed in the table of Animal Health Division, MAFF, Japan that cause severe animal disease of veterinary importance (listed here as Appendix 4).

Organisms are designated as plant pathogens by the Minister of Agriculture, Forestry and Fisheries, Japan.

Plant protection law and enforcement regulations are promulgated by the Ministry of Agriculture, Forestry and Fisheries, Japan. Plant material cannot be imported into Japan without a phytosanitary certificate (or a copy) issued by the government agency of the exporting country certifying that it has been found free or believed to be free of harmful animal or plant pathogens. Permits to import prohibited material for experimental or research purposes can be obtained from the Ministry of Agriculture and Forestry Plant Protection Station which exercises jurisdiction over the destination area. The prohibited material must be sent to the Plant Protection Station. A list of organisms designated as plant pathogens by the Minister of Agriculture, Forestry and Fisheries can be found in the *Bulletin of the*

Japanese Federation for Culture Collections 1, 79-85 (1985), inbid2, 32-33 (1986), inbid3, 53 (1987), inbid 5, 52-53 (1989), inbid 7, 55 (1991), inbid 8, 54 (1992), 9, 160-161 (1993).

There are proposed changes being discussed (Spring 1996) by the Japanese government on plant protection law that will bring Japan's Plant Quarantine Regulations in line with International Regulations.

Biological weapons

Japan is proposing to regulate the trade of microorganisms that could possibly be used as biological weapons, as proposed by the Australian Group.

The safe handling of microorganisms

The Ministry of Education are currently responsible for promulgating *Guidelines for the safe handling of research microorganisms*.

UK

Classification of Biological agents

The lists of biological agents have now been revised and individual countries in Europe are implementing legislation for the handling of these organisms. The UK have raised the categorisation of some of the biological agents. The major changes implemented in the UK are given in Appendix 2.

Control of Substances Hazardous to Health (COSHH) Regulations (1995)

All employers are required to observe the provisions of COSHH if there is a risk of exposure of their employees to hazardous substances. The COSHH (1988) legislation first came into force on 1 January 1990 from which point no work which was liable to expose anyone to substances hazardous to health was to be carried out unless an assessment evaluating risks to health was first performed and that the requirements to meet the COSHH regulations had been established. If it is reasonably practicable the hazard should be eliminated altogether but if not, adequate controls must be put in place. In 1995 the COSHH 1994 regulations superseded the 1988 Regulations particularly in respect to Biological Agents and Carcinogens. The new legislation is published in *Statutory Instruments 1994 No. 3246. Health and Safety : The control of Substances Hazardous to Health (Amendment) Regulations 1994. London: HMSO and COSHH (General ACOP) and Control of Carcinogenic substances: Approved Codes of Practice (1995). London: HSE. ISBN 0 11 885468 2.*

Chemical (Hazard Information and Packaging) Regulations 1993

This legislation covers the classification labelling and packaging of chemicals and chemical preparations. Microorganisms that produce known toxins (hazardous substances) for example *Aspergillus flavus* which normally produces aflatoxin must be labelled with the risk 45 statement "may cause cancer". The legislation also covers the need to provide safety data sheets under a standard format.

New Zealand

Amendments in legislation and guidelines

a. The Biosecurity Act (New Zealand)

In 1993, all legislation previously covering the introduction of animals, plants and microorganisms was incorporated into the Biosecurity Act. This act sets down the conditions under which microorganisms can be imported into the country and the conditions under which organisms can be studied in quarantine. Several national culture collections for microorganisms have been identified as "contaminant facilities" under the act. They are repositories for medical, veterinary and plant-related microorganisms which are needed for research but which are deemed hazardous to the New Zealand environment. The management and curation of these collections is required to fulfill defined criteria connected with security and microbiological quality control. The

collections also provide a containment service to other research users who need to investigate microorganisms in quarantine.

b. The Hazardous Substances and New Organisms Bill (New Zealand)

This parliamentary bill is in the process of being passed into law. Insofar as this act considers microorganisms, its primary focus is on the implications of the importation of organisms new to the New Zealand environment and of genetically modified organisms. This legislation sets in place a delegated procedure by which the risk of such organisms can be assessed in consideration of their importation.

USA

Etiologic agents, infectious materials or vectors containing infectious agents originating from foreign locations into the United States must have an importation permit issued by the United States Public Health Service. Importation permits are issued only to the importer who must be located in the United States. The importation permit, with the proper packaging and labeling, will expedite clearance of the package of infectious materials through the US Public Health Service Division of Quarantine and release by US Customs. Infectious materials imported to the USA must be packed to withstand breakage and leakage of contents. The application for a permit to import or transport agents or vectors of human disease can be obtained from US Department of Health and Human Services, Public Health Service, Centre for Disease Control and Prevention, Office of Health and Safety FO5, Atlanta, Georgia 30333.

Lists of etiologic agents can be found in Public Health Service HHS 42 CFR Edition 10-1-87 p 60-61 and in the Federal register Volume 52, No. 115, June 16 1987, Rules and Regulations p 22909-22911, however, this list is extremely old and does not follow current approved names and classifications.

The Environmental Protection Agency proposed a rule under section 5 of the Toxic Substances Control Act (TSCA), 15 U.S.C 2604 to screen microorganisms before they are introduced into commerce. This rule was designed to prevent unreasonable risk to human health and the environment without imposing unnecessary regulatory burdens on the biotechnology industry.

Major changes since January 1995 on the transport of infectious substances by air

A UN label/mark is required on all packages containing infectious substances. The marking is intended to allay fears of handlers of pathogenic shipments as it indicates that the package has been put through performance tests. These tests are not new, they have been included in regulations for several years and shippers should have been using pre-tested containers since these regulations were introduced.

IATA have made indications that they will correlate hazard/risk group of organisms with packing groups with the potential result of making package performance tests more stringent for high risk pathogens. At present there is no relationship between risk group and packing group.

Further information on these two issues can be found in: Dangerous Goods Regulations (DGR) January 1995. International Air transport Association (IATA).

Regulatory Alert - June 10, 1996 Important notice of proposed rulemaking from the Centres for Disease Control (CDCP).

The proposed rule is being promulgated by the CDCP to place additional shipping and handling requirements on laboratory facilities that transfer or receive select infectious agents capable of causing substantial harm to human health. There has been considerable concern over the potential shipping of such organisms 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 (see appendix 5 for select infectious agents list). The proposed rule will apply to laboratory facilities such as Universities, Research Institutions, Commercial entities and Government Agencies who would all be required to register with the Secretary of HHS or designate.

The proposed rule includes:

1. A comprehensive list of select infectious agents.
2. Registration of facilities
3. Transfer requirements
4. Verification procedures
5. Agent disposal requirements
6. Research and clinical exemptions
7. Criminal and civil penalties
8. Request for public comment on the proposed amendment, which was required on or before July 10, 1996.

Reference: Department of Health and Human Services, Public Health Service, 42 CFR Part 72, RIN 0905-AE70. Additional requirements for facilities transferring or receiving select infectious agents. Federal Register: June 10, 1996, Vol. 61 (112) Proposed Rules p 29327-29333.

