Human Health Considerations in the Use of Btk-Based Insecticide Foray 48B for Asian Gypsy Moth in Hamilton

Summary report prepared for the Ministry of Health, Ministry of Agriculture and Forestry, and Waikato DHB Public Health Unit.

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Auckland Regional Public Health Service

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1 Outline

This document compiles and summarises available information on the human health issues related to the use of Btk-based sprays for aerial application in moth control operations. The information comes from a number of sources, including:

- health risk assessments (HRAs) prepared for the 2 aerial spray programmes in Auckland
- HRAs prepared for moth control programmes in North America and Europe
- Research information on the biology, ecology and human health effects of the *Bacillus thuringiensis* organism
- Toxicological information on spray ingredients
- Health surveillance and research information from New Zealand and elsewhere, including preliminary analysis of records from the Painted Apple Moth Health Service in Auckland
- Reports and community feedback related to the PAM eradication programme

As with the 3 HRAs carried out for the Auckland spray programmes, ARPHS has had access to the ingredient list for Foray 48B, but not to information held by ERMA and ACVM supplied by the company as part of product registration.

We have prepared some preliminary projections of health service use and health issues that might be expected in Hamilton. However, caution is needed in interpretation because of the different population and community characteristics and spray programme differences.

2 Foray 48B and Btk-based insecticides

Biology of Btk as an insecticide

The biology, ecology and safety of *Bacillus thuringiensis*, are extensively described in a monograph by Glare and O'Callaghan from AgResearch, Lincoln[1]. In summary:

Bacillus thuringiensis var *kurstaki* is a relatively widespread soil organism which is used primarily as a biological insecticide against caterpillars of Lepidoptera (moths and butterflies). In soil it is found as a spore, with an associated protein crystal inclusion, which contains an insecticidal delta-endotoxin, the main biologically active agent. The delta-endotoxin is activated in the gut of caterpillars, and severely disrupts gut function by binding with a specific receptor, disrupting water and nutrient absorption and also allowing spore germination. The Btk endotoxin is highly specific for Lepidoptera caterpillars and has little effect on other insect genera or non-target organisms. There is no equivalent effect on mammals because of the absence of receptors and the different conditions in the mammalian gastrointestinal tract. Btk is not used as an adult insecticide.

Although the organism persists in the environment after spraying (mostly in soil and leaf litter), the main effect on target caterpillars is from direct ingestion of spores adhering to leaves. There seems to be little or no medium or long-term larvicidal protection for target plants, hence the need for repeated application.

[1] Glare TR, O'Callaghan M. *Bacillus thuringiensis* Biology, Ecology and safety. 2000. Chichester. John Wiley and sons Ltd.

General description of Foray 48B:

- biological insecticide based on *Bacillus thuringiensis kurstaki*, a soil organism with wide distribution.
- Manufacturer: Valent Biosciences (previously Abbott Laboratories), part of Sumitomo Corporation.
- F48B is mainly used in commercial and non-commercial forestry protection and urban tree protection, mostly by aerial application.

The Material Safety Data Sheet is included in Appendix B, and summary of physical, chemical and toxicological information prepared for the Ministry of Agriculture and Forestry is included in Appendix C.

Formulation

The manufacturer has not released the formulation or ingredient list publicly. It has been released to ERMA and ACVM as part of product registration, and to selected Ministry of Health, ARPHS and AerAqua Medicine staff, and the Minister and Associate Minister of Biosecurity. We understand that the Hamilton Medical Officer of Health has been briefed in general terms, but has not seen the ingredient list.

General information on Foray 48B production and ingredients is given in the 2002 Health Risk Assessment and Appendix C.

Registration

Foray 48B was registered under the Pesticides Act, and is in process for transfer to the HSNO regime under ERMA. The Agricultural Compounds and Veterinary Medicines (ACVM) group at the NZ Food Safety Authority holds current registration information. ERMA NZ considered that the new formulation did not change the hazard profile and the two formulations could be considered to be the same for the purposes of the HSNO Act.

Use in Hamilton

We understand that the Hamilton moth spray operation will use the same material and application rate as the PAM operation, i.e. undiluted liquid F48B, as manufactured, with an application rate of 5-7 litres per hectare.

Other Btk formulations in New Zealand

- DIPEL ES, suspension concentrate, Sumitomo Chemical Co Ltd/Nufarm NZ Ltd
- DIPEL DF water dispersible granules, Sumitomo Chemical Co Ltd/Nufarm NZ Ltd
- DELFIN, water dispersible granules, Mitsui & Co (NZ) Ltd
- Bactur, water dispersible granules, Grosafe Chemicals Ltd

DiPel has organic certification for horticultural use

Other Bt insecticides registered in New Zealand

- *Bt aizawai* - Xentari (Nufarm NZ Ltd)
- *Bt aizawai* with *Btk* - Agree (Elliott)
- *Bti* – Vectobac (Nufarm NZ Ltd)

Bti products are used for mosquito control, and would be expected to have similar manufacture and formulation to Btk products such as F48B.

3 Previous Health Risk Assessments and Related Reports

A number of Health Risk Assessments have been prepared on Foray 48B and Btk-based sprays both in New Zealand and elsewhere. The following reports are attached:

New Zealand Reports

- Health Risk Assessment of the 2002 Aerial Spray Eradication Programme for the Painted Apple Moth in Some Western Suburbs of Auckland: a Report to the Ministry of Agriculture and Forestry. Public Health Service, Auckland District Health Board, March 2002
- Health Risk Assessment of *Btk* spraying in Auckland's Eastern Suburbs to Eradicate White-Spotted Tussock Moth (*Orgyia thyellina*). Report to the Ministry of Health and the Ministry of Forestry, commissioned by the Northern Regional Health Authority, North Health, 4 September 1996 (ISBN 0-473-05908-8), with Addendum
- Health Risk Assessment of the Proposed 1997-1998 Control Programme for the White-Spotted Tussock Moth in the Eastern Suburbs of Auckland, Report to the Ministry of Forestry, Public Health Protection Service, Auckland Healthcare Ltd, September 1997
- Aer'aqua® Medicine Ltd (formerly Jenner Consultants Ltd). Health Surveillance following Operation Ever Green: A programme to eradicate the white-spotted tussock moth from eastern suburbs of Auckland, May 2001 (also available on the MAF website)

In summary, the main conclusions of these reports are that:

- *Btk* is not a human pathogen. Bt species have rarely been found as an opportunistic organism, mainly in wounds. Btk is not pathogenic for people with immunocompromising conditions or those on stomach acid-suppressing medication.
- The Btk delta endotoxin is not active in mammalian gut and has no other known effect on mammals
- The quality control processes in F48B manufacture and testing required by regulatory processes in NZ and the USA (where the material is made) are sufficient to prevent contamination by other organisms and Bacillus toxins, including bacillus enterotoxins, B cereus and B anthracis. Toxin production is determined by plasmids, and the culture and QA processes would prevent introduction of these plasmids.
- The inert ingredients are variously registered for use in cosmetics, pharmaceuticals and food in NZ, and their concentrations in F48B are within regulatory requirements.
- Some people may experience minor eye, nose, throat and respiratory irritation. The HRAs raised the possibility of asthma aggravation of asthma, which was considered biologically plausible, although epidemiological research and surveillance from the WSTM operation did not support this.
- The HRAs raised the possibility of atopic/allergic reactions for previously sensitised people, although MoH toxicological advice was that the exposure would be insufficient for people to become sensitised.
- Some people would find the odour of F48B unpleasant. Some people may experience nausea, headache or other symptoms if exposed to unpleasant smells. The PAM HRA raised this as a possibility, but there was no research or surveillance information on this.
- Available evidence does not support any effects during pregnancy on either mother or fetus, or effects on prematurity, miscarriage rates, birth weights, congenital abnormalities.

In particular, the evidence (epidemiological and toxicological) is against a causal link between F48B exposure and congenital hypothyroidism.

- There is no evidence that F48B exposure causes thyroid dysfunction, gastroenteritis, neurological or autoimmune effects. An immunological response has been observed following exposure in some situations, but always in the absence of clinical infection.
- Spray programmes are likely to cause considerable anxiety, particularly around exposure during pregnancy, children's exposure and fear of long term effects.
- Long term effects have not been described in published literature, and there is little reliable information. There are no known or suspected carcinogens, mutagens or teratogens in the ingredient list, and the spent culture material would not be expected to be carcinogenic, mutagenic or teratogenic.
- Risks of skin irritation from exposure to caterpillar stellae are small, except when there is massive caterpillar proliferation.
- Noise from low flying aircraft can be annoying and could produce anxiety in people with war experience. Aircraft crashes are rare, and aircraft have to meet CAA requirements.
- The HRAs included advice and recommendations on risk communication, reducing exposure and support for people with various pre-existing medical conditions. The HRAs recommended a precautionary approach for reducing exposure.

