Antibiotics in Agronomy and Horticulture

The objective of the National Health and Medical Research Council is to advise the Australian community on the achievement and maintenance of the highest practicable standards of individual and public health and to foster research in the interests of improving those standards.

Glossary of Terms

Antibiotic	Antibiotics are selective antimicrobial agents other than disinfectants, antiseptics and substances used solely as antineoplastics, that, on application to living tissue or by systemic administration, kill or prevent the growth of susceptible microorganisms.
Antibiotic resistance	An organism is said to have acquired resistance to an antibiotic when the minimum inhibitory concentration (MIC) for that strain is significantly higher than the MIC normally found in the same species of organism for that antibiotic.
Bacteria	Bacteria are unicellular prokaryotic organisms or simple associations of similar cells based upon growth habit, planes of division and cell separation. With few exceptions the cells are contained within a rigid or semirigid cell wall and with few exceptions the cell wall polymers include eptidoglycans. They show a variety of nutritional and physical requirements. Those that perform photosynthesis do so under anaerobic conditions requiring an electron donor other than water and do not produce oxygen in the process, utilize one or more of the bacteriochlorophylls and never contain chlorophyll or phycobili proteins. Those that perform chemosynthesis may require either aerobic or anaerobic conditions or be facultative. Bacteria are widely distributed throughout the environment. They may occur within the bodies of animals causing no harm to their host while others cause disease in their hosts (animal and plant). They are present in the soil and compost heaps, bringing about the breakdown of complex animal and plant tissue.
Fungicide	Any substance or mixture of substances intended for preventing, destroying or controlling fungi.

Maximum Residue Limit	Maximum Residue Limit (MRL) is the maximum of a residue (expressed as mg/kg) recommended by the Chemical Safety Unit of the Department of Human Services and Health to be permitted in, or on, a food or a primary feed Commodity. In Australia, MRLs are incorporated into the NFA Food Standard Code and then into State Food and Drug Regulations
Pathogens	Pathogens Disease producing organisms affecting plants or animals, but not higher organisms such as nematodes.
Phytotoxic	Causing damage to plants. Any substance which exerts a deleterious effect on plant tissues.

Working party on the use of antibiotics in agronomy & horticulture

Terms of reference

The formation of the WorkingParty on the Use of Antibiotics in Agronomy and Horticulture was endorsed by the National Health and Medical Research Council at its 104th Session in November 1987. This followed a recommendation from the Antibiotics Committee (renamed during the inquiry as the NHMRC Expert Panel on Antibiotics) for the need to examine and report on the application of antibiotics in the plant industry. Council endorsed the following terms of reference:

- To assess the role of antibiotics in the treatment, prevention, and control of diseases in plants.
- To identify public health issues arising out of the application of antibiotics to plants, eg. antibiotic resistance, toxicity.
- To recommend strategies for ensuring appropriate use of antibiotics in the plant industry, and to report to the Antibiotics Committee.

Membership

Dr D Bryden (Chairman)	The Postgraduate Foundation in Veterinary Science, The University of Sydney
Dr P Fahy	Biological & Chemical Research Institute, NSW Department of Agriculture and Fisheries, Sydney
Mr L C Jones	Agriculture & Forestry Group, Department of Primary Industries & Energy, Canberra
Professor P J McDonald	Department of Clinical Microbiology, Flinders Medical Centre, Adelaide
Dr M L Moffett	Plant Pathology, Queensland Department of Primary Industries, Brisbane (Retired June 1988)
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Introduction

Antibiotics have had a long history of use in agriculture and have been responsible for a marked increase in livestock production. They have had a more limited role in plant production.

Plant pathologists over many years have been interested in the efficacy of antibiotics in controlling plant diseases and in particular their possible systemic action. The advent of systemic eradicant fungicides made a significant improvement in the control of fungal diseases. There are no such chemicals available for the control of bacterial or viral diseases.

Australia's quarantine laws have been relied upon to minimise the threat of introduced plant pathogens and particularly those not yet recorded in this country. Quarantine detection procedures have had considerable success. However, where disease symptoms are not readily expressed or are carried symptomlessly, the possibility of the introduction of a pathogen is greatly increased. Antibiotics could assist in minimising the risk of such introductions.

In Australia there has been increased interest in the use of antibiotics to control plant diseases, particularly bacterial diseases of fruit trees and ornamental plants.

Antibiotics have had successful application in plant disease control overseas where the more traditional plant protection methods have been inadequate. On overseas experience antibiotics could have a beneficial role in the agricultural and horticultural industries in Australia. However such usage raises concern over their uncontrolled use, safe practices in their application, and their effectiveness in the control of plant diseases.