SAFE HANDLING OF MICROORGANISMS

The safe handling and distribution of microorganisms is of concern to all microbial resource collections who have a particular duty of care to ensure that not only their staff are safe but also those who handle packages on route and the recipients are not put at risk. Safe practices, provision of information and training are all required for good laboratory practice and to comply with legislation. Some of the new regulations covering safe handling of microorganisms have been raised above and some specific topics are covered in the following section. New controls and concerns about the potential harm particular organisms can cause may require the production of a manual of health and safety standards for microbial resource collections. From allergies through toxicoses to infection there is a need for containment and safe practices to reduce the risk of harm during work with microorganisms. The following does not provide a complete guide on safe practices but raises issues that are of concern.

Allergic reactions

The new COSHH (1995) regulations of the UK now incorporate regulations to control exposure to respiratory sensitisers and allergenic properties of microorganisms and their products. Allergic reactions to fungi or chemicals may occur, but only certain individuals will react while the majority of other people remain unaffected. Those who suffer allergic reaction to a particular fungus must avoid coming in contact with it. Some allergic reactions may be recognised by a reddening and possible swelling of the skin after contact or, if an aero-allergen, by an increased flow of secretions in the nose and to the eyes and possible respiratory distress such as coughing or difficulty in breathing. Sensitisation and the development of allergen reaction take a considerable time. Extreme reaction can often lead to severe shock. The person affected should avoid contact with the fungus or chemical concerned. The UK Advisory Committee on Dangerous Pathogens (ACDP) have also produced documentation that for the first time includes the now mandatory containment level required for each category of organism.

The spores of fungi (including *Alternaria*, *Aspergillus*, *Cladosporium* and *Penicillium*) and cereal rusts and smuts in the air are able to induce allergy asthma and hay fever in man. There are also a number of special pulmonary conditions, to which certain industrial workers are subject, caused by fungal spores. These include cheese washer's lung (*Penicillium verrucosum*), maltster's lung (*Aspergillus clavatus*), mushroom worker's lung (*Doratomyces* sp.) and suberosis (*Penicillium glabrum*).

Respiratory sensitisers include: air borne spores and other propagules of microorganisms including the fungi mentioned above and the bacterium, *Pseudomonas*; chemicals are also responsible and these can include: mycotoxins, other metabolites (e.g. ampicillin, penicillin, streptomycin sulphate), cobalt salts; dusts, mists, cutting fluids and enzymes are also considered sensitisers. Health surveillance is required where staff may come into contact with respiratory sensitisers. This can initially take the form of a questionnaire issued to staff on a regular basis (6 weekly or quarterly); an example questionnaire is provided in *Preventing Asthma at Work: How to control respiratory sensitisers (HSE)*.

Sensitivity to latex gloves can develop and even those who do not wear them can be affected. Powdered gloves will release excess powder into the atmosphere when put on or removed. The extractable proteins absorbed by the powder may cause allergic reaction in susceptible persons. Gloves that are powder free and low in allergen content should be used. The following has been recommended to prevent latex sensitisation (*Nursing Times* **91** (46), 1995):

- Avoid the use of powdered latex gloves where possible.
- Ascertain the allergenicity of the glove.
- Do not use cheap gloves as these are likely to be allergenic.
- Report any irritation that may be related to wearing of gloves immediately.
- Wash hands immediately after wearing gloves.
- Avoid oil-based emollients as this may enhance absorption of the proteins.
- Do not wear latex gloves unless you have to.

Hazard groups and containment levels

Microorganisms are divided into four hazard groups as designated by the Advisory Committee on Dangerous Pathogens (ACDP 1996) and the EU Directive 93/88/EEC.

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 list of bacteria and fungi falling into hazard groups 2 or 3 is given Appendix 1. In the case of fungi it is recognised that many organisms infect following traumatic inoculation through the skin, or infect the compromised patient. Most fungi from clinical specimens require Containment Level 2 (ACDP 1996) unless a higher degree of containment is specified. Genetically Modified Organisms (GMO's) also require containment level 2 for handling.

The containment level numbers correlate with the risk group in which the organism falls (i.e. organisms in Risk Group 1 require Containment level, 1 and so forth). Details are presented in Table 5.

Table 5. Summary of laboratory containment levels

CONTAINMENT REQUIREMENT	CONTAINMENT LEVEL			
	1	2	3	4
Laboratory site: isolation	No	No	Partial	Yes
Laboratory: sealable for fumigation	No	No	Yes	Yes
Ventilation: inward airflow/negative pressure	Optional	Optional	Yes	Yes
Ventilation: through safety cabinet	No	Optional	Optional	No
mechanical: direct	No	No	Optional	No
mechanical: independent ducting	No	No	Optional	Yes
Airlock	No	No	Optional	Yes
Airlock: with shower	No	No	No	No
Wash hand basin	Optional	Yes	Yes	Yes
Effluent treatment	No	No	No	Yes
Autoclave site: on site	Yes in suite	No	No in lab	Free standing in lab:
	No	Yes	Yes	No
	No	No	Optional	No
	No	No	No	Yes
Microbiological safety cabinet/enclosure	No	Optional	Yes	Yes
Class of cabinet/enclosure*	-	Class I	Class I/III	Class I/III

* Guidance on the use of Class II microbiological safety cabinets is given in the The Advisory Committee on Dangerous Pathogens Report (1996).

Mycotoxins

There are at least 300 different mycotoxins produced by fungi and there are hundreds of species known to produce them. The fumonisins from *Fusarium* were discovered relatively recently and are considered to be potentially hazardous. The most well known mycotoxin producers are *Aspergillus*, *Penicillium*, and *Fusarium* and the most well known mycotoxin is aflatoxin from *Aspergillus flavus* and *A. parasiticus*. Other well known toxins are ochratoxin A, patulin, and citrinin, produced by *Penicillium* and trichothecenes, fumonisins, and zearalenone produced by *Fusarium*. Many of these compounds can also be produced by other fungi.

Potential exposure to mycotoxins in the laboratory is mainly by:

- i. ingestion or inhalation of contaminated dust or fungus spores
- ii. through the skin when the fungi are extracted into solvents.

Individuals who are immuno-compromised or with other relevant medical conditions may be at greater risk and several of the compounds may cause or promote cancers. Pregnant women and children might also be at particular risk. The effects of low levels of mycotoxins or of mixtures on humans is largely unknown. It is worth noting that even the most poisonous mycotoxins found in food are a factor of about one million times less toxic than the most virulent of the botulinum toxins from the bacterium *Clostridium botulinum*. However, the effects of exposure to low levels over long periods must also be considered.

Precautions to minimise exposure to toxins

- i. Aerosol formation from liquid systems must be guarded against.
- ii. Direct contact with the pure and diluted toxins must be avoided by the use of safety equipment such as mechanical pipetting devices.
- iii. Microbiological safety cabinets should be used whenever possible.
- iv. Personal protective equipment such as laboratory coats, gloves, and masks should be used at all times (*NB*: vinyl gloves can allow solvents to penetrate therefore they should be changed immediately if they become contaminated).
- v. Disposable laboratory coats can be worn and disposed of after use otherwise laboratory coats should be regularly decontaminated.
- vi. Commodities containing fungi or those suspected of contamination by mycotoxins should never be handled without protective gloves.
- vii. Procedures involving grinding cultures or commodities should ensure operator safety particularly from inhalation of particles.
- viii. All work surfaces and equipment used during extraction should be correctly decontaminated after use, and hazardous wastes must be correctly disposed of.
- ix. Analytical equipment such as Thin Layer Chromatography (TLC) plates and High Performance Liquid Chromatography (HPLC) columns may retain contamination, and have to be disposed of properly. Similarly, equipment used for other forms of analysis (e.g. electrophoresis gels) may become contaminated and need to be disposed of with a view to removing or de-activating mycotoxins.
- x. Workers should be aware of scientific literature on the mycotoxins produced by the fungi with which they are concerned, irrespective of whether mycotoxins are the reason for studying the particular fungus.