Other NZ reports attached:

- *Clarification of Issues raised in "Our Case Against Moth Spraying"*. Report to the Ministry of Forestry, Jenner Consultants Ltd. January 1998.

This report analysed the claims made on the Canadian STOP website about Btk/F48B. While there was some valid material on the website, many claims were based on invalid interpretations of research, and misquotation and distortion was common.

Risk assessments and related reports on *Btk*-based insecticides from other countries include:

- International Programme On Chemical Safety (IPCS). Environmental health criteria for *Bacillus thuringiensis*. WHO/IPCS 1999 (available from http://www.inchem.org)
- Report of Health Surveillance Activities, Aerial spraying for Asian Gypsy moth – May 200, Seattle, WA. Washington State Department of Health, July 2001 (attached – available from www.doh.wa.gov/ehp/ts/pest.htm)

Many of the references cited in the HRAs are available on the internet, and all would be available through libraries.

4 Published literature on Btk-based sprays and spray programmes since 2002 HRA

Appendix D summarises research and other literature published since the preparation of the HRA for the PAM Aerial Spray programme, plus one review (no original research) not included in the PAM report. AerAqua and ARPHS have undertaken periodic literature searches. Separate Medline/PubMed and internet searches were done by ARPHS for this report.

The more recent literature does not identify new health effects, but gives some further quantification in some cases. Most health risk assessment documents from other countries use similar source materials to the 3 Auckland HRAs.

5 Health Monitoring and Support During the 2 Spray Programmes in Auckland

Operation Evergreen

During Operation Evergreen, health enquiries were largely handled by the Public Health service and primary care services. A health surveillance programme was set up after the spray programme, and included: review and analysis of two sentinel general practices to assess whether there was any pattern of illness related to spraying, and epidemiological analysis of available health information sources, including hospital admissions, birth effects, and infectious diseases. No patterns could be found to indicate an effect at the population level. A copy of the surveillance report is attached (Health Surveillance Following Operation Evergreen, May 2001), and available from the MAF website.

Painted Apple Moth Health Service

The PAM Health Service was set up prior to the start of the PAM spray programme to provide health advice and support services. A detailed analysis of information gathered by the service is underway currently. An excerpt from a recent report is attached (Appendix E), indicating the range of enquiries and health concerns which people have contacted the PAM Health Service about.

Note: the tables in that report give numbers of people seen about each health concern, but this does not indicate the number of people with clinically significant reactions following spray exposure.

Practical Support Plans, including those for temporary relocation, are precautionary and pre-emptive in most cases. Most people have not had reactions at all because they have been prevented from any exposure to the spray. The severity table in Appendix E refers to severity of underlying condition, such as past history of specific food allergies, and not severity of reaction following spray exposure since most people in the table have had no reaction. It is not known whether these people would actually have a reaction if they were to be exposed.

Waitakere City Council

Early in 2003, the Waitakere City Council invited people to write to the Council, describing symptoms they may have had following spraying. In all, about 200 people wrote in. A summary (prepared by ARPHS) is included in Appendix F. The symptoms were mostly as described in the HRA (see below re asthma).

6 Health Effects and Concerns Related to Foray 48B/Btk

This section summarises the current understanding of each of the health topics. The information is drawn from the 3 NZ HRAs and surveillance report from Operation Evergreen, North American HRAs, WHO reports and research papers, along with knowledge gained from the 2 spray operations in Auckland. Clinical information is from the PAM Health Service.

Condition	Analysis
Asthma and respiratory conditions	Asthma is often raised as a potential risk factor. The spray is moderately acidic and is (mildly) irritant to mucosae, so an effect is plausible. The HRAs took a cautious approach and recommended people with asthma update their asthma management plans and seek advice. Epidemiological field research however, shows no detectable effect. The only epidemiological study with control group is from

	Vancouver Island, British Colombia, Canada, where asthmatic children inside and outside the spray area were assessed before, during and after a spray programme and no effect on symptoms or peak flows from spray exposure was found. The children were recruited via a hospital asthma programme, and had varying severity of symptoms, with 31% on daily inhaled steroids and a mean of 1.1 hospitalisations in the previous year (paper attached). The Operation Evergreen health surveillance programme did not find any increase in asthma presentations to GPs or hospital after spray days. The paper by Petrie et al in Auckland found no significant increase in asthma symptoms among asthmatics. Diagnosis of past or current asthma used by the PAM Health Service is based on: • self reported statement of doctor's diagnosis • anyone on asthma preventive medication • confirmation from person's own GP • specialist diagnosis via letter • or PAM health service GP diagnosis after clinical assessment When the PAM Health Service receives a report of possible asthma aggravation they actively follow up for medical diagnosis with GP assessments and referral to specialists if there is any possibility. No asthma aggravation events have been confirmed by the respiratory specialists. Among the people with asthma justification for a practical support plan there is one person with asthma triggered by eating some maize products who had asthma aggravated on the first two sprays days, and has since been in relocation for spray day itself with no further exacerbations. One person with asthma as a justification for a Practical Support Plan and a relevant allergy history had asthma symptoms after inadvertent outdoor exposure, but these settled without medical intervention. This person had been in relocation and returned home on the understanding that spraying was complete. However the following day a second spray was delivered to a localised area by helicopter while the person was outside. Symptoms settled with normal medication and without medical intervention. One person had a history of asthma with very impaired peak flows and symptoms on spray days, who was referred to a specialist, had sequential assessments with lung function tests over several sprays with no change found. A few people with self-managed mild asthma have experienced irritant type short term symptoms while outdoors during spraying, eg in cars, and have since avoided the area completely on spray days. All such events settled spontaneously on the day with self management.

	Severe, unstable asthmatics have been advised to avoid exposure, as a precaution, rather than being based on research evidence or history of reaction to the spray. 192 of the 629 people with practical support plans had asthma or asthma + eczema as the reason for support. These support plans were based on taking precaution for these people, rather than effects from exposure. As part of the Waitakere City Council's request for people to write in about symptoms, six people with possible new adult onset asthma were identified. These people were offered independent assessment, and 3 people took up the offer. They were seen by a doctor nominated by the Asthma Society, and were assessed as not having new adult onset asthma. Spray can cause throat or large airway irritation, which is generally mild and short lived. The spray droplet size is calibrated for ~120 µm, far larger than respirable size of <10µm. Approximately 0.17% of the volume of spray is <14 µm in size in bench tests done for MAF/AgriQual. Droplet sizes may change after spraying depending mainly on humidity (evaporation would be expected to reduce droplet size to some degree, although one of the "inerts" is a humectant). The make-up of the smaller particles may differ from the larger droplets, which are more likely to consist of solids and materials clumped by the sticking agent. Small particles would include water, spores (which are about 2-5 µm) and soluble components. *Hyperventilation syndrome* A number of people have been diagnosed with hyperventilation, which can present with symptoms similar to asthma. This diagnosis is based on written opinion from a specialist or respiratory physiotherapist after appropriate clinical assessments.
Congenital hypothyroidism	A possible cluster was identified by a critic of the WSTM programme following discussions with a local pharmacist. Using the Ministry of Health's guidelines for cluster investigation, ARPHS reviewed information from the National Testing Centre. 8 cases of congenital hypothyroidism were identified among children born in the spray area between 1993 and 2001. One of these children had a genetic condition, which could not have been caused by spray exposure, and so was excluded. A baby of a woman who had been in the spray zone frequently during the spray programme was also included, although her exposure was more than a year prior to pregnancy. The cluster started over a year before the WSTM operation in 1997 (3 cases prior to spraying) and only 1 case was exposed during the thyroid developmental period. The expected pattern of sub-types of congenital hypothyroidism was evident, rather than an increase in one type which might have been expected in a cluster with a single cause. A link with spray is not considered plausible.
Thyroid disease	The possibility of thyroid effects was raised by a WSTM programme critic, but without any indication of a cluster existing.