The use of antibiotics in livestock production has been examined in depth during the last 20-30 years. In Australia, in terms of kilogram amounts, approximately one third of the bulk antibiotic imports are consumed by the feed additives industry. Antibiotic use in the control of plant diseases may increase overall antibiotic use in the rural sector.

Decisions have to be taken on what controls, if any, need to be introduced to safeguard the continuing effectiveness of antibiotics. Also of importance is the absence of detectable levels of antibiotics in both meat and other agricultural produce entering the food chain. The absence of antibiotic residues is particularly important to Australia in preserving good relationships with overseas trading partners.

The NHMRC has addressed the continuing use of antibiotics in primary production in Australia as an adjunct for significantly increasing the production of meat, poultry, eggs and milk. The NHMRC Report, *Antibiotics in Stockfeeds* (Approved by the Council at its 101st Session, June 1986) recognised a role for antibiotics in primary products, and that controls needed to be exercised over which antibiotics are used and the conditions which should apply to their availability.

The lead-up to theformation of the NHMRC Working Party on the Use of Antibiotics in Agronomy and Horticulture identified similar concerns for the plant industry**.** Furthermore, the Commonwealth Department of Community Services and Health (now the Commonwealth Department of Human Services and Health) had sought the views of the then NHMRC Antibiotics Committee on a number of issues relating to the importation of antibiotics for use in agronomy and horticulture. The Department administers the permit system for these drugs which are controlled by the C*ommonwealth Customs and Prohibited Imports Act and Regulations*.

The Antibiotics Committee foresaw the need for a detailed review of the issues arising from the use of antibiotics in agronomy and horticulture before informed advice could be given to any regulatory agency in Australia. The Antibiotics Committee also believed guidelines should be established well before there is a widespread demand for antibiotics in the treatment of plant diseases.

Definition of an antibiotic

The meaning of the term *antibiotic* has undergone considerable revision over the past few decades to reflect contemporary usage. The term was originally associated with substances produced exclusively by microbial fermentation and used for the treatment of microbial infections. These days many of these substances are produced by chemical synthesis and some are not used for the treatment of microbial infections, eg. the antineoplastic antibiotics.

The National Health and Medical Research Council, at its 109th Session in May 1990, developed a compromise definition which addressed contemporary usage of the term but excluded uses other than those associated with killing or preventing the growth of susceptible micro-organisms. Council endorsed the following definition:

‘Antibiotics are selective antimicrobial agents other than disinfectants, antiseptics and substances used solely as antineoplastics, that, on application to living tissue or by systemic administration, kill or prevent the growth of susceptible microorganisms.’

The Working Party considered that some chemicals commonly used in agronomy to control plant diseases, could come within the scope of the antibiotic definition. These chemicals could attract the same government controls applied to the traditional antibiotic compounds as concerns their availability, application and importation into Australia. While the Working Party is supportive of government controls over antibiotics, it recognises that some chemicals such as the commonly used chemical fungicides, should not be unduly restricted.

Biological control agents, whose effective mode of action may be either wholly of partly through antibiotic production, are excluded from the definition of an antibiotic.

Public health issues - arising from the use of antibiotics in agronomy & horticulture

The on farm preparation and application of antibiotics in agronomy and horticulture raises some issues relating to public health, particularly in relation to the method of application and the type of antibiotic selected.

Broadly, risks relate to the exposure of workers to antibiotics through:

- inhalation, ingestion and skin contact during the preparation and application of liquids, slurries and sprays containing antibiotics

- exposure to residues or wastes resulting from these applications.

The implications of these public health and safety issues need to be addressed in relation to each specific application procedure. These implications will be discussed in more detail in the section, ‘Use of Antibiotics in Horticulture’ (Page 7).

Guiding principles of antibiotic use

The aims of the NHMRC Expert Panel on Antibiotics (EPOA) are:

- to advise on ways to minimise the antibiotic burden in the Australian community and environment. The antibiotic burden is a combination of the total amount of antibiotics used and the breadth of the spectrum of those antibiotics
- to advise on ways to minimise the rate of development of antibiotic resistance and the spread of that resistance, and thereby preserve the utility of older, narrower-spectrum, safer and less expensive antibiotics

In the context of the availability of antibiotics for use in agronomy and horticulture, the EPOA and the Working Party felt that antibiotic use should be restricted to those areas of use where:

- productivity would be severely affected without their use
- no satisfactory alternative treatments are available
- risks of antibiotic exposure to users and consumers could be adequately minimised
- development of antibiotic resistance would be minimal and, or of no consequence to human, veterinary, or plant health

Important principles need to be taken into account before approving an antibiotic for use in agronomy and horticulture. These are:

- The antibiotic should be rapidly degraded in the environment by chemical or microbiological means
- The use of antibiotic will not add unnecessarily to the antibiotic burden. This means that it will not be prescribed, dispensed or used where it is not needed. It also means that a broad spectrum agent will not be used when a narrow spectrum agent would be adequate
- When the rate of development of microbial resistance is likely to be high when the agent is used alone, then it should not be used unless used in combination with another agent able to minimise the effect
- Use of the antibiotic will not encourage the selection of microbial cross-resistance to a wide spectrum of unrelated antibiotics
- Antibiotics will not be used in combination unless:
  (i) it is proven that a combination of agent is essential for the treatment of a single organism in order to guarantee efficacy or prevent the emergence of resistance
  (ii) more than one pathogen organism is expected in the relevant circumstances and these cannot be treated effectively with a single agent.

Brief review of microbial plant diseases where antibiotics have been used

There are a number of plant pathogens worldwide which are sensitive to antibiotics and where the application of antibiotic preparations has proved valuable in the control of the diseases caused by those pathogens.

Fungal diseases are of far greater economic significance than bacterial or viral diseases. However due to the availability of highly effective fungicides, there are only a few instances where antibiotics have been used commercially for the control of fungal diseases. Antibiotics have mainly been targeted against bacterial pathogens. Antibiotics have not been successfully applied for the control of viral diseases.

Streptomycin and oxytetracycline have been used to control the fire blight bacterium, *Erzvinia amylovora,* in pear and apple trees. These antibiotics have also been employed to control bacterial speck of tomato caused by *Pseudomonas syringae pv. tomato,* bacterial canker (blast) P. *syringae pv. syringae,* and bacterial spot *Xanthomonas camprestris pv. pruni* of stone fruit. Streptomycin was used in an attempt to control angular leaf spot *Pseudomonas syringae pv. tabaci* on tobacco seedlings. Streptomycin as a seed dressing has been used on beans, tomatoes and cotton, but problems associated with phytotoxicity has limited its use particularly in beans.

To prevent stem rot caused by *Erwinia chrysanthemi* in Dieffenbachia (ornamental house plant), dipping of cuttings followed by five weekly sprays of streptomycin has been used by nurserymen.

Bacterial leaf blight of rice *(Xanthomonas campestri pv. oryzae) is* an important disease in rice, particularly where high yielding varieties have been introduced. Antibiotics such as cellocidin and chloramphenicol have been used in Japan for the control of this disease.

Rice blast caused by the fungus *Pyricularia oryzae is* the most harmful disease of rice in Japan. The Japanese formerly controlled this disease by applying mercury compounds as a seed dressing or as a spray application to the plant. However, the use of mercury compounds has not been possible for many years. The antibiotics blasticidin-S and kasugamycin have been found to be effective against P. *oryzae* and have replaced the mercury fungicide.

Use of antibiotics in field crops and postures

Following a review of world literature and an assessment of the situation in Australia, the Working Party agreed that there did not appear to be any current need for antibiotic use in this area except for quarantine purposes.

Use of antibiotics in horticulture

The Working Party considered seven areas of use of antibiotics in horticulture.

These are:

1. Soil applications
2. Seed treatments
3. Spray applications to growing plants
4. Dipping propagation material

5. Hydroponics
6. Post-harvest applications
7. Tissue culture.

The Working Party took into account the following aspects.

- Different methods of application
- Risk to operators applying antibiotic
- Environmental impact and public health implications of antibiotic applications in agronomy and horticulture.

1 Soil applications

Continued application of antibiotics and possible build up of antibiotic residues in the soil may have an effect on the size of the microbial population and on the diversity and nature of the species within that population. Ingham and Coleman (1984)[1] showed that commercial rates of application of streptomycin to soil did not have significant effect on total bacterial and fungal numbers in the short term (over several weeks). However, the nature of the bacterial population would appear to have been changed. Other studies (see Anderson & Domsh, cited in Ingham and Coleman 1984) using different soil types have observed more dramatic effects.

The risks to people making these applications should not be great provided that standard safety precautions are followed.

It is recommended that:

Soil applications of antibiotics for the treatment of plant diseases should not be permitted until adequate environmental studies are conducted to indicate that this is a safe and satisfactory method of administration.

1. Ingham ER, & Coleman DC, 1984, 'Effects of streptomycin, cycloheximide, fungizone, captan, carbofuran, cygon and PCNB on soil microorganisms', *Microb. Ecol*, 10, 345-358.

2 Seed treatment using liquids, sprays or powders

The Working Party noted that the antibiotics streptomycin, tetracycline and oxytetracycline are used in seed treatments.