Decontamination procedures after working with mycotoxins

The following procedures have been developed for use with aflatoxin and may not be effective against all mycotoxins. Glassware which has been used to extract fungi should be soaked in 5% sodium hypochlorite. All exposed surfaces should be swabbed with 5% sodium hypochlorite. Fungal material should be autoclaved prior to the addition of 5% sodium hypochlorite. Spills of pure toxin should be absorbed with diatomaceous earth, carefully collected and placed in a bucket. The spillage area should be cleaned with 5% sodium hypochlorite. In the case of aflatoxin spillage or contamination, add 5% sodium hypochlorite followed, after 30 min, by acidification to pH 7.8-8.8 with 2M hydrochloric acid and then the addition of acetone to a final concentration of 5% by volume, this should be left for 30 min prior to safe disposal. Further information in SIGMA *Fungal Toxin Data Sheet* (1986)

Alternative methods of decontamination have been published (Castagnaro, et al. 1991, World Health Organisation) which involve analysis for decontamination by HPLC. A method using alkaline potassium permanganate is effective against citrinin, ochratoxin A, patulin, sterigmatocystin, and aflatoxin B1, B2, G1, G2. Effectiveness against other mycotoxins has yet to be determined. However, this method is not effective for TLC plates, solutions in DMF and DMSO, and solutions in non-volatile organic solvents miscible with water. The method is suitable for protective clothing, and for the removal and subsequent decontamination of mycotoxins in solvents. This avoids the risk of transporting the waste to an incinerator site. Incineration of contaminated TLC plates may be more convenient than laboratory decontamination.

References

- Advisory Committee on Dangerous Pathogens. (1996) *Categorisation of pathogens according to hazard and categories of containment*. Fourth edition. London: HMSO.
- Castegnaro, M., Berek, J., Frey, J.-M., La fontaine, M., Miraglia, M., Sansone, E. B. & Telling, G. M. (1991) *Laboratory Decontamination and destruction of carcinogens in laboratory waste: some mycotoxins*. IARC Scientific Publications No. 113. pp63. Lyon: International Agency for Research on Cancer.
- Fungal Toxins: Safety Data Sheet. (1986) St Louis, USA: SIGMA Chemical Company.
- Key precautions to prevent latex sensitisation(1991) *Nursing Times* **91** (46).
- Preventing asthma at work. How to control respiratory sensitisers. Health and Safety Executive. Sudbury, UK: HSE Books.

SOME INFORMATION SOURCES

The following are information sources highlighted by the members of the Postal, Quarantine and Safety committee and there are no doubt many more. The increasing use of World Wide Web to disseminate such information is often helpful.

The USA National Biological Impact Assessment Program (NBIAP)

NBIAP have a variety of information resources on biosafety. UNIDO has set up a Biosafety Information Network and Advisory Service (BINAS). These services are available on INTERNET.

The Health and Safety at Work Directory 1995/96. Kingston upon Thames: Croner Publications Ltd.

This provides access to essential sources of information, services and advice in the field of occupational health and safety in the UK. Where to find information on authorities, enforcing agencies, professional bodies and health and safety training. It also has two sections on health and safety in Europe, covering the European Union listing health and safety contacts in the Council, the Commission, the Economic and Social Committee and other relevant sources of information and it also lists the European Health and Safety Organisations.

Safety Software Directory.

This directory lists software for use in safety management and data storage and is available from: J. Kibblewhite, PO Box 3, Bracknell RG12 3FE, UK.

Database on the safety aspects of biological experiments

This database comprises 1600 literature citations on animal, plant and microbial projects published over the period 1974 to 1994. Contact and further information is available from Genzentrum, Ludwig-Maximilians-University Munich.

PUBLICATIONS: SOME ARTICLES, BOOKS AND PAPERS OF RELEVANCE

This section lists relevant publications with short notes on their contents. The committee would like feedback on its usefulness and additions to give better coverage. Quite often publications become well known in particular countries or regions but fail to reach a worldwide audience. This section is an attempt to bridge that gap.

HEALTH AND SAFETY

Advisory Committee on Dangerous Pathogens (1996). Categorisation of biological agents according to hazard and categories of containment. Fourth edition. London: HMSO.

The UK Advisory Committee on Dangerous Pathogens (ACDP) was set up in 1981 following a second outbreak of laboratory-acquired smallpox. There are eight expert members including four representatives of employers and four representing employees. Their terms of reference are to advise the Health and Safety Commission, the Health and Safety Executive and the Health and Agriculture Ministers, as required, on all aspects of hazards and risks to workers and others from exposure to pathogens in the UK. This new edition of the Categorisation of biological agents according to hazard and categories of containment reflects the implementation of two European Community Directives concerned with biological agents. The UK COSHH regulations have been strengthened (see above) and now include mandatory containment measures for laboratories (also reproduced in the above document). The European Directive (93/88/EEC) contains the Community classification of biological agents which forms the Approved List specifically invoked by the new COSHH regulations and has legal status (the Approved Lists of bacteria and fungi are given here as Appendix 1). The modifications to the European status implemented in the UK are given in Appendix 2.

Boleij, J., Buringh, E., Heederk, D. & Kromhout, H. (1995) Occupational hygiene of chemical and biological agents. Amsterdam: Elsevier, 283 pages.

This monograph covers exposure assessment for occupational hygiene in areas such as compliance and control measures and their application in occupational epidemiology. Chapters on occupational hygiene, workplace surveys, monitoring and measurement methods, exposure assessment and control give a blend of theory and practice in the most part based on results of research projects carried out in the Departments of Air Quality and Epidemiology and Public Health over a period of 15 years to 1994. The book provides some information on approaches to hazard monitoring in the laboratory.

Current topics. Commerce officials want tighter controls on microbe exports. ASM News 62, 124.

This short article expresses concern over the potential use of biological agents as weapons and that commerce officials want tighter controls. See also Satcher (1996) below.

Fleming, D.O., Richardson, J.H., Tulis, J.J. & Vesley, D. (eds). (1995) Laboratory safety: principles and practices. Second edition. Washington D.C.: ASM Press, 406 pages.

This book provides a resource for laboratory directors, biosafety officers, engineers, researchers and anyone associated with assuring personnel safety in biomedical or biotechnical laboratories. The epidemiology of laboratory associated infections including some previously unreported cases are covered. Hazard assessments of a wide range of pathogens and toxic chemicals are presented. The book will assist in the identification and the assessment of work related hazards, provide information on working with hazardous agents and on administrative controls proposed for use in safety management.

Fungal Toxins: Safety Data Sheet. St Louis, USA: SIGMA Chemical Company.