	This was assessed by inviting people who had recently developed thyroid conditions to contact the PHU. Twenty on people were interviewed and information obtained from their GPs, but no unusual pattern could be detected, and no evidence of a cluster could be found, using the MoH Guideline for cluster investigation.
Infection	No evidence of *Btk* being a pathogen. Some *Bt* subspecies/serovars have been found in opportunistic infections in unusual circumstances, usually involving wounds (often as a co-infection) – e.g. land mine explosion, accidential injection (mixed culture, with known pathogenic organism), eye injury of high pressure spray in spray worker. These are not comparable to exposure during aerial spray operations. Studies of agricultural workers using Bt-based spray have not found evidence of infection, although persistence or temporary colonisation in bowel, nose and conjunctiva has been found. Bt species can be found transiently on mucosal surfaces (eye, nose, bowel), but with no evidence of invasive disease. Infection in immunocompromised people has not been shown in research literature. In the PAM programme, the 30 people listed as avoiding the spray because they are medically immuno-compromised include those with SLE, Sjogrens Syndrome, a range of cancers, HIV, poorly controlled diabetes, hepatitis C, cytomegalovirus, fibromyalgia, inflammatory bowel disease, epilepsy, polyarthritis, dermatomyositis, Hashimoto's thyroiditis (predating the spray), and rheumatoid arthritis. The disease alone is often not the complete explanation for their relocation. Situational factors may also contribute. None has had an infection related to the spraying. None is in an avoidance plan because they have had exacerbation of their illness. There are published reports of Bt species being found in cultures obtained from normally sterile sites, not necessarily in association with spray programmes. These have generally been in mixed cultures, and the microbiologists and clinicians involved have concluded that the Bt is a contaminant rather than a pathogen, based on clinical and laboratory evidence. Antibody response has been found in people with large exposure to Bt products (e.g. spray workers), as could occur to any antigen, but consistently in the absence of infection.
Gastrointestinal: nausea, diarrhoea, wind	Feeding studies of Btk products show no increase in GI symptoms including diarrhoea. Btk can persist in the bowel, but do not appear to cause gastroenteritis. Nausea and intestinal gas have been reported by people calling the PAM Health Service and in information requested by the Waitakere City Council and spray opponents. Enterotoxins. Some Bacillus species, including Bt, can produce

	enterotoxins. Foray 48B production and QA methods are aimed at excluding enterotoxins. See attached summary of research information prepared for MAF (Appendix G).
Irritation (eyes, skin, mucosa)	Spray is mildly irritant probably because of pH and organic breakdown products of culture broth, or being hypertonic. Usually transient (few seconds). The MSDS identifies transient skin and eye irritation, but no corrosive or toxic effect.
Allergy and related	Spent broth material was identified as a potential trigger for an allergic response in people already sensitised and highly allergic. PAM Health Service criteria for accepting diagnosis of past or current allergy are: • self reported statement of doctor's diagnosis or • confirmation from person's own GP or • specialist diagnosis via letter or • PAM health service GP diagnosis after clinical assessment • NOT self diagnosis or by naturopath Among the 55 people listed as having a food or non food product allergy as a justification for relocation or warning call, a few have had a possible reaction to the product. (a) A young person with a previously undiagnosed food allergy developed symptomatic illness during the early sprays. A specialist physician (allergist) concluded that the reaction may have been to peanuts (which is not an ingredient of the spray) and the spray was coincidental. (b) a person had urticaria during spraying and it was possibly related although specialist immunologist did not confirm this (c) a person with multiple food allergies had aggravation of general symptoms over the months of spraying. There are a small number of other people (approximately 10) with symptoms that have a temporal association to possible Foray 48B exposure but a causative relationship cannot be confirmed or excluded until patch testing is implemented. A suitable patch test antigen is being prepared. Other people with known severe allergies to broth components have been assisted to avoid exposure, so the true rate of serious reactions is not known.
Headaches, other constitutional symptoms	Headache has been reported relatively commonly. Several people with “multiple chemical sensitivity/chronic fatigue”-spectrum have contacted the PAM Health Service re change of symptoms. Assessments done by immunologists and rheumatologists have not identified a link with spray exposure (e.g. symptoms deteriorated without exposure, no temporal pattern).
Situational stress	This is common. Spray programmes are disruptive – to home, work, school, transport, walking etc. 70/629 people with support

	plans have had these because of situational stress.
Pregnancy Miscarriages	No increase or unusual pattern of birth defects found following the WSTM spray programme. There are no known teratogens or mutagens in the spray ingredients. No effect on gestation or birth weight could be found from the WSTM health surveillance. Concern about miscarriage is often raised. Miscarriage is common, and would be expected to occur commonly during the spray programme. There is no evidence that miscarriages increase following spray programmes from international or NZ sources.
Endocrine disruption	This concern is commonly raised, but without evidence being presented. The inert ingredients are not known endocrine disrupters.

7 Other information and commentary sources

Schools: Two surveys have been done. The NZEI conducted a survey of members, and found a proportion had experienced irritant symptoms, and that children had been off school during spray days. In the second survey, done for ARPHS, 25 school principals or secretaries were contacted post spray. This survey found that the spraying had not caused significant disruption to school functioning, although were some student and staff absences.

Report by Hana Blackmore: see separate review

Report by Meriel Watts: see separate review

The Health Advisory Group (HAG) has been established to advise MAF on a health surveillance and research programme. Highest priority has been given to analysis of PAM Health service information and doing research on social impact of the PAM programme.

8 Projections of health service utilisation for Hamilton, based on PAM Health Service information

Population

Appendix H shows a comparison between the population structures of the spray zones in Hamilton with those of the initial PAM spray zone and the Operation Evergreen spray zone in the Eastern suburbs of Auckland. The Hamilton population is intermediate between the others, with the PAM spray zone population being younger, and the Evergreen population being on average older. The Hamilton area has a higher proportion of Maori than the two zones in Auckland, but lower proportion of Pacific people. The PAM HRA only covered the initial spray programme, and population figures were not revised for the expanded programme.

NZDep Index of socio-economic status was included in the PAM HRA, but not the Operation Evergreen HRA. NZDep was charted for each Census Area Unit in the PAM HRA report, and not reported as an average or detailed table given.

Projections of the scope of health and support service utilisation are based on information from the PAM Health Service. Appendix E includes tables from a recent PAM Health Service monthly report showing

(1) the number of people who have contacted the service;

(2) the number of people who have had practical support plans developed with the PAM Health Service (which range from phone calls informing people of day of spraying, to breakfast venues outside the spray area, to social supports, to relocation during and after spray days), and;

(3) assessed medical severity of risk, which includes a small number of those who have had reactions, but is mainly those considered to be at risk because of pre-existing conditions.

Extrapolation to the Hamilton situation has a number of major caveats.

- The denominator population in West Auckland varies significantly, in part because of the change of spray programme size, but also because of the large numbers of people going in and out of the spray zone (e.g. commuters to Auckland City).
- The spray areas have different population characteristics - socio-demographics, community characteristics etc – which could affect people's response to the spray programme and access to health and support services.
- The spray programmes are very different. The PAM programme has involved nearly 2 years of spraying, initially on a limited area, but then expanding to a larger urban area, with spraying at approximately 3-4 week intervals. The Hamilton operation is shorter (approximately 2 months), but with more frequent spraying (weekly).

The West Auckland spray zone population is approximately 160,000, and approximate figures of possible health support service demand have been calculated compared with the 30,600 population in the Hamilton spray zone. The resident population in the WSTM spray area was approximately 80,000. Projections (with a 95% confidence interval) in the following tables might be expected for a spray programme equivalent to the PAM programme.

Activity	**PAM Health Service**	**Hamilton Projection (95% CI)**
Practical Support Plans	633	117 (96-138)
Medical Assessment	1265	237 (207-267)
Specialist assessment	196	36 (24-48)

Primary medical justification for a practical support plan:			
Condition	***PAM HS***	***Rate/1000 total population***	***Hamilton Projection (95% CI)***
Allergy – prior history of allergy to relevant food or preservative	55	0.34	10 (4-16)
Asthma – prior history of any severity	192	1.2	36 (24-48)
Skin condition including eczema, but not concomitant asthma	34	0.19	6 (1-10)
Lower or upper respiratory but not asthma	45	0.28	8 (3-14)
General symptoms including irritant type at spray time	122	0.76	23 (13-32)
CFS or chemical sensitivities	64	0.4	12 (5-19)
Medical illness with immune suppression	30	0.19	6 (1-10)
Situational stress or pregnancy	87	0.54	16 (8-24)

Description of health events

Medical severity among those who receive Practical Support Plans, based on proportional extrapolation from the PAM Health Service. These figures do not represent the number of people who have had a reaction, rather the severity of the identified risk condition.