In considering the current practice of including marker dyes in antibiotics used for seed treatment, the Working Party agreed that it is desirable that this practice should be continued where practicable, particularly in food crops.

Little risk to the operator is foreseen providing standard safety precautions are observed. It was noted that the use of powders may result in the accumulation of powder deposits and air borne dust, which may have further health and safety implications.

It is recommended that:

i. The practice of including marker dyes in antibiotic treatments for seeds should be continued, particularly in the case of food crops.

ii. The thorough cleaning of premises and work areas where seed treatments are being conducted should be mandatory.

iii. Operator protection and occupational health and safety procedures should be strictly followed.

iv. Antibiotic preparations for seed treatments should be labelled with appropriate warnings and packaged in suitable containers.

3 Dipping propagation material

Antibiotics used for this application will be in the form of solutions or slurries. The Working Party considered that health and safety problems would be minimal, however the disposal of spent slurry or solution was considered to be an environmental issue requiring attention.

It is recommended that:

i. Antibiotic concentrates for such applications should be dispensed in appropriate containers with suitable labelling to reduce the likelihood of skin contact, ingestion or inhalation of antibiotic.

ii. Operator protection and occupational health and safety procedures should be followed while plant material is being treated.

iii. Guidelines for the disposal of spent antibiotic solution and slurry should be drawn up to address environmental and safety issues.

4 Spray applications to growing plants

Application of antibiotics to growing plants is mostly through a spray application process which may pose occupational health risks to the worker. The Working Party also notes the use of tree injections of antibiotics for the treatment of mycoplasma diseases of tree crops.

The Working Party recognises that there is a possibility of the build up of antibiotic residues resulting from spray applications to growing plants.

The probability of microbial resistance developing was considered to be high, particularly in the glass house environment where temperature and humidity are high.

Protection of workers applying antibiotics by sprays to plants was highlighted as an important consideration.

It is recommended that:

i. Prior to the approval of spray applications, residue data studies should be conducted and appropriate Maximum Residue Limits (MRL) established for each antibiotic. Withholding periods should be established for edible produce as appropriate. The approval procedure for spray applications should take into consideration the method of application and the extent of application with a view to minimising the risk of increasing antibiotic resistance in pathogens.

ii. Operator protection and occupational health and safety procedures would be required for workers involved in spray applications.

iii. Antibiotics for spray applications should be suitably packaged and labelled with appropriate warnings.

5 Hydroponics

The use of antibiotics in the hydroponic culture of plants is recognised as a possible risk, as nutrients are recirculated and losses are replaced by a topping up process. There is a possibility of antibiotic accumulation induced by evaporative loss which could ultimately cause phytotoxicty.

The Working Party considered two major areas in which hydroponics are used:

a) ornamentals
b) food producing plants

The use of antibiotics to treat bacterial diseases in ornamental plants is an acceptable use of antibiotic products in horticulture. However, due to the high risk of antibiotic accumulation in the culture solution and plants, the use of antibiotics in the hydroponic culture of food plants could involve dangerous levels of exposure to the consumer and thus may not be a desirable application.

It is recommended that:

i. The use of antibiotics in hydroponic solutions for food producing plants in general should be prohibited, except in situations where it can be shown to be therapeutically effective without risk to public health. In these uses appropriate withdrawal periods would need to be established.

ii. Operator protection and occupational health and safety procedures should be required for all workers handling the antibiotic preparation.

iii. Guidelines are needed for the disposal of waste hydroponic water containing antibiotics.

6 Post-harvest applications

The occupational health and safety risks to workers are considered to be high for such applications, particularly because of the risk of splashes and spills involving antibiotic solutions. Antibiotic residues, when present, could be a risk to consumers.

The Working Party considers there is a high risk of resistant strains of microbial flora developing as a consequence of the dipping of fruits and nuts etc. in antibiotic solutions. This has been illustrated by the resistance shown to develop in parallel chemical dips such as fungicides. The Working Party considered that the beta-lactam, antibiotics should not be used and that if streptomycin is to be considered for this application then a MRL should be established.

It is recommended that:

Antibiotics generally should not be used for post-harvest applications. Should antibiotics be used at any time for such applications their use should be strictly controlled, and MRL's established.

7 Tissue culture and biological research

It was recognised that antibiotics are already widely used in plant tissue culture and biological research. The risks involved in this usage are minimal provided good laboratory practice is followed.

The Working Party agreed that problems could arise from resistant organisms developing in laboratories undertaking this work where good laboratory or experimental practice was not followed.

The need for care in the correct disposal of tissue culture media and other contaminated biological material containing antibiotics should also be stressed.