Many fungi produce extremely hazardous toxins, this data sheet gives information on safe handling and disposal of such toxins (for further information see section on mycotoxicosis above).

Laboratory Biosafety Manual (1993). Second edition. UK: World Health Organisation.

WHO have produced this manual to help establish international standards in health and safety. The book covers basic principles in health and safety in the handling of hazard group 1-4 organisms, animal facilities, safe

laboratory techniques, safe shipment of materials, emergency procedures, disinfection and sterilisation, laboratory equipment, hazardous chemicals, fire, electrical safety, training and it also provides a safety checklist.

Medical aspects of occupational asthma. Guidance Note MS25 from the Health and Safety Executive. 1991. London: HMSO.

This is a particularly relevant guidance note when considering the potential for microorganisms and their products to cause respiratory sensitisation and that may cause asthma (see Respiratory protection below).

Occupational safety & health handbook and catalogue 1994-95. Royal Society for Prevention of Accidents (ROSPA). Birmingham: ROSPA.

The full range of ROSPA services and products are covered by this catalogue including ROSPA membership, training, safety audits, publications and several topics including a suppliers guide.

Preventing asthma at work. How to control respiratory sensitisers. Health and Safety Executive. Sudbury, UK: HSE Books.

This document gives advice on how to reduce the exposure to respiratory sensitisers to protect the worker. It supplements the information given in the Guidance Note MS25, *Medical aspects of occupational asthma* and provides guidelines for practices that will control respiratory sensitisers (also see Respiratory protection below).

Respiratory protection: Good working practice. A step by step guide for small and medium size companies. 1991. Bracknell, UK: Occupational Health Group, 3M United Kingdom plc.

The information provided by this companies catalogue and associated information booklets is invaluable in helping select the most suitable respiratory protection. Although Personal Protective Equipment (PPE) comes rather low on the control or containment equipment or practices list (COSHH) it is essential that in the case of emergency or spillage that PPE provided gives adequate protection.

Respiratory protective equipment. A practical guide for users (1990) HSC HS(G)53.

This is a useful supplement to the above documents on respiratory protection and control of respiratory sensitisers. Presented with a wide choice of respiratory protective equipment it is often difficult to select the most appropriate. Help is provided.

Safety in biological fieldwork - Guidance notes for codes of practice. Third edition 1990. London: Institute of Biology.

The Institute of Biology Committee on Safety in Biological Fieldwork provide information and input to these guidance notes. The safety advisers of several research councils have also provided assistance in the production of this booklet. The booklet covers safety in particular habitats and in the use of special procedures relevant to collecting of biological specimens.

Samson, R.A., Flannigan, B., Flannigan, M.E., Verhoeff, A.P., Adan, O.C.G. & Hoekstra, E.S. (eds) (1994) Air Quality monographs Vol 2 Health implications of fungi in indoor environments. Amsterdam: Elsevier (602 pages).

Health implications of fungi in indoor environments are discussed along with current methodology on isolation and detection of moulds, the fungal diversity in indoor environments, respiratory symptoms caused by moulds, the role of fungal metabolites, fungal growth on interior finishes. Recommendations are made for standard methods for work and assessment on contaminated indoor environments. The extracts of fourteen fungal species isolated from air conditioning systems were cited as giving positive skin and respiratory challenge in a patient with allergic symptoms.

Penicillium chrysogenum
P. brevicompactum
P. frequentans

A. amstelodami
A. flavus
A. ruber

Aspergillus niger
A. versicolor
A. fumigatus
A. repens

Cladosporium herbarum
Alternaria tenuis
Aureobasidium pullulans
Wallemia sebi

Mycotoxins present in or on spores cause many problems. Various toxins have an effect on pulmonary alveolar macrophage cells. Volatiles produced by moulds have been associated with health problems. Bacteria were also considered to be a problem particularly *Pseudomonas* which contains lipopolysaccharide endotoxins. The major part of the text is concerned with methodology for the evaluation, monitoring of environments and analysis. Chapter 4 covers respiratory symptoms caused by fungi. Home dampness was associated with symptoms in children and sensitisation to fungi is shown to be age dependent, younger age groups being more sensitive and susceptible to asthma. Larsen and Frisvad conclude in their paper on volatiles and mycotoxins of indoor *Penicillium* and *Aspergillus*, that volatiles produced might be toxic/allergenic and might pose a human and animal health problem.

Mycotoxins such as macrocyclic trichothecenes have been detected in the airborne particles collected on membrane filters. Satratoxin G and H, verrucarol and trichothecenes have been detected in air above toxigenic cultures of *Stachybotrys atra*. However, authors state that the work supports the previously reported finding that mycotoxins are concentrated in airborne fungal propagules and are not present as free aerosols in the air.

Satcher, D. (1996) Shipment of human pathogens. ASM News 62, 168.

This short article expresses concern over the shipment of dangerous pathogens that could then be used as biological weapons. The American Society for Microbiology (ASM) is working in collaboration with the Centers for Disease Control (CDC) and offers advice to ASM members. It is recommended that increased vigilance is required to reduce the risk of illicit access to dangerous pathogens and toxin producers. CDC will soon be proposing new regulations regarding acquisition and transfer of certain biological agents.

Smith, D. & Onions, A.H.S. (1994) The preservation and maintenance of living fungi. Second edition. IMI Technical Handbook, No. 1. Wallingford, UK: CAB INTERNATIONAL.

This book provides the background for the management of a collection of microorganisms both safely and effectively as well as describing techniques for their preservation and maintenance. The chapter *Microbial resource collections: aims management and information* provides information on the distribution of strains, quarantine and postal restrictions for plant, human and animal pathogens giving contacts for information and permits. An appendix is devoted to safety in which health and safety regulations are discussed and their impact on the handling and distribution of cultures is covered.

Stricoff & Walters (1995) Handbook of laboratory health and safety. Second edition. NY, USA: Wiley Interscience.

This book discusses management, leadership and employee involvement in health and safety management. The book includes a sample laboratory health and safety assessment questionnaire designed for use as a tool to evaluate health and safety standards. It suggests that health and safety responsibilities should be delegated to specific people and task descriptions written. Hazard evaluation and evaluation are also discussed and goes on to cover all aspects of containment and control.

Smith, J.M.B. (1989) Opportunistic mycoses of man and other animals. Wallingford, UK: CAB INTERNATIONAL.

There are only a few fungi that are listed as pathogenic in the classification of biological agents. However, there are many opportunist fungi that are normally saprobic but on occasion are able to cause disease or grow on man or an animal rendered susceptible by predisposing factors. This book describes such relationships.

Transport of Biological Agents

K. Bostian & D. Fleming (1993). More on mailing Microorganisms. A letter in ASM News 59, 587-588.

The authors reported on a meeting "Transport of Pathogenic Materials" convened by the Public and Scientific Affairs Board (PSAB), Atlanta Ga. USA. The meeting resulted in a working group consisting of representatives of Centres for Disease Control and Prevention (CDC), Department of Transportation (DOT), US Postal Services (USPS) and US Department of Agriculture (USDA), Animal Plant and Health Inspection Service. Recommendations for uniform definitions for materials (potentially pathogenic microorganisms) were developed and revision of 42 CFR (CDC) and 49 CFR (DOT-HM181) were published in 1994.