Severity	Description	% of PAM HS PSPs	Rate per 1000 population	Hamilton Projection
Highest severity	Eg anaphylaxis to relevant foods, multiple severe food allergies in child, very severe asthma	7%	0.27	8 (3-14)
Significant medical	Eg definite or unstable asthma, eczema or upper respiratory with significant severity	29%	1.1	33 (22-44)
Other medical	Eg short-term irritant symptoms or mild respiratory, mild skin problems, headaches,	29%	1.1	33 (22-44)
Precautionary because of previous medical diagnosis	Eg lower respiratory: alveolitis, emphysema, bronchiectasis; lichen planus, immune disorders, rheumatoid arthritis, SLE, past/current history of Chronic Fatigue Syndrome, and major medical problems not known to be at specific risk of aggravation by spray exposure	19%	0.74	22 (13-31)
Mainly psychosocial justification	Eg pregnancy or situational stress as justification, general concerns about spraying	16%	0.62	19 (10-27)

9 Appendices

A. Abbreviations

ACVM	Agricultural Compounds and Veterinary Medicines Group of the NZ Food Safety Authority, which administers pesticide regulations.
F48B	Foray 48B, the Btk-based insecticide used in the 3 aerial spray operations in New Zealand to date.
PAM HS	Painted Apple Moth Health Service, operated by Aer'aqua Medicine Ltd
PSP	Practical Support Plans, developed for individuals with concerns about or reactions to F48B spray. Range from phone calls on spray mornings, assistance with closing windows, social supports for transport, to providing alternative day-time venue outside the spray area, to relocation in motels during and after spray day
WSTM	White Spotted Tussock Moth. Operation Evergreen was the programme to eradicate the WSTM in the eastern suburbs of Auckland in 1996/97. An extension was proposed, but not needed in 1998.

B. Material Safety Data Sheet for Foray 48B (US Version)

C. Summary of Foray 48B Information from MAF

Report prepared for MAF by Aer'Aqua Medicine

Foray 48 B

The following tables and references provide the most up to date information available on the properties, components and effects of Foray 48B.

The Ministry of Agriculture and Forestry has commissioned the preparation of this information in order to provide the public with a definitive source of scientific data on the spray used in the Painted Apple Moth eradication programme.

Foray 48B: Statement of Use and Ingredients from the Manufacturer

Foray 48B is formulated with an understanding of its potential for widespread use. To ensure minimal risk to the environment and health of exposed individuals, careful consideration is given to minimizing the quantity of inert ingredients added and ensuring that the inerts used have been thoroughly tested and pose minimal risk. The majority of the formulation, more than half, is made up of water. In addition to residual fermentation growth material and food carbohydrate, preservatives and anti-evaporants are added to maintain formulation stability and ensure it can be adequately dispersed in order to maximize effectiveness at the lowest possible use rate. The inerts used in preserving the formulation are all approved for use in pesticides by the US Environmental Protection Agency (EPA). None appear on the US EPA's list 1,inerts of toxicological concern, or list 2, inerts considered potentially toxic and a high priority for further testing. All except for one of the inerts used are approved by the US Food and Drug Administration (FDA) as food additives in the U.S. and appear in the US Federal Register as general food additives or as preservatives Generally Recognized as Safe (GRAS). Similarly, most of these components are also listed in the Canada Food and Drugs Act as Class II preservatives approved for food use.

FORAY 48B: PHYSICAL AND CHEMICAL CHARACTERISTICS

Characteristic	**Data**	Reference
Name: (Trade Name):	Foray® (Foray 48B)	Valent BioSciences, Inc., 2000
Active ingredient:	2.1% - *Bacillus thuringiensis* subsp. *kurstaki,* Lepidopteran Active toxin	Valent BioSciences, Inc., 2000
Inert ingredients:	97.9% "Foray's inert ingredients, which include various carriers, suspension agents, and stabilizers are classified by the Environmental Protection Agency (EPA) as inert ingredients of minimal toxicological concern to non-target organisms and the environment (EPA's List 4B and 3)" "All inert ingredients in Foray formulations are included in 40 CFR 180.1001. This list has been designed by the EPA as 'exempt from the requirements of a residue tolerance on raw agricultural commodities" VBC verifies that none of its Btk formulations contain toxic inert ingredients, such as benzene, xylene, or formaldehyde"	Valent BioSciences, Inc., 2000 Valent BioSciences, Inc., 2001
EPA Reg. No.	73049-46	Valent BioSciences, Inc., 2000
EPA Est. No.	33762-IA-001	Valent BioSciences, Inc., 2000
Appearance	Tan to light coloured liquid	Valent BioSciences, Inc., 2001
Potency	10 600 IU/mg or 48 BIU/gal (12.7 BIL/L)	Valent BioSciences, Inc., 2001
Specific gravity	1.14 ±0.05	Valent BioSciences, Inc., 2001
Weight	9.51 ±0.42 lbs/gal (1.14 ±0.05 kg/L)	Valent BioSciences, Inc., 2001
PH	4.7 ±0.3	Valent BioSciences, Inc., 2001
Dispersibility	Disperses readily into water	Valent BioSciences, Inc., 2001
Viscosity @ 25ºC Viscosity @ 5ºC	150 – 800 cP (centipoise) 150 – 1000 cP	Valent BioSciences, Inc., 2001

* BIU – Billion International Units

ENVIRONMENTAL CHARACTERISTICS

Characteristic	Environment/ Studied Organism	Data reported	Reference
Concentration	Air during spray campaign / Btk	Occupational exposure results ranged from 0 to 5600 CFU/m^3 of sampled air General public exposure results ranged from 0 to 1600 CFU/m^3 of sampled air Spray workers experienced mean exposures from 3000 to 5.9 x 10^6 CFU/m^3 of sampled air	Siegel, 2001 [Elliott et al., 1988] Siegel, 2001 [Noble et al., 1992]

* CFU – Colony Forming Units

TOXICOLOGICAL CHARACTERISTICS

Characteristic	Data	Reference
δ-endotoxins and their effect on the target organisms	Bt produces a parasporal inclusion body during sporulation usually referred to as a crystal. This crystal is made of proteins. A large number of related crystal proteins are known and more than one protein type can co-assemble in one crystal. These crystalised proteins need to be solubilized in a caterpillar's gut in order to be activated as toxins Caterpillars need to ingest the Btk crystal in order to be killed by it. Upon ingestion, the crystals solubilise in the highly alkaline environment of the host insect midgut. Producing the fragments . (δ-endotoxins) that actually exerts the toxic effect in the larvae. The toxins binds to specific receptors present on the gut membranes of the caterpillar's epithelial midgut cells. Finally, the membrane-bound δ-endotoxin induces the formation of pores (holes) in the midgut epithelial cell membrane. As a result of pore formation the cells die, eventually leading to death of the larvae.	Joung & Cote, 2000
alkali solubilization is a laboratory generated process. Similar processes never occur in the environment nor in mammals (mammalian "gut" is acidic)	Alkali-soluble fraction from the parasporal crystal delta-endotoxin of B.thuringiensis var. kurstaki showed no in vitro or in vivo toxicity, and no haemolytic activity.	Thomas & Ellar, 1983

HUMAN HEALTH OUTCOMES FROM EXPOSURE TO Btk

Human Health Outcomes For Oral Exposure

Dose/ Level of exposure [duration]	Studied (exposed) group	Effects observed	Reference
Human studies:			
1 gram of formulated Btk (3 x 10^9 viable spores Btk) per gram) in capsules [daily for 5 days]	18 volunteers	All of the subjects remained well during the course of the experiment. The physical examinations (a detailed history and records of height, weight, temperature, blood pressure, respiratory rate, pulse rate immediately after exercise and 30 and 60 seconds thereafter, evaluations of the genitourinary, the gastrointestinal, the cardiorespiratory, and the nervous systems) before, at the end of the 5th day test period and in 4 or 5 weeks later, did not show any adverse effects. All laboratory findings (including routine urinalysis, with qualitative and quantitative (when indicated) urobilinogen determination, complete blood count, sedimentation rate, blood urea nitrogen, glucose, bilirubin, and thymol turbidity tests) were negative.	Fisher R & L. Rosner, 1959
Animal studies:			
Doses up to 24 grams of formulated Btk (2 x 10^{12} viable spores of Btk per kilogram of body weight)	Groups of 10 rats	No fatalities occurred nor were there any outward symptoms of toxicity. Gross and histological examination of tissues revealed no differences from the tissues of control animals.	Fisher R & L. Rosner, 1959
10^{12} spores of Btk [daily for 5 months] (cumulative dose: 1.5 x 10^{14} CFU)	Mixed Rambouillet /Merino sheep, male	No signs of illness were reported	Siegel, 2001 [Hadley et al., 1987]
5000 mg of Foray 48B (commercial product containing B.t.k spores)/kg body weight	Rats	No oral toxicity has been demonstrated	Valent BioSciences, Inc., 2001