It is recommended that:

> A survey of antibiotic use in tissue culture should be undertaken with a view to establishing a code of good laboratory practice for their handling.

The need for antibiotics for control of microbial plant diseases

Global usage of antibiotics

Plant pathologists throughout the world have over the years investigated the potential of antibiotics for the control of plant diseases. Their major interest in such antimicrobial agents related to the need for eradicant compounds which were highly selective as well as being translocated through the plant.

Despite the extensive testing of the efficacy of a wide range of antibiotics against plant pathogens there are relatively few that are routinely applied for the control of plant diseases.

Streptomycin sprays are used against fire blight in all countries where outbreaks of the disease has been reported. It is the only effective control measure available. A streptomycin formulation is used in New Zealand for the control of bacterial canker (blast) P *syringae pv. syringae* and bacterial spot X. *campestris pv. pruni.* It is also used in the USA and New Zealand to control bacterial diseases of tomato seedlings and as a bean seed dressing.

Oxytetracyclines are used experimentally for the control of mycoplasma diseases.

In commercial tissue culture, penicillin, streptomycin and the tetracyclines as well as other antimicrobial agents are commonly used.

Antibiotics have been employed in Japan and India for the control of rice diseases. Agrimycin 100 (streptomycin and oxytetracycline formulation) has been used to control bacterial blight X. c. pv. *oryzae* of rice in India[2] while kasugamycin and blasticidin-S are used to control rice blast (P. *oryzae)*[3]

2. Thirmalachar MJ, Antibiotics in the control of plant pathogens, *Advances in Applied Microbiology*, 1968; 10: 313-337.

3. Misato T, The development of agricultural antibiotics in Japan, *Japan Pesticide Information*, 1969.

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Use of antibiotics in Australia

Antibiotics are currently widely used in experimentation and in laboratory media. However their use in the commercial situation is limited.

In Queensland streptomycin sulphate has been used by the Navy Bean Marketing Board as a seed treatment to reduce the incidence of common blight (X. *campestris pv. phaseoli*).

Antibiotics are employed by nurserymen in the horticulture industry for the treatment of plant cuttings.

Fire blight, the major disease of pears and apples in the USA, England and Europe, hasnot been recorded in Australia. Until now quarantine restrictions have been successful in preventing the entry of *E. amylovora*. With the current freeing of entry restrictions on rosaceous planting material and the possible import of apples from countries with fire blight, the probability of fire blight outbreaks has increased. In that event, plant pathologists will require an immediate effective control measure. The only control measure is the use of streptomycin sprays. There is an urgent need for the mechanisms to be put in place whereby this antibiotic or a formulation with oxytetracycline is available with adequate safeguards if such an outbreak should occur.

Antibiotics which have been used in horticulture

Blasticidin-S

Blasticidin-S inhibits the growth of many Gram positive and Gram negative bacteria. It is also active against fungi with variable effectiveness. This antibiotic is toxic to plants.

It is also toxic to mammals. Carp are killed at a concentration of 8.7 micrograms per ml in water and the LD50 for mice is 39 mg/kg. Blasticidin-S is also toxic for humans, affecting the mucous membranes, skin and lungs. The antibiotic is rapidly broken down after application to plants reducing the danger of food contamination.

Blasticidin-S is selective in its action with the minimal inhibitory concentration for *P. oryme*, being 5 to 10 micrograms per mI while the growth of *Pellicularia sasakii* was not inhibited even at 100 micrograms per ml.

The drug shows some antiviral activity with inhibition of the synthesis of tobacco mosaic virus at a concentration of only 0.05 micrograms per ml. Blasticidin-S is applied as a dust or wettable powder.

Cellocidin

Cellocidin is active against X. *campastris pv. oryme*, the cause of rice bacterial leaf blight, but is phytototoxic and is also toxic to mammals.

Chloramphenicol

Chloramphenicol has been used to protect rice plants against bacterial leaf blight caused by X. *campestris pv. oryzae* However chloramphenicol is an antibiotic, which for public health reasons, should not be used in the treatment of plant diseases.

Cycloheximide

Due to its phytotoxicity, cycloheximide is likely to be more valuable in the treatment of woody plants than herbaceous species.

Cycloheximide has been found to be effective against rust on a number of woody plants including the rust on lodgepole pine caused by *Cronartium comandrae* and in young loblolly pines caused by *Cronartium fusiforme.* It is also effective against Hypoxylon cankers in aspen. Cycloheximide is phytotoxic when used on the leaves of woody plants or herbaceous plants. It has a strong activity against powdery mildews, but because of the phytotoxicity is not a practical control measure in these diseases.