Brown, E.M. & Simione, F.P. (eds) (1994) ATCC Guide to packaging and shipping of biological materials. Rockville, Maryland: American Type Culture Collection.

This provides guidelines to comply with postage and package legislation for Canada and the USA and is extremely useful for all who distribute and receive microorganisms.

The Biosecurity Act. 1993. NZ Government Publication, Wellington.

This act sets down conditions under which microorganisms can be imported into New Zealand. In the legislation several National Collections have been designated as containment facilities and conditions for their operation have been laid down.

Chemicals (Hazard Information and Packaging) Regulations 1993: Approved Supply List: Information approved for the classification and labelling of substances and preparations dangerous for supply. Health and Safety Executive. Sudbury: HSE Books.

This UK legislation classified several substances as carcinogens for the first time. The legislation came into force in January 1995. CHIP 2 continues the practice established under CHIP 1, of dividing carcinogenic substances into three categories for the purposes of classification and supply labelling. Category 1 carry the "Toxic" symbol plus Risk Phrase R49 "may cause cancer by inhalation". Category 2 carry the "Toxic" symbol plus Risk Phrase R45 "may cause cancer". Category 3 carry the "Harmful" symbol plus Risk Phrase R40 "possible risk of irreversible effects". Microorganism toxins may fall into these categories. It is therefore necessary to label those organisms that produce such toxins and the packages in which they are despatched with the relevant risk phrase and symbol where these toxins are likely to be present.

CHIP 2 legislation requires suppliers to identify the hazards (or dangers) of the chemicals they supply (this will include metabolic products of microorganisms), use labels and safety data sheets to give information about the hazards and to package them safely.

This document lists substances that are dangerous for supply and provides information on how to derive the correct label and therefore triggers the right response of the recipient so that COSHH is complied with. Aflatoxin is not listed, but as this may cause cancer a suitable label must be derived which would include the risk phrase "May cause cancer".

CHIP for Everyone. Chemicals (Hazard Information and Packaging) Regulations 1993). Health and Safety Executive. Sudbury: HSE Books.

This informative booklet outlines the actions necessary to comply with the CHIP 2 legislation (see above).

Approved guide to the classification and labelling of substances and preparations dangerous for supply. Chemicals (Hazard Information and Packaging) Regulations 1993. Guidance on regulations. HSE Books, UK: Health and Safety Commission.

This document gives guidance on how substances should be classified and labelled to comply with the CHIP regulations which came into effect on 1 September 1993. This affects all who send microorganisms that produce toxic substances or where there are toxic components in the growth medium. There is a significant amount of aflatoxin in the freeze-dried samples of *Aspergillus flavus* and also in the agar medium when cultures are sent in universal bottles. The packages and bottles must therefore be appropriately labelled.

Biosafety in microbiological and biomedical laboratories (1993). The US Department of Health and Human Services, Public Health Service, Centres for Disease Control and Prevention (CDC), and National Institute of Health (NIH). Washington: US Government Printing Office. HHS Publication No. (CDC) 93-8395.

This publication sets down guidelines for the safe handling of microorganisms in biomedical laboratories.

Conference paper (1993) Export Controls to Prevent the Proliferation of Biological Weapons. The Genetic Engineer and Biotechnologist 13 (4), 271-283.

A seminar to raise the awareness in the academic and research community of new export controls on biological materials and equipment that could be used in the proliferation of biological weapons was held 10 March 1993 in London. On 31 December 1992 the UK government introduced legislation, The Export of Goods (Control) Order 1992 to control such exports which resulted from discussions of the Australia Group (an informal group of 24 country representatives). The paper presents lists of the organisms and toxins which require a license from the Department of Trade and Industry to export.

European Plant Protection Organisation. (1990) Phytosanitary Regulations of EPPO Member Counties. Paris, France: European and Mediterranean Plant protection Organisation.

This text gives a summary of the Phytosanitary Regulations provided for in the Directive 77/93/EEC and includes amendments upto 26 June 1989, Council Directive 89/439/EEC. It gives an overview of the European Community (EC) requirements and covers the legislation, permits, prohibitions, points of entry, transit and the commodities themselves. Amongst the commodities covered are packing material and soil, wood and bark, woody plants, herbaceous plants, cut flowers and branches, flower bulbs and tubers, vegetables and fruit, potatoes and seeds. Under sections on prohibitions and restrictions it lists the pests and diseases (including bacteria, fungi and viruses) whose introduction is prohibited in all or specified EC member states.

Guidelines for Packaging and Shipping of Infectious Substances. 1993. New Zealand Communicable Disease Centre, Institute for Environmental Health and Forensic Sciences, Porirua, New Zealand. 12pp.

This document provides packaging and shipping information for the transport of infectious substances in New Zealand.

Guidelines for Packaging and Shipping of Infectious Substances. 1995. Update No.2. New Zealand Communicable Disease Centre, Institute for Environmental Health and Forensic Sciences, Porirua, New Zealand. 3pp.

This document provides an update on the packaging and shipping information for the transport of infectious substances in New Zealand outlined in the 1993 edition above.

Procedures for the Handling and Transport of Diagnostic Specimens and Etiologic Agents. Third Edition: Approved Standard. Pennsylvania: The National Committee for Clinical Laboratory Standards. NCCLS document H5A3.

This describes a practical and systematic method for ensuring the integrity of the specimen from the point of origin to the laboratory. The document offers descriptions of handling procedures, packaging, labelling the package, transportation and handling procedures on arrival. It is intended for international as well as domestic use and provides a resource for clinical laboratories, physicians, hospitals, transport services and other persons or institutions that ship, handle or receive specimens.

Rohde, C. & Claus, D. (eds) (1995) *Shipping of infectious, non-infectious and genetically modified biological materials. International Regulations. ECCO. Available from: Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ), Braunschweig, Germany.*

This booklet is revised on a regular basis and this revision is a valuable source of information on international shipping regulations. For further information and supply contact C. Rohde, *Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ), Mascheroder Weg 1b, D-38124, Germany.*

Rohde, C., Claus, D. & Malik, K.A. (1995) *Technical Information Sheet No. 14: Packing and shipping of biological materials: some instructions, legal requirements and international regulations. World Journal of Microbiology & Biotechnology 11, 706-710.*

This paper was originally published by UNESCO/WFCC Education Committee 1995 and reproduced in the World Journal of Microbiology and Biotechnology. It covers the procedures for packaging and transport of biological materials according to the legal regulations and requirements of the relevant international and governmental (national) agencies and refers to Rhode & Claus (1995) and Brown & Simione (1994) for further information. It presents an extremely useful table listing the countries with restrictions on the receipt and despatch of non-infectious biological substances or infectious perishable biological substances and transport by internal postal services.

Safe Biotechnology (5) Recommendations for safe work with animal and human cell cultures concerning potential human pathogens.

This provides an update on biological risk and handling recommendations but does not cover aspects of transportation between laboratories.

Smith, I.M, McNamara, D.G., Scott, P.R. & Harris, K.M. (eds) (1992) *Quarantine Pests for Europe. Wallingford, UK: CAB INTERNATIONAL.*

This book provides essential information on pests and diseases in Europe. The movement of pest organisms from country to country within Europe is restricted, it is essential for laboratories who supply organisms to be aware of these restrictions.