10^8 Btk CFU	Rats	A dose did not cause any toxic or pathogenic effects	Valent BioSciences, Inc., 2001
1.4 x 10^7 CFU of Btk (washed cells, 24-h laboratory grown culture) per animal [acute exposure]	Female Sprague-Dawley rats	No mortality reported	WHO, 1999 [Shadduck, 1980]

Human Health Outcomes For Inhalation Risk

Dose/ Level of exposure [duration]	Studied (exposed) group	Effects observed	Reference
Human studies:			
100 mg. of formulated Btk (3 x 10^9 viable spores per gram) [daily for 5 days]	5 volunteers	All of the subjects remained well during the course of the experiment. The physical examinations (a detailed history and records of height, weight, temperature, blood pressure, respiratory rate, pulse rate immediately after exercise and 30 and 60 seconds thereafter, and vital capacity, evaluations of the genitourinary, the gastrointestinal, the cardiorespiratory, and the nervous systems as well as x-ray examinations) before, at the end of the 5th day test period and in 4 or 5 weeks later, did not show any adverse effects. All laboratory findings (including routine urinalysis, with qualitative and quantitative (when indicated) urobilinogen determination, complete blood count, sedimentation rate, blood urea nitrogen, glucose, bilirubin, and thymol turbidity tests) were negative	Fisher R & L. Rosner, 1959
3.0 x 10^3 to 5.9 x 10^6 Btk spores/ m^3 sampled air. (maximal exposure values: 5.4 x 10^6 to 7.2 x 10^7 organisms)	Spray operators General population	During the spray programme, some workers experienced chapped lips, dry skin, eye irritation, and nasal drip and stuffiness, but no serious health problems reported. The symptoms were transient and frequently occurred during the beginning of a spray run and when Btk spray concentrations were increased. No significant differences were found with respect to gender or smoking status. Nearly all the workers exposed to higher concentrations for several shifts (5 to 20) were culture-positive for Bt; majority of the workers remained culture-positive for 14 to 30 days. Of those who were culture positive, eight workers reverted to a culture-negative status during a project or within 30 days of project completion. Examining the records of 3500 hospital emergency room admissions, 1140 family practice patients, over 400 bacterial cultures from 10 hospitals showed no evidence for community illness or infections attributed to Btk	WHO, 1999 [Noble et al., 1992]
Commercial product: Foray 48B	Workers	No overt symptoms of toxicity have been reported by individuals during the use of this or other Btk containing products	Valent BioSciences, Inc., 2001

Aerial spraying of *Bacillus thuringiensis* var. *kurstaki*	Residents of Oregon, Lane County (1985 year - about 80000 people; 1986 year – about 40000 people)	Of 95 subcultures of *Bacillus* species obtained from patient cultures (18 different body sites or fluids), 55 were identified as B.t – positive cultures and 52 (95%) of the B.t. isolates were assessed to be probable contaminants and not the cause of clinical illness. For three patients, B.t. could neither be ruled in nor out as a pathogen. Each of these 3 B.t. positive patients had pre-existing medical problems: an elderly immunocompromised person with underlying lung disease (B.t. cultured from blood); a mentally retarded person with a spastic hemiplegia and seizure disorder secondary to bilateral subdural hemorrhages suffered in a motor vehicle accident 10 years before (B.t. cultured from gallbladder contents); an intravenous drug user (B.t. cultured from an antecubital abscess. Telephone surveillance did not reveal any pattern of predominance of any one symptom complex or of involvement of any single organ system. Symptoms were those common to any community (e.g., nausea, headache/ dysphoria, rash, angioedema)	Green et al., 1990
Aerial applications of Foray 48B (containing Bacillus *thuringiensis* strain HD1) over 12 203 ha in Victoria, British Columbia, Canada	Residents of Victoria region, (approx. 75,420 people)	The study identified bacteria with genetic patterns consistent with those of *Bacillus thuringiensis* subsp. *kurstaki* HD1 in 9102 of 10659 (85.4%) isolates obtained from the air samples, 13 of 440 (2.9%) isolates obtained from the water samples, and 131 of 171 (76.6%) isolates from the nasal swab samples. The analysis data suggest that bacteria with genetic patterns consistent with those of *Bacillus thuringiensis* subsp. *kurstaki* HD1 were present both in the environment and in the human population of Victoria prior to aerial applications of Foray 48B. The presence of *Bacillus thuringiensis* subsp. *Kurstaki* HD1-like bacteria in human nasal passages increased significantly after the application of Foray 48B, both inside and outside the spray zone. Despite this exposure, the human health surveillance program failed to detect any correlation between the aerial application of *Bacillus thuringiensis* subsp. *kurstaki* HD1 and short-term health effects in the general adult population, in emergency room visits, or in aggravation of asthma symptoms in children. While *Bacillus thuringiensis* subsp. *Kurstaki* HD1-like bacteria were detected in the nares of the human population, the available evidence suggests that its presence was transient, as clinical symptoms of active nasal-pharyngeal infection were not reported. Overall, the human health surveillance program did not detect any short-term change in health status that could be associated with the aerial application of Foray 48B.	Valadares de Amorim et al., 2001 [the Capital Health Region Office, 1999-2001]
Aerial and Ground spraying application of Btk (1996/1997)	A urban population of over 80000, of whom approx. 5000 were subject to longer duration spraying	"A comprehensive health surveillance programme has examined health outcomes for a period of two years afterwards –using individual, local, regional and national health information. This included investigating residents' self-reported health concerns, consultation rates at sentinel family doctors, and a review of health data sources to establish birth outcomes and other events of community concern. No adverse health patterns were found, once patterns were examined at a population level. The frequency of occurrence of the following was no different from natural variation: early births; small babies; birth defects; consultation rates with sentinel family doctors for asthma, other respiratory problems, headaches, skin or eye symptoms, and autoimmune disorders. There was a pattern of self-reports by residents for irritant respiratory, skin and eye symptoms at the time of spraying and a level of expressed concern about potential future disease. A voluntary register of residents exposed to the longer duration programme	MAF, 2001

		was well supported and has been placed in the National Archives (Auckland Regional Office) to assist with any future health studies."	

Aerial spraying of Foray 48B containing *B. thuringiensis* subspecies *kurstaki* HD1 as the active ingredient	86 children with asthma	There were no differences in asthma symptom scores between subjects and controls, neither before nor after the spray; nor were there significant changes in Peak Expiratory Flow Rates for subjects after the spray period.	Pearce, M. 2002
Animal studies:			
10 grams of formulated Btk sample (9 x 10^9 viable spores per gram) [4 times over a period of 6 days; duration of each exposure- 15 min]	10 mice	During repeated exposures of the mice to inhalation of the test material, no untoward reaction was observed in either group. Observations of animals' well-being throughout the test period showed no departure from normal in either group, as was demonstrated also by normal weight gains for both groups. Gross pathology findings were negative.	Fisher R & L. Rosner, 1959
Approx. 10^8 CFU of Btk /L of air [4 hours]	Rats	The low pathogenic potential was demonstrated	Valent BioSciences, Inc., 2001
Approx. 7 mg of Foray/L air [4 hours]	Rats	No toxic effects were observed	Valent BioSciences, Inc., 2001

Human Health Outcomes For Skin Exposure

Dose/ Level of exposure [duration]	**Studied (exposed) group**	**Effects observed**	**Reference**
Human studies:			
Bacillus thuringiensis var. *kurstaki* (commercial product)	Spray project worker	After a splash of Btk mixture to face and eyes, a worker developed dermatitis, severe itching (pruritis), burning, swelling and erythema, with conjunctival injection. B.t. was cultured from his conjunctiva. After the treatment of eyelid and skin with steroid cream, symptoms disappeared.	Green et al., 1990
Animal studies:			
Formulated Btk (approximately 9 x 10^9 viable spores per gram)	20 white male guinea pigs	"Administration of a commercial Btk product by injection or by application to abraded skin caused a slight erythema and edema, indicative of local irritation. There was no reaction from its application on intact skin. There was no evidence of any allergenic response by any route of administration."	Fisher R & L. Rosner, 1959
2.5 gram of Foray/ kg of body weight [single dose exposure]	Rats	No toxic effects were observed	Valent BioSciences, Inc., 2001
Foray 48B [4 hours]	Rabbits	Very mild, temporary dermal irritation was seen. All signs of irritation cleared in all animals within 2 days after application	Valent BioSciences, Inc., 2001