Cycloheximide may be effective against downy mildew on onion, and in shoot blight of Japanese larch caused by *Guignarida laricini.* Cycloheximide has also been found to be active against the neck rot of onions caused by *Botrytis allfl* and as a seed treatment against rust on safflower caused by *Puccinia carthami.*

It is recommended that:

> The antibiotics cycloheximide and chloramphenical, while used in several other countries, are unsuitable for use in agronomy and horticulture in Australia, and their use should not be considered.

Griseofulvin

Griseofulvin shows fungistatic action against most phytopathogenic fungi. The phytotoxicity of griseofulvin is low.

The drug has had some use against apple blossom blight which is caused by *Sclerotinia mah* and against Fusarium wilt of melon.

Kasugamycin

Kasugamycin is less phytotoxic than blasticidin-S with a wider margin between curative and phytoxtoxic concentrations.

It does not show acute or chronic toxicity to mice, rats, rabbits, dogs, monkeys or humans and no toxicity to fish. Kasugamycin is mainly applied as a dust and can also be used as a seed treatment as a wettable powder. Kasugamycin is used in Japan to control rice blast (P. *oryme).*

Oxytetracycline

Oxytetracycline has been used for the treatment of bacterial spot on peach and also for the control of *Agrobacterium tumefaciens* in pecan trees.

Oxytetracycline is also used in combination with streptomycin in the treatment of Fire blight of pears and apples.

Polyene macrolides

Polyene macrolides which act as systemic fungicides against plant diseases are usually absorbed in plant roots or the aerial parts of plants. They penetrate after seed treatment into the tissue. The polyene macrolides have limited possibilities for use in agriculture.

Polyoxins

Polyoxins are active against *Pellicularia filamentosa* the cause of rice sheath blight and are used for the control of this disease in Japan.

They are active against *Alternaria mali*, the cause of apple cork rot and *Alternaria kikuchiana*, the cause of black spot in Asian pears.

Neither of the polyoxins are toxic to mice, although polyoxin D showed a slight toxicity to fish.

Streptomycin

Streptomycin was one of the first antibiotics used in the treatment of plant diseases. The most common use of streptomycin is in the control of fire blight which is caused by *Envinia amylovora* in rosaceous plants such as pears and apples. Fire blight is a serious disease which can be effectively controlled by use of streptomycin, although it is also used in combination with oxytetracycline. If fire blight should be found in Australian apple and pear crops it is certain that its control would depend on the use of either streptomycin or streptomycin and oxytetracycline in combination.

Commercial suppliers

There are no known Australian manufacturers of antibiotic products commercially available for use in agronomy and horticulture. All products in use are imported, mostly from the United States of America.

Regulatory agency attitudes

Overseas agencies

The Working Party sought the views and practices of various regulatory agencies around the world, concerning the use of antibiotics in the fields of agronomy and horticulture, A summary of these is included below.

Agency	Comments
United Kingdom Ministry of Agriculture, Fisheries & Food (MAFF)	• MAFF is responsible for approval of pesticides in U K (Pest Regulations 986) Key issues in approval process: toxicology, residues, environmental and efficacy • U K working party concerning use of microbial pesticides (1976). Data requirements for Control of Pesticide Regulations 1986, added to cover use of bacteria fungi and viruses. Procedures now available to handle antibiotic agents if these are notified for plant disease

	control. To date the use of antibiotics which may be used in the medical field are not encouraged for use in crop protection in the UX, except on an experimental basis.
Canada, Pesticides Directorate	• Two products registered for sale, with restrictions governing conditions -'Terramycin' (oxytetracycline hydrochloride) tree injection formula (21.6%) - 'Agrimycin 17' agricultural streptomycin (17% activity), wettable powder. Use: fire blight (apples, pears), bacterial black rot (seed treatment of Brassica), bacterial blight (seed treatment of beans)
Belgium	• Antimicrobial agents are not approved for the treatment of plant diseases
United States Department of Agriculture, Agriculture Research Service	• Federal responsibility regulating and monitoring pesticides is given to the U S Environment Protection Agency (EPA) • Antibiotic usage confined to streptomycin, tetracyclines, kasugamycin • Main uses in USA; control of fire blight disease in apples and pears Streptomycins used in some States to control locally important bacterial diseases. Streptomycines, tetracyclines, and kasugamycin have all been applied to seeds of vegetable and field crops to eradicate seed-borne *Pseudomonas spp.* and *Xanthomnonas spp.* Oxytetracycline used commercially to treat plant diseases of known or suspected mycoplasma etiology • Applications include: seed treatments (solution or slurry), injections, sprays • Problems include: development of antibiotic resistance in target and non-target organisms, genetic resistance to antibiotics, pathogen resistance.
New Zealand Pesticides Board	• Usage controlled by NZ Pesticides Board. Only antibiotic registered for use in New