Transportation of Dangerous Goods Act and Regulations, 1992, Registration SOR 85-77 as amended in 1994 (SOR 94-264). (Canada Gazette Part II, Vol. 128, No. 7 (SOR/94-264 24 March, 1994) (Original document SOR/85-77, 1985 Canada Gazette Part II)

This is an amended version of the regulations and the content has been extensively covered earlier in this report under the section *Changes in Guidelines or Regulations: Canada*. The publication also includes lists of infectious substances which are not listed here and which are prohibited from shipment by Canadian Post.

National Standard of Canada CAN/CGSP-43, 125-M90, Packaging of Infectious Substances and Diagnostic Specimens, dated November 1990. Canada, Ottawa: Standards Council of Canada.

The standards for the packaging of infectious substances and diagnostic specimens are defined in this document and must be complied with when shipping such materials into and throughout Canada.

Laboratory Biosafety Guidelines (1996). 2nd edition. Canada, Ottawa: Laboratory Centre for Disease Control, Health Protection Branch, Health Canada.

This document defines the risk groups and their assignments for Canada. It outlines:

a) containment of biohazards, b) regulations for import, export, transportation, c) classification of biological agents according to risk [see above under Transport of Dangerous Goods], d) physical containment levels (1

through 4), e) containment for animal biohazard facilities and large scale production of microorganisms, f) laboratory design.

Human Pathogens Importation Regulations, Registration SOR/94-558, 16 August, 1995. Canada Gazette Part II, Vol. 128, No. 18.

Regulations to control the importation of human pathogens came into effect in Canada in 1994 and these were published in the above. Further information is given under the section *Changes in Guidelines or Regulations: Canada..*

APPENDIX 1. Classification of Biological agents for Europe (Council Directive 93/88/EEC Annex 1)

HAZARD GROUP 2 BACTERIA

<i>Actinobacillus actinomycetemcomitans</i>	<i>Edwardsiella tarda</i>
<i>Actinomadura madurae</i>	<i>Ehrlichia sennetsu</i> (<i>Rickettsia sennetsu</i>)
<i>Actinomadura pelletieri</i>	<i>Ehrlichia</i> (other species which are known pathogens of man)
<i>Actinomyces gerencseriae</i>	<i>Eikenella corrodens</i>
<i>Actinomyces israelii</i>	<i>Enterobacter aerogenes/cloacae</i>
<i>Actinomyces pyogenes</i>	<i>Enterobacter</i> (all species)
<i>Actinomyces</i> (other species which are known pathogens of man)	<i>Enterococcus</i> (all species)
<i>Arcanobacterium haemolyticum</i> (<i>Corynebacterium haemolyticum</i>)	<i>Erysipelothrix rhusiopathiae</i>
<i>Bacteriodes fragilis</i>	<i>Escherichia coli</i> (except those known to be non-pathogenic)
<i>Bartonella bacilliformis</i>	<i>Flavobacterium meningosepticum</i>
<i>Bordetella bronchiseptica</i>	<i>Fluoribacter bozemanai</i> (<i>Legionella</i>)
<i>Bordetella parapertussis</i>	<i>Francisella tularensis</i> (Type A)
<i>Bordetella pertussis</i>	<i>Francisella tularensis</i> (Type B)
<i>Borrelia burgdorferi</i>	<i>Fusobacterium necrophorum</i>
<i>Borrelia duttonii</i>	<i>Gardnerella vaginalis</i>
<i>Borrelia recurrentis</i>	<i>Haemophilus ducreyi</i>
<i>Borrelia</i> spp. (all species known to be pathogens of man)	<i>Haemophilus influenzae</i>
<i>Campylobacter fetus</i>	<i>Haemophilus</i> spp. (all other species known to be pathogens of man)
<i>Campylobacter jejuni</i>	<i>Helicobacter pylori</i>
<i>Campylobacter</i> spp. (all other species known to be pathogens of man)	<i>Klebsiella oxytoca</i>
<i>Cardiobacterium hominis</i>	<i>Klebsiella pneumoniae</i>
<i>Chlamydia pneumoniae</i>	<i>Klebsiella</i> spp. (all other species known to be pathogens of man)
<i>Chlamydia psittaci</i> (avian strains)	<i>Legionella pneumophila</i>
<i>Chlamydia psittaci</i> (other strains)	<i>Legionella</i> spp. (all other species known to be pathogens of man)
<i>Clostridium botulinum</i>	<i>Leptospira interrogans</i> (all serovars)
<i>Clostridium perfringens</i>	<i>Listeria ivanovii</i>
<i>Clostridium tetani</i>	<i>Listeria monocytogenes</i>
<i>Clostridium</i> spp. (all other species known to be pathogens of man)	<i>Moraxella catarrhais</i>
<i>Corynebacterium diphtheriae</i>	<i>Moraxella lacunata</i>
<i>Corynebacterium minutissimum</i>	<i>Morganella morganii</i>
<i>Corynebacterium pseudotuberculosis</i>	<i>Mycobacterium africanum</i>
<i>Corynebacterium</i> spp. (all other species known to be pathogens of man)	<i>Mycobacterium avium/intracellulare</i>

APPENDIX 1 (continued).

<i>Mycobacterium bovis</i> (except BCG strain)	<i>Pseudomonas aeruginosa</i>
<i>Mycobacterium chelonae</i>	<i>Rhodococcus equi</i>
<i>Mycobacterium fortuitum</i>	<i>Rochalimaea quintana</i>
<i>Mycobacterium marinum</i>	<i>Salmonella arizonae</i>
<i>Mycobacterium paratuberculosis</i>	<i>Salmonella enteritidis</i>
<i>Mycoplasma pneumoniae</i>	<i>Salmonella typhimurium</i>
<i>Neisseria gonorrhoeae</i>	<i>Salmonella</i> (other serovars)
<i>Neisseria meningitidis</i>	<i>Serpulina</i> spp. (all species known to be pathogens of man)
<i>Nocardia asteroides</i>	<i>Shigella boydii</i>
<i>Nocardia brasiliensis</i>	<i>Shigella flexneri</i>
<i>Nocardia farcinica</i>	<i>Shigella sonnei</i>
<i>Nocardia nova</i>	<i>Staphylococcus aureus</i>
<i>Nocardia otitidiscaviarum</i>	<i>Streptobacillus moniliformis</i>
<i>Pasteurella multocida</i>	<i>Streptococcus pneumoniae</i>
<i>Pasteurella</i> spp. (all other species known to be pathogens of man)	<i>Streptococcus pyogenes</i>
<i>Peptostreptococcus anaerobius</i>	<i>Streptococcus</i> spp. (all species known to be pathogens of man)
<i>Plesiomonas shigelloides</i>	<i>Treponema carateum</i>
<i>Porphyromonas</i> (all species known to be pathogens of man)	<i>Treponema pallidum</i>
<i>Prevotella</i> (all species known to be pathogens of man)	<i>Treponema pertenuis</i>
<i>Proteus mirabilis</i>	<i>Treponema</i> (all species known to be pathogens of man)
<i>Proteus penneri</i>	<i>Vibrio cholerae</i> (inc EL Tor)
<i>Proteus vulgaris</i>	<i>Vibrio parahaemolyticus</i>
<i>Providencia alcalifaciens</i>	<i>Vibrio</i> (all species known to be pathogens of man)
<i>Providencia rettgeri</i>	<i>Yersinia enterocolitica</i>
<i>Providencia</i> (all species known to be pathogens of man)	<i>Yersinia pseudotuberculosis</i>
	<i>Yersinia</i> (all species known to be pathogens of man)