Human Health Outcomes For Ocular Exposure

Dose/ Level of exposure [duration]	Studied (exposed) group	Effects observed	Reference
Human studies:			
Dipel [Btk product]	A farmer	Corneal ulcer developed after an accidental splash of the product in the face. To relieve irritation in his eye, the farmer applied a corticosteroid ointment for 7 days before the ulcer developed. The ulcer healed following injection of gentamicin and cephazolin. In this case it is difficult to evaluate what actually caused the ulcer formation for the following reasons: - corticosteroids may have contributed to the formation of the ulcer (one of the side effects of corticosteroids is delayed flattening and movement of the corneal epithelium, which is essential to wound healing); - the possibility that Bt may have simply persisted in the farmer's eye following exposure and that a different micro-organism was responsible for the ulcer.	Siegel, 2001 [Samples & Buettner, 1983]
Animal studies:			
10^9 CFU of Btk	Rabbits	Foray was moderately irritating in a rabbit eye irritation test. No apparent redness or other ocular findings remained 7 days after the application of reported dose of Btk to the eye.	Valent BioSciences, Inc., 2001

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D. Summary of reports published since the 2002 Auckland HRA

Reference	Abstract/Summary and Comment
Pearce M, Habbick B, Williams J, Eastman M, Newman M. The effects of aerial spraying with Bacillus thuringiensis Kurstaki on children with asthma. Can J Public Health. 2002 Jan-Feb;93(1):21-5.	Abstract: OBJECTIVE: To determine if aerially spraying a biological pesticide was associated with an increase in the symptoms or change in the Peak Expiratory Flow Rate of children with asthma. METHODS: A pre/post matched pairs cohort design was used. Children living in the spray zone were matched with children outside of the spray zone. Peak Expiratory Flow Rates, asthma symptoms and non-asthma symptoms were recorded in diaries. RESULTS: There were no differences in asthma symptom scores between subjects and controls, neither before nor after the spray; nor were there significant changes in Peak Expiratory Flow Rates for subjects after the spray period. CONCLUSIONS: No evidence of adverse effects from the use of the biological pesticide was found. We believe that this is the first paper to address the issue of whether or not aerial spraying with Btk has a harmful effect on children with asthma. Comment: This prospective cohort study found no affect on children with pre-existing asthma from Foray 48B spray exposure. It is the largest study of this type to date. The PAM HRA was more cautious in its recommendation for people with asthma as it seemed biologically plausible that the irritant effect of the spray could affect people with pre-existing asthma. (more summary re severity of the asthma in the study population)
Petrie K, Thomas M, Broadbent E. Symptom complaints following aerial spraying with biological insecticide Foray 48B. N Z Med J. 2003 Mar 14;116(1170):U354.	Abstract: AIM: To investigate the effect of aerial Bacillus thuringiensis (Foray 48B) spraying on self-reported symptom complaints, health perceptions, and visits to healthcare providers. METHODS: Two hundred and ninety two residents within the Ministry of Agriculture and Forestry (MAF) West Auckland spray zone were recruited by a door-to-door survey of homes within the most intensively sprayed area ten weeks prior to the first aerial spraying. Participants completed a symptom checklist and a questionnaire measuring health perceptions. Three months after the start of spraying, 181 (62%) of the original participants responded to a similar postal questionnaire. Symptom reports, health perceptions and visits to healthcare providers were compared between the baseline and the follow-up questionnaire. Rates of symptom complaints in respondents with previously diagnosed asthma, hay fever, or other allergies were compared to those in respondents without these prior health conditions. RESULTS: Symptom complaints increased significantly following the aerial spraying, in particular: sleep problems, dizziness, difficulty concentrating, irritated throat, itchy nose, diarrhoea, stomach discomfort, and gas discomfort. Analyses showed a significant increase in symptoms in those participants with a previous history of hay fever. While overall self-ratings of health decreased following the spraying, most residents saw their health as unaffected by the spray programme, and there was no significant increase in visits to general practitioners or alternative healthcare providers. CONCLUSIONS: Aerial spraying with Foray 48B is associated with some adverse health consequences in terms of significant increases in upper airway, gastrointestinal, and neuropsychiatric symptoms, as well as a reduction in overall perception of health in the exposed population. Comment: This paper produced useful information on the level of symptoms in the community. Irritant symptoms (irritated throat, itchy eyes) were described in the PAM HRA. The gastrointestinal symptoms were not expected (feeding

	studies of Btk-containing preparations have not found GI symptoms, even at high exposure levels), and the significance of the other symptoms would need further assessment because of the methodological limitations of the study. Interestingly, no significant difference was found in respiratory symptoms, consistent with other research. The main limitation with the study is the absence of a non-exposed control group for contemporaneous comparison. The two surveys were carried out nearly 3 months apart, and several of the symptoms included in the study have seasonal variation. A repeat study with control group has been proposed by the PAM HAG as part of the health surveillance programme.
Siegel JP. The mammalian safety of Bacillus thuringiensis-based insecticides. J Invertebr Pathol. 2001 Jan;77(1):13-21.	Abstract: The United States Environmental Protection Agency between the years 1961 and 1995 registered 177 products containing viable Bacillus thuringiensis (Bt). Numerous laboratory studies have demonstrated that Bt and Bt products are noninfectious and are toxic to mammals only at a dose > or =10(8) colony forming units (cfu) per mouse (a human equivalent based on the weight of >10(11) cfu). In contrast, as few as three vegetative cells of Bacillus anthracis can kill mice (a human equivalent of >10(3) cfu). There are only two literature reports of Bt infection in man between the year 1997 and the present, and all infected individuals had experienced either extensive burns or a blast injury, which predisposed them to infection. Two epidemiology studies conducted during large-scale aerial Bt serovar kurstaki spray campaigns reported no increased incidence of illness. Some recent papers have expressed concern about the production of Bacillus cereus enterotoxins by Bt isolates. Laboratory studies found no evidence of illness in rats and sheep fed Bt products, nor have epidemiology studies found increased incidence of diarrhea during Bt aerial spray campaigns. Increases in human antibody levels following exposure to Bt products have been reported but there was no increased incidence in asthma or other illness. Based on laboratory studies and field experience, Bt insecticides have an excellent safety record. Comment: This is one of several reviews of research literature on Bt product safety. The information identified in this paper was included in the Auckland HRAs from other sources.
Smith RA, Barry JW. Environmental persistence of Bacillus thuringiensis spores following aerial application. J Invertebr Pathol. 1998 May;71(3):263-7.	Abstract: Soil and leaf populations of Bacillus thuringiensis (Bt) were monitored following aerial application of commercial Bt formulations at the rate of 72 billion international units per acre per year during a 5-year period. Data from soil sample spore counts suggested that Bt spores persisted in Wasatch forest soils for up to 2 years but they did not proliferate. Bt isolates were recovered from leaf samples 12 months post application from sprayed, previously sprayed and from nonsprayed areas. The frequency and diversity of Bt isolates recovered from leaves was independent of sample area spray history. In accordance with U.S. Forest Service criteria, aerial application of Bt during a 5-year period resulted in the eradication of gypsy moth (Lymantria dispar, L) from the Wasatch Front region of the Wasatch Mountain Range, Utah.
van Netten C, et al The measurement of volatile	The full report behind this paper is referenced in the PAM HRA – reference 85. The researchers were attempting to identify a volatile component in F48B to use as a marker for assessing spray drift,