	Zealand is 'Agrimycin 17' (170g/kg streptomycin as the sulphate salt in the form of a wettable powder), used to control fire blight in apples and pears, diseases of stonefruit trees, and bacterial diseases in seedling tomatoes. Kasugamycin is currently being used experimentally. • Policy is not to grant any further clearances for antibiotics in horticulture or agriculture used as plant therapeutics. • A panel of experts met in 1978 to consider use of antibiotics in horticulture. Panel recommended that the use of oxytetracycline in horticulture should be discouraged; registration of streptomycin for control of bacterial diseases in horticulture to be continued but that 'efforts be made to limit the necessary use of such products'
Sweden, National Chemicals Inspectorate	• Antibiotics not approved for use against plant disease in Swedish forestry, agronomy or horticulture. No antibiotics currently listed as approved pesticides.
West Germany, Federal Ministry of Health	• Clearances for plant protection substances involves two agencies: Federal Biological Research Centre and Federal Ministry of Health. • Antibiotics employed in human and/or veterinary medicine are generally excluded from use in plant protection. Other antibiotics can only be used where there is no danger of cross-resistance developing. Special microbiological investigations are taken into account before approval is given. Only those compounds with different characteristics to those used in medicines can be considered. Selection is based on key factors such as concentration, chemical properties, stability in the environment and metabolism. • No antibiotic has yet been cleared for use as a plant protection substance.

Netherlands	• No clear policy developed on registration of antimicrobial agents as pesticides. Cautious approach taken eg. limited use with tight controls. Before approval is granted it has to be demonstrated that it is improbable that the intended agricultural use will give rise to the development of resistance in humans. • Two antibiotics are registered. Streptomycin is approved for use in flower culture, tree nurseries and for control of fire blight in apple & pear. Validamycin is used as a fungicide for potatoes.

Australia

Responsibility for approval and registration of antibiotics for use in agronomy and horticulture lies with the Commonwealth and States. However, under the national registration arrangements announced in August 1991 the Commonwealth is assuming responsibility for approval and registration of agricultural and veterinary chemicals up to 9 the point of retail sale. The National Registration Authority (NRA) commenced operations on 15 June 1993 as the body to undertake this responsibility. The complete legislation for the new arrangements has not yet been enacted and in the interim, the NRA is undertaking the assessment function with the States still responsible for the administrative step of issuing registrations in accordance with the NRAs clearance.

Clearance by the NRA involves an examination of the physical and chemical properties of a chemical product as well as an assessment of efficacy and of toxicological data to determine whether there may be any affect on public health (eg toxic residues); occupational health and safety; or the environment. There is also an assessment of possible trade implications resulting from use of products in Australia.

The NRA is assisted in the assessment process by other agencies including the Chemicals Safety Unit, the National Occupational Health and Safety Commission (Worksafe Australia), the Commonwealth Environmental Protection Agency and the States/ Territories.

Any antibiotic used in agronomy and horticulture must be approved and registered for that purpose in Australia. Such uses may not be permitted at this time in Australia.

The Working Party considers that no antibiotic should be used in agronomy or horticulture until appropriate consideration has been given to its approval and registration for that purpose in Australia.

It is recommended that:

> Current mechanisms for the clearance of antibiotics for use in veterinary applications should be used for the approval of antibiotics for use in agronomy and horticulture.

The Working Party also notes that there appears to be no mechanism for the legal prescribing of antibiotics attracting the S4 Poisons Schedule for use in agronomy and horticulture.

Schedule 4 poisons are those which are restricted in the public interest to medical, dental or veterinary prescription for supply.

The Working Party considers that none of the nominated groups are appropriately qualified to determine whether or not an antibiotic preparation should be prescribed for use in agronomy and horticulture.

Modification of State and Territory legislation could be required if another professional group e.g. plant pathologists, are to prescribe antibiotics for agronomy and horticulture.

An alternative could be to re-schedule some of the currently restricted antibiotics to enable their use without prescription.

It is recommended that:

The States and Commonwealth should develop mechanisms whereby appropriately qualified professionals can legally use antibiotics in agronomy and horticulture.

Antibiotic products, including generic products, offered specifically for the agricultural market, should be true to label claim and standard as is the case for all other agricultural and veterinary chemical products.

An appropriate body should oversee and monitor patterns of antibiotic usage in agronomy and horticulture.

Consideration be given by the Commonwealth and States regulatory authorities to ensure that Agricultural chemical usage legislation provides sufficient controls over the use of Antibiotics in agronomy and horticulture.