HAZARD GROUP 3

Bacteria

<i>Bacillus anthracis</i>	<i>Mycobacterium tuberculosis</i>
<i>Brucella canis</i>	<i>Mycobacterium ulcerans</i>
<i>Brucella melitensis</i>	<i>Rickettsia akari</i>
<i>Brucella suis</i>	<i>Rickettsia canada</i>
<i>Burkholderia mallei</i> (<i>Pseudomonas mallei</i>)	<i>Rickettsia conorii</i>
<i>Burkholderia pseudomallei</i> (<i>Pseudomonas pseudomallei</i>)	<i>Rickettsia montana</i>
<i>Chlamydia psittaci</i> (avian strains)	<i>Rickettsia prowazekii</i>
<i>Coxiella burnetii</i>	<i>Rickettsia rickettsii</i>
<i>Francisella tularensis</i> (Type A)	<i>Rickettsia tsutsugamushi</i>
APPENDIX 1 (continued).	<i>Rickettsia typhi</i> (<i>Rickettsia mooseri</i>)
<i>Mycobacterium africanum</i>	<i>Salmonella typhi</i>

Mycobacterium bovis (except BCG strain)
Mycobacterium leprae
Mycobacterium microti

Shigella dysenteriae (Type 1)
Yersinia pestis

Hazard Group 2 Fungi

Aspergillus fumigatus
Candida albicans
Cryptococcus neoformans var *neoformans*
(*Filobasidiella neoformans* var *neoformans*)*
Cryptococcus neoformans var *gatti*
(*Filobasidiella bacillispora*)
Emmonsia parvum var *parva*
Emmonsia parvum var *crecens*
Epidermophyton floccosum
Fonsecaea compacta

Fonsecaea pedrosoi
Madurella grisea
Madurella mycetomatis
Microsporium (all species known to be pathogens of man)
Neotestudina rosatii
Sporothrix schenckii
Trichophyton rubrum
Trichophyton (all species known to be pathogens of man)

*Safety cabinet is essential

Hazard Group 3 Fungi

Blastomyces dermatitidis
(*Ajellomyces dermatitidis*)
Coccidioides immitis
Histoplasma capsulatum var. *capsulatum*
(*Ajellomyces capsulatus*)

Histoplasma capsulatum var. *duboisii*
Histoplasma capsulatum var. *farcinimosum*
Paracoccidioides brasiliensis

Footnote:

- Any strains of pathogenic organisms in the hazard categorisation list which have been attenuated or genetically modified and granted a Clinical Trials Certificate or Products Licence may be recategorised into a lower hazard group when used for the approved therapeutic purposes.
- Some recent publications have described the possible association of an apparently new species of *Mycoplasma* with acute fatal disease. *M. incognitus* cannot be categorised until more is known but caution in handling is advised. DNA hybridisation studies appear to indicate a relationship with *M. fermentans*.

APPENDIX 2. Additions and Changes in Hazard Categorization of Microorganisms in the UK

Hazard Group 2 (additional)

Acinetobacter calcoaceticus
Acinetobacter lwoffii
Aeromonas hydrophila
Alcaligenes (all species known to be pathogens of man)
Arizona (all species known to be pathogens of man)
Bacillus cereus
Bacteriodes (all species known to be pathogens of man)
Burkholderia cepacia
Burkholderia (all species known to be pathogens of man)
Chlamydia psittaci (excludes avian strains)
Chlamydia trachomatis
Francisella tularensis (Type B only)
Fusobacterium (all species known to be pathogens of man)
Mycoplasma hominis
Neisseria elongata
Nocardia (all species known to be pathogens of man)
Peptostreptococcus (all species known to be pathogens of man)
Rochalimaea (all species) (*Bartonella*)
Serratia liquefaciens
Serratia marcescens
Shigella dysenteriae (other than Type 1)
Stenotrophomonas maltophilia
Ureaplasma urealyticum

Bacteria raised to category 3

Brucella abortus
Ehrlichia sennetsu (*Rickettsia sennetsu*)
Mycobacterium avium/intracellulare
Mycobacterium kansasii
Mycobacterium malmoense
Mycobacterium scrofulaceum
Mycobacterium simiae
Mycobacterium szulgai
Mycobacterium xenopi
Rickettsia (all species other than those listed as 3 that are known to be pathogens of man)
Salmonella paratyphi A,B,C

Fungi raised to category 2

Candida (all species known to be pathogens of man)
Xylohypha bantiana

Fungi raised to category 3

Penicillium marneffeii

APPENDIX 3. Level of Biosafety of Human Pathogens by the National Institute of Health (NIH), Japan

Virus, Chlamydia and Rickettsia

Level 1

Live Vaccine virus (except *Vaccinia*)

Level 2

Adeno-associated

Batai

Bunyamwera

California encephalitis

Corona

Cowpox

Coxsackie (A, B)

Creutzfeldt-Jacob disease agent

Dengue

Echo

Eastern equine encephalitis

Enterovirus (68-71)

Epstein-Barr (EB)

Gibbon ape lymphosarcoma

Hepatitis (A, B, C, D, E)

Herpes saimiri

Herpes simplex (1, 2)

Human cytomegalo

Human herpes 6

Human papilloma

Human parvo

Human rhino

Human rota

Human T-cell leukemia-lymphoma
(HTLV 1, 2)

Influenza (A, B, C)

Japanese encephalitis

JC

La Crosse

LCM

Measels (SSPE)

Molluscum contagiosum

Monkeypox

Mumps

Murray Valley encephalitis

Newcastle disease

O'Nnyong-Nnyong

Orbivirus

Parainfluenza (1-Sendai 2-4)

Polio (1-3)

Rabies (fixed, attenuated)

RS

Rubella

Semliki forest

Simian immunodeficiency virus (SIV)

Simbu

Sindbis

St Louis encephalitis

Tanapox

Vaccinia

Varicella-zoster

Vesicular stomatitis

Western equine encephalomyelitis

West Nile fever

Yaba monkey tumor pox

Chlamydia psittaci

Chlamydia trachomatis

Level 3

Chikungunya

Colorado tick fever

Hantaan

Human immunodeficiency (HIV 1, 2)

Kyasanur Forest fever

Negishi

Powassan

Rabies (street strain)

Rift Valley fever

Tick-borne encephalitis

Venezuelan equine encephalitis

Coxiella burnetii

Rickettsia spp.

APPENDIX 3 (continued).