constituents in Foray 48B, an insecticide prepared from Bacillus thuringiensis var. kurstaki. Sci Total Environ. 2000 Dec 18;263(1-3):155-60.	since Btk was widespread in the environment. Field samples from an aircraft flyover did not detect any volatile markers. The samples from the vapour in the F48B containers was analysed and contained a range of 38 volatile organic compounds. Comment: Only 2 of the 38 identified compounds were in the ingredient list for F48B, the others presumably were from the spent broth material, or may be produced during sample processing (which includes heating the sample to 280^{o}C). At least ten (mostly siloxanes) may be related to plastics used for storage or sampling. Only 2 (acetic acid and benzoic acid) are on the EPA list 4B. The list included butylated hydroxytoluene (BHT), and trimethyl phospine, but neither are among the listed ingredients. The analysis was not able to detect 5 of the seven listed ingredients nor did it quantify concentrations.
Dewhurst IC. Toxicological assessment of biological pesticides. Toxicol Lett. 2001 Mar 31;120(1-3):67-72. Pesticides Safety Directorate, Mallard House, Kings Pool, YO1 7PX, York, UK. i.c.dewhurst@psd.maff.gsi.gov.uk	Abstract: The majority of pesticides are based on synthetic chemicals. Regulatory assessments are performed by comparing the findings in a range of routine toxicity studies, designed for testing chemicals, with estimates of exposures. Recently there have been significant moves towards developing natural/biological alternatives. Biological pesticides (those based on viable organisms) present the regulator with a different set of challenges to those raised by most chemical pesticides. The concerns associated with biological pesticides can vary greatly from one organism to another, requiring an almost case-by-case approach. The known toxicity of certain bio-molecules and the pathogenicity of certain organisms underlines the need for a risk assessment of biological pesticides. The main aspects of a health risk assessment are characterisation of the organism, infectivity, pathogenicity, sensitisation and production of toxic secondary metabolites. Obtaining information or data on these areas is not always easy as there are no widely accepted test schemes or protocols for organisms, though guidelines are being developed for the European Commission (EC). Predicting exposure following pesticidal use of an organism is made more complex if it multiplies or secretes toxic metabolites. Reliable data on effects (lack of) associated with naturally occurring (background) exposures can sometimes provide considerable reassurance. This paper describes the background to the proposed EC scheme, which has much in common with current UK practices, and presents three examples of biological pesticides which have been assessed under the existing UK procedures. Comment: The paper discusses assessment frameworks for biological pesticides, and only briefly describes the approval of a bacillus-species based product for use on crops, based on biological research and epidemiology.
Assessment of Environmental and Human Health Effects from Proposed Application of Foray 48B in Waskesiu, Prince Albert National Park of Canada: draft for public consultation, Prepared for: Parks Canada Western Region	This is a (draft) risk assessment prepared for a spray programme in Alberta, Canada. It does not contain new health information.

Office, Calgary, AB. Prepared by: AXYS Environmental Consulting Ltd. Calgary, AB, in Association with: Cantox Environmental Ltd. North/South Consultants Inc. March 2003	
GB Jensen, P. Larsen,et al Bacillus thuringiensis in fecal samples from Greenhouse Workers after Exposure to B.thuringiensis-Based Pesticides Applied and Environmental Microbiology, 2002; 68(10 October): 4900-4905	Abstract: In a study of occupational exposure to *Bacillus thuringiensis*, 20 exposed greenhouse workers were examined for *Bacillus cereus*-like bacteria in fecal samples and on biomonitoring filters. Bacteria with the following characteristics were isolated from eight individuals: intracellular crystalline inclusions characteristic of *B. thuringiensis*, genes for and production of *B. cereus* enterotoxins, and positivity for *cry11* as determined by PCR. DNA fingerprints of the fecal isolates were identical to those of strains isolated from the commercial products used. Work processes (i.e., spraying) correlated with the presence of *B. thuringiensis* in the fecal samples (102 to 103 CFU/g of feces). However, no gastrointestinal symptoms correlated with the presence of *B. thuringiensis* in the fecal samples. Comment: This research is consistent with that reported in the PAM HRA, that Bt species can colonise human intestine without producing gastrointestinal symptoms. This report concerns the use of 2 Bti products; occupational exposure would have been higher than in the PAM spray area. Bacillus enterotoxins were detected in this study. F48B manufacturing quality assurance programme includes testing for enterotoxins and exotoxins (see p 23 of PAM HRA). EPA regulations include criteria for acceptance. ERMA/ACVM should have details on regulatory requirements for NZ.

E. Excerpt from PAM Health Service Reports to MAF and Ministry of Health

The report contains the numbers and estimated rates of:

- people who have called and/or been assessed by the PAM Health Service
- reasons for people having Practical Support Plans; and
- Severity of the reasons for the Plans

These figures do not represent the number of people who have had actual reactions to the spray – this is far fewer (see table in Section 6).

The information has been supplied by the PAM Health Service, Aer'aqua Medical Services.

Numbers of people assessed by the PAM Health Service

The following table summaries the information contained in Appendix A "Health Service Activity Report.

A denominator of 160,000 resident population is assumed for the entire programme although any particular spray will involve some varying proportion of the overall population.

Cumulative number of new people calling the service with health concerns (from 30 Dec 01 to 28 Sept 03)	3,385	21 per thousand
Cumulative number of new people with Practical Support Plans (from 30 Dec 01 to 28 Sept 03)	633	3.9 per thousand
Cumulative number of residents assessments by a doctor in conjunction with the PAM support service (from 30 Dec 01 to 28 Sept 03)	1,265	7.9 per thousand
Cumulative number of specialist medical assessments to 28 Sept 03	196	1.2 per thousand

A practical support plan includes anything from a warning call to inform of spray schedule to relocation in a motel

Primary medical justification for a practical support plan:

Allergy – prior history of allergy to relevant food or preservative	55	0.34 per thousand
Asthma – prior history of any severity	192	1.2 per thousand
Skin condition including eczema, but not concomitant asthma	34	0.19 per thousand
Lower or upper respiratory but not asthma	45	0.28 per thousand
General symptoms including irritant type at spray time	122	0.76 per thousand
CFS or chemical sensitivities	64	0.4 per thousand
Medical illness with immune suppression	30	0.19 per thousand
Situational stress or pregnancy	87	0.54 per thousand

Medical justification for the Practical Support Plans

The "justification" listed is the one overriding reason for each person to receive a PSP, not the presence or otherwise of each condition or occurrence of a reaction

Note: *Epidemiological patterns, among the residents with self-reported concerns, is part of Health Service Monitoring and reported separately*

Patterns of justification cumulative to date

Food allergy relevant to spray constituents, including asthma from food and multiple food allergies in young children where there is a likelihood of further manifestations of allergy developing.	38
Allergy relevant to non-food constituents of the spray, includes specific medically recognised allergy to preservatives etc.	17
Skin condition, pre-existing skin condition where precautions to prevent direct spray contact are in place, includes eczema.	34
Asthma, medical history of asthma of any severity and spray exposure precautions are in place. This is not a measure of people with aggravation of asthma due to spraying.	161
Asthma and eczema, Both asthma and eczema are medical problems and spray exposure precautions are in place.	31
Lower respiratory other than asthma, where there is a medical diagnosis of such conditions as bronchiectasis, congenital lung conditions, emphysema, alveolitis and spray exposure precautions are in place.	24
Upper respiratory, where there is a medical diagnosis of such pre-existing conditions as chronic sinusitis, tonsillitis, rhinitis, and spray exposure precautions are in place.	21
Irritant symptoms post spray including confirmed, suspected or clearly not spray related, includes sore or puffy eyes, sneezing, cough, sore throat, nausea, headaches, gastric upset, itching, transient rash, also odour problems.	122
Chronic fatigue syndrome or multiple chemical sensitivities, including self declared ME, history of spray poisonings, fibromyalgia not associated with underlying connective tissue disorder, sensitive to sprays.	64
Immune suppression of medical significance including leukaemia, HIV, post chemotherapy, SLE, fibromyalgia secondary to underlying connective tissue disorder, autoimmune disease.	30
Situational stress associated with contemporaneous medical illness or underlying psychological morbidity relevant to spraying for example war trauma, anxiety disorder.	70
Pregnancy and baby where there is no other medical problem and spray exposure precautions are in place.	17
Total*	629

** This figure represents the total number of people who have had any category of justification at any point where they have a Practical Support Plan.*

Some people may have consecutive justifications. The total is slightly greater than the number of people who have ever had a Practical Support Plan (626).