Guidelines concerning the disposal of solutions and products containing antibiotics are needed. These guidelines will need to address occupational health and safety and environmental issues arising from the disposal of sprays, solutions, slurries and hydroponic water containing antibiotics.

Recommendations

Specific Antibiotic Usage

In accordance with the guiding principles of antibiotic use (Page 5) Council recommends that:

1 Soil Applications

Soil applications of antibiotics for the treatment of plant diseases should not be permitted until adequate environmental studies are conducted to indicate that this is a safe and satisfactory method of administration.

2 Seed Treatments

i. The practice of including marker dyes in antibiotic treatments for seeds should be continued, particularly in the case of food crops.

ii. The thorough cleaning of premises and work areas where seed treatments are being conducted should be mandatory.

iii. Operator protection and occupational health and safety procedures should be strictly followed.

iv. Antibiotic preparations for seed treatments should be labelled with appropriate warnings and packaged in suitable containers.

3 Dipping Propagation Material

i. Antibiotic concentrates for such applications should be dispensed in appropriate containers with suitable labelling to reduce the likelihood of skin contact, ingestion, or inhalation of the antibiotic.

ii. Operator protection and occupational health and safety procedures should be followed while plant material is being treated.

iii. Guidelines for the disposal of spent antibiotic solution and slurry should be drawn up to address environmental and safety issues.

4 Spray Applications to Growing Plants

i. Prior to the approval of spray applications, residue data studies should be conducted and appropriate Maximum Residue Limits (MRL) established for each antibiotic. Withholding periods should be established for edible produce as appropriate. The approval procedure for spray applications should also take into consideration the method of application and the extent of application with a view to minimising the risk of increasing antibiotic resistance in pathogens.

ii. Operator protection and occupational health and safety procedures would be required for workers involved in spray applications.

iii. Antibiotics for spray applications should be suitably packaged and labelled with appropriate warnings.

5 Hydroponics

i. The use of antibiotics in hydroponic solutions for food producing plants in general should be prohibited except in situations where it can be shown to be therapeutically effective without risk to public health. In these uses appropriate withdrawal periods would need to be established.

ii. Operator protection and occupational health and safety procedures should be required for all workers handling the antibiotic preparation.

iii. Guidelines are needed for the disposal of waste hydroponic water containing antibiotics.

6 Post-Harvest Applications

Antibiotics generally should not be used for post-harvest applications. Should antibiotics be used at any time for such applications their use should be strictly controlled and MRLs established.

7 Tissue Culture and Biological Research

A survey of antibiotic use in tissue culture should be undertaken with a view to establishing a code of good laboratory practice for their handling.

General Recommendations

8. Council recommends that the antibiotics cycloheximide and chloramphenicol, while used in several other countries, are unsuitable for use in agronomy and horticulture in Australia, and their use should not be considered.

9. Council advocates that current mechanisms for the clearance of antibiotics for use in veterinary applications should be used for the approval of antibiotics for use in agronomy and horticulture.

10. Council endorses the advice of the Working Party on the Use of Antibiotics in Agronomy and Agriculture that the States and Commonwealth should develop mechanisms whereby appropriately qualified professionals can legally use antibiotics in agronomy and horticulture.

11. Council recommends that antibiotic products, including generic products, offered specifically for the agricultural market, should be true to label claim and standard as is the case for all other agricultural and veterinary chemical products.

12. Council recommends that an appropriate body oversee and monitor patterns of antibiotic usage in agronomy and horticulture.

13. Council recommends that consideration be given by the Commonwealth and States regulatory authorities to ensure that agriculture and veterinary chemical usage legislation provides sufficient controls over the use of antibiotics in agronomy and horticulture.

14. Council recommends that the relevant authorities promulgate guidelines concerning the disposal of solutions and products containing antibiotics. These guidelines will need to address occupational health and safety and environmental issues arising from the disposal of sprays, solutions, slurries and hydroponic water containing antibiotics.

15. Council recognises the threat posed by exotic pests, diseases and weeds and the success of the Australian Quarantine and Inspection Service in preventing the entry of these through their regulatory activities. However the increasing interest that is being shown in the use of antibiotics as protectants, particularly for the treatment of systemic infections in plants, and the potential for deleterous consequences, is of concern to Council. This concern is brought to the attention of the Australian Quarantine and Inspection Service, the States, and plant pathologists.

16. In noting that guidelines are needed for the use and disposal of solutions and products containing antibiotics, Council is concerned about the occupational health and safety and environmental issues that arise. These concerns are brought to the attention of the Commonwealth and States' Environmental Protection Agencies and the National Registration Authority for Agricultural and Veterinary Chemicals.