Level 4

Crimean Congo hemorrhagic fever
Ebola
Herpes B
Junin
Lassa

Machpo
Marburg
Variola (major, minor)
Yellow fever (except 17D vaccine strain)

Mycoplasma and Bacteria

Level 1

Bacteria except those listed under levels 2 and 3

Level 2

Actinobacillus actinomycetemcomitans
Actinomadura madurae
A. pelletieri
Actinomyces bovis
A. israelii
A. pyrogenes
A. viscosus
Aeromonas hydrophila
A. sobria
Bacillus cereus
Bordetella bronchiseptica
B. parapertussis
B. pertussis
Borrelia
Baranhamella catarrhalis
Calymmatobacterium granulomatis
Campylobacter coli
C. jejuni
Clostridium botulinum
C. difficile
C. haemolyticum
C. histolyticum
C. novyi
C. perfringens
C. septicum
C. sordelli
C. sporogenes
C. tetani
Corynebacterium diphtheriae
C. jeikeium
C. pseudodiphtheriticum
Erysipelothrix rhusiopathiae
Escherichia coli (except *E. coli*,
Strain K12 and derived organisms)

Francisella novicida

APPENDIX 3 (continued).

Pasteurella multocida (except
serotypes causing animal disease)
P. pneumotropica
P. ureae

Fusobacterium necrophorum
Haemophilus ducreyi
H. influenzae
Helicobacter pylori
Klebsiella oxytoca
K. pneumoniae
Legionella (all species
including legionella-like organisms)
Leptospira interrogans (all serotypes)
Listeria monocytogenes
Mycobacterium avium
M. chelonae
M. fortuitum
M. haemophilum
M. intracellulare
M. kansasii
M. leprae
M. lepraemurium
M. malmoense
M. marinum
M. paratuberculosis
M. scrofulaceum
M. simiae
M. szulgai
M. ulcerans
M. xenopi
Mycoplasma fermentans (Lo)
M. hominis
M. pneumoniae
Neisseria gonorrhoeae
N. meningitidis
Nocardia asteroides
N. brasiliensis
N. farcinica
N. otitidiscaviarum

Plesiomonas shigelloides
Pseudomonas aeruginosa
P. cepacia
Salmonella all serotypes

except those in level 3

Serratia marcescens
Shigella all species
Staphylococcus aureus
Streptobacillus moniliformis
Streptococcus pneumoniae
S. pyrogenes
Treponema carateum
T. pallidum

Level 3

Bacillus anthracis
Brucella all species
Francisella tularensis
Mycobacterium africanum
M. bovis (except BCG)
M. tuberculosis

Fungi

Level 1

Not listed

Level 2

Aspergillus fumigatus
Candida albicans
Cladosporium carrionii
C. trichoides (*C. bantianum*)

Level 3

Blastomyces dermatitidis
Coccidioides immitis
Histoplasma capsulatum
(*H. capsulatum* var. *capsulatum*,
H. capsulatum var. *duboisii*)
H. farciminosum
Paracoccidioides brasiliensis
Penicillium marneffeii

T. pertenuae
Vibrio cholerae
V. fluvialis
V. mimicus
V. parahaemolyticus
V. vulnificus
Yersinia enterocolitica
Y. pseudotuberculosis

Pseudomonas mallei
P. pseudomallei
Salmonella paratyphi A
S. typhi
Yersinia pestis

Cryptococcus neoformans
Exophiala dermatitidis
Fonsecaea pedrosoi
Sporothrix schenckii

Toxin producing strains of:
Aspergillus spp.
Chaetomium spp.
Fusarium spp.
Myrothecium spp.
Penicillium spp.

APPENDIX 3 (continued).

Nematodes

Level 1

Nematodes excluded from level 2

Level 2

Acanthamoeba spp.
Cryptosporidium spp. (oocyst)
Entamoeba histolytica
Giardia lamblia
Leishmania spp.
Naegleria spp.
Plasmodium spp.
Toxoplasma gondii
Trichomonas vaginalis

Trypanosoma
Schistosoma spp. (cercaria)
Echinococcus spp. (egg, hydatid sand,
protoscolex)
Hymenolepis spp. (egg, cysticercoid)
Taenia solinum (egg, cysticercus)
Angiostrongylus spp.
Strongyloides spp.
Trichinella spiralis

**APPENDIX 4. Animal pathogens of Class 4 by the Culture Collection Committee
of the Animal Health Experimental Station, MAFF, Japan**

Virus

African swine fever
Rinderpest

African horse sickness
Foot and mouth disease

Bacteria

Mycoplasma mycoides subsp. *mycoides*

Pseudomonas mallei

APPENDIX 5. Select Infectious Agents listed in proposed rule on additional requirements for facilities transferring or receiving select infectious agents.

Viruses

1. Crimean-Congo haemorrhagic fever virus
2. Chikungunya virus
3. Ebola virus
4. Hantaviruses
5. Japanese encephalitis virus
6. Lassa fever virus
7. Marburg virus
8. Rift Valley fever virus
9. Tick-borne encephalitis viruses
10. Variola major virus (Smallpox virus)
11. Yellow fever virus
12. South American haemorrhagic fever virus (Junin, Machupo, Sabia, Guanarito and those yet to be described).
13. Encephalitis viruses (Venezuelan, Western, Eastern)
14. Kyasanur Forest Disease Virus

Exemptions: Vaccine strains of these viral agents as described in the third edition of the CDC/NIH *Biosafety in microbiological and biomedical laboratories* are exempt.

Bacteria

1. *Bacillus anthracis*
2. *Brucella abortus*, *B. melitensis*, *B. suis*
3. *Chlamydia psittaci*
4. *Clostridium botulinum*
5. *Francisella tularensis*
6. *Burkholderia (Pseudomonas) mallei*
7. *Burkholderia (Pseudomonas) pseudomallei*
8. *Yersinia pestis*

Rickettsiae

1. *Coxiella burnetii*
2. *Rickettsia prowazekii*
3. *Rickettsia rickettsii*

Fungi

1. *Histoplasma capsulatum* (inc. var. *duboisii*)

Toxins

1. Abrin
2. Botulinum toxins
3. *Clostridium perfringens* toxin
4. *Corynebacterium diphtheriae* toxin

APPENDIX 5 (continued).

5. Cyanginosins
6. Staphylococcal enterotoxins

7. *Shigella dysenteriae* neurotoxin
8. Ricin
9. Saxitoxin
10. Shigatoxin
11. Tetanus toxin
12. Tetrodotoxin
13. Trichothecene mycotoxins
14. Verrucologen

Exemptions: Toxins for medical use, inactive for use as vaccines, or toxin preparations for biomedical research use at an LD₅₀ for vertebrates of more than 100 nanograms per kilogram body weight (e.g. microbial toxins such as the botulinum toxins, tetanus toxin, diphtheria toxin and *Shigella dysenteriae* neurotoxin) are exempt.

Recombinant organisms/molecules

1. Genetically modified microorganisms or genetic elements that contain nucleic acid sequences associated with pathogenicity from organisms on restricted list.
2. Genetically modified microorganisms or genetic elements that contain nucleic acid sequences coding for any of the toxins on the restricted list or their toxic subunits.

The deliberate transfer of a drug resistance trait to microorganisms on this list that are not known to acquire the trait naturally is prohibited by NIH *Guidelines for research involving recombinant DNA molecules* if such acquisition could compromise the use of the drug to control these disease agents in humans or veterinary medicine.

Reference: Department of Health and Human Services, Public Health Service, 42 CFR Part 72, RIN 0905-AE70. Additional requirements for facilities transferring or receiving select infectious agents. Federal Register: June 10, 1996, Vol. 61 (112) Proposed Rules p 29327-29333.