Description of health events

Medical severity among those who have ever received Practical Support Services

All householders who have ever had a Practical Support Plan have been assigned one of the following categories of severity:

Highest severity	Eg anaphylaxis to relevant foods, multiple severe food allergies in child, very severe asthma	**7%**	**0.27 per thousand**
Significant medical	Eg definite or unstable asthma, eczema or upper respiratory with significant severity	**29%**	**1.1 per thousand**
Other medical	Eg short-term irritant symptoms or mild respiratory, mild skin problems, headaches,	**29%**	**1.1 per thousand**
Precautionary because of previous medical diagnosis	Eg lower respiratory: alveolitis, emphysema, bronchiectasis; lichen planus, immune disorders, rheumatoid arthritis, SLE, past/current history of Chronic Fatigue Syndrome, and major medical problems not known to be at specific risk of aggravation by spray exposure	**19%**	**0.74 per thousand**
Mainly psychosocial justification	Eg pregnancy or situational stress as justification, general concerns about spraying	**16%**	**0.62 per thousand**

HEALTH SERVICE MEDICAL UPDATE

	Totals	Jan-02	Feb-02	Mar-02	Apr-02	May-02	Jun-02	Jul-02	Aug-02	Sep-02	Oct-02	Nov-02	Dec-02	Jan-03	Feb-03	Mar-03	Apr-03	May-03	Jun-03	Jul-03
Individuals with new medical condition		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Individuals with pre-existing condition aggravated by spray		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Medical problems assessed																				
No of new residents with health concerns		206	121	81	45	42	33	42	27	126	504	492	403	189	423	290	174	92	23	27
Cumulative no. of residents with health concerns	**3,340**																			
No of new PSPs		15	14	35	16	18	0	23	3	7	74	82	110	30	68	58	61	5	3	4
Cumulative no. of PSPs	**626**																			
No assessed by GP – PAM support service		59	29	27	38	23	13	5	9	27	70	127	184	90	101	184	56	106	51	34
Cumulative no. assessed by GP	**1,233**																			

F. Summary of Letters on Health Related Concerns to Waitakere City Council, 2003.

Summary prepared by ARPHS for Waitakere City Council

The 200 or so letters concern the symptoms from approximately 235 people. In the table below, the first number relates to the main or first symptom reported in a letter, and the number in brackets to the number of other people reporting these symptoms. Numbers are approximate, as some people had several symptoms but the table is generally indicative of the scope of symptoms:

Irritant symptoms	
• Nose, throat, sinuses	51 (19)
• Eyes and eyelids	31 (8)
• Mouth	1 (1)
• Nose bleeds	3 (4)
Headache and migraine	28 (14)
Respiratory	
• Asthma exacerbation (2 with evacuation recommendation from chest specialist)	29 (4)
• Possible new asthma (no previous asthma)	3 (1)
• Cough	15 (6)
• 'Flu-like symptoms	5 (1)
• Short of breath, other breathing symptoms	10 (2)
• Other	1 (1)
Gastrointestinal	
• Nausea (some with vomiting)	6 (5)
• Diarrhoea	3 (2)
• Abdominal ache/pain	(1)
• Bloating	(1)
• Mouth ulcers	1 (1)
Dermatological (skin conditions)	
• Rash	15 (7)
• Rash from specific spray component (fish)	1
• Eczema (mostly exacerbation)	6
• Exacerbation of other skin condition	1
Allergy-related	
• Reaction with previous history of allergy	1 (2)
• Positive allergy tests (including fish)	2

• Hayfever-type symptoms, sneezing	3
Pregnancy	
• Miscarriage	3
Constitutional symptoms	
• Fatigue	9 (3)
• ME/Chemical sensitivity/chronic fatigue	4 (1)
• Faintness/dizziness	2 (2)
• Anxiety	Several
• Sleep disturbance	Several
Other symptoms	
Joint ache	(1)
Taste in mouth	1 (1)
Voice loss	1

Ten writers described effects on pets.

The writers are mainly reporting irritant symptoms (eye, nose, throat and skin irritation and rashes, cough, airways irritation). These symptoms are largely as outlined in the PAM health risk assessment report (HRA), and the previous HRA for the White Spotted Tussock Moth spray programme in 1996/7.

Exacerbation of existing asthma was one of the commonest symptoms, but for three people the primary complaint was of new asthma symptoms. Further assessment would be needed to differentiate between new asthma (which has long term health implications) and short term irritant effects.

The PAM HRA was cautious about asthma, indicating that asthmatics could be affected, although the HRA didn't expect severe exacerbation to be common. For instance, there was no increase in hospital or GP presentations for asthma during the 1996/7 White Spotted Tussock Moth spray programme in Auckland City, and Canadian research found no increase in asthma among children compared with those outside the spray zone.

The PAM Health Service has been assisting a number of people with severe allergies (producing skin or anaphylactic reactions), several of whom wrote to the Council detailing their symptoms. These have primarily been people with known allergies. Others with allergies have been relocated as a precaution (rather than because of symptoms), and so avoided (or reduced) their risk of reaction.

Three women reported miscarriages. Unfortunately, miscarriage is very common in the general population (around a quarter of pregnancies are affected), and the information to hand from North America and the Tussock Moth programme does not indicate a link between Foray 48B or other Bt insecticides and effects on pregnancy.

Many writers had found the spray programme disruptive for daily activities, especially those who left the area (several writers were on the PAM Health Service temporary relocation scheme). They also reported disruption to schooling, work, business, transport around the area, and recreational activities etc. Some also described additional expenses, mainly for health services.

G. Is Commercial Btk Product Associated With Gastro-Enteritis In Humans?

Bacillus thuringiensis, like other bacteria, produces a number of different toxins (WHO, 1999; Glare 2000; Siegel, 2001). These toxins may include enterotoxins (diarrhoeal type) 'similar to those produced by *B. cereus'* (Glare, 2000). However, as a condition for registration for pesticide use on food in the USA, *Bt* active ingredients must be tested to show the absence of metabolites that are considered hazardous to humans and the environment (Laird, 1990; EPA RED, 1998; WHO, 1999; Glare 2000).

Although, the *Bacillus thuringiensis* species is very close to *B. cereus* in its cultural and biochemical characters, it differs by the ability of *Bt* to produce parasporal crystalline inclusions known for their insecticidal activity. *Bt* isolates can be easily and quickly identified by H-serotyping, which is not a routine laboratory test (WHO, 1999; de Barjac H).

Pathogenic *B. cereus* is characterised by the presence of specific plasmids, which are not present in *Btk*. These plasmids are the primary determinants of the toxins, which cause the specific pathogenicity of *B. cereus*.

Evidence to date suggests that food poisoning associated with *Bt* exposure would be unlikely to occur. Siegel offers an explanation why *Bt* isolates have not been associated with food borne illness in man. He suggested that either the isolates used in commercially produced *Bt* did not produce enterotoxins under commercial fermentation conditions, or that enterotoxins were absent from the final product because they were degraded by the end of the fermentation run. His argument was supported by the numerous laboratory safety studies that were used to register Bt insecticides (Siegel, 2001).

Foray 48B uses a long established specific strain of *Btk* known to produce a relatively low amount (if any) of enterotoxin. There is no valid evidence to link commercial *Btk* product with any episodes of diarrhoea.

References

de Barjac H, Identification of H-serotypes of Bacillus thuringiensis, chapter 3, pp 37-43)

EPA (1998) *Bacillus thuringiensis*. Registration Eligibility Decision (RED) EPA738-R-98-004, March 1998

Laird M. et al, Safety of Microbial Insecticides, CRC Press, Inc. Boca Raton, Florida, 1990

Siegel J.P (2001) The Mammalian Safety of *Bacillus thuringiensis* - Based Insecticides, Journal of Invertebrate Pathology, 77, pp 13 –21

Travis R. Glare and M. O'Callaghan *Bacillus thuringiensis*: Biology, Ecology and Safety, John Wiley & Sons, Ltd., 2000, p.350

WHO, Environmental Health Criteria 217 *Bacillus thuringiensis*. World Health Organization, Geneva, 1999

H. Demographic Comparisons between Auckland and Hamilton Spray Zones

Age Structure

	Hamilton		***PAM, initial zone***			***Eastern Suburbs***	
	Numbers	%	Numbers	%		Numbers	%
Age group					Age group		
0-4	2298	7.5	1236	9.0	0-4	5889	7.3
5-9	2145	7.0	1161	8.4	5-14	10299	12.8
10-14	2322	7.6	984	7.2			
15-19	2676	8.7	957	7.0	15-64	52836	65.6
20-29	5409	17.7	2484	18.1			
30-39	4683	15.3	2376	17.3			
40-49	4026	13.1	1725	12.5			
50-59	3006	9.8	1251	9.1			
60-69	1884	6.1	855	6.2	65-74	6342	7.9
70-79	1461	4.8	564	4.1	75-84	4020	5.0
80+	735	2.4	153	1.1	85+	1209	1.5
Total	30645	100	13746	100		80595	100
Source	*WDHB (Census 2001)*		*PAM HRA (Census 96)*		*WSTM HRA (Census 91)*		

Ethnicity profile of 3 spray zones

Ethnicity	Hamilton (%)	PAM 1 (West Auckland) (%)	Evergreen (Eastern suburbs) (%)
Pakeha/European	70	56.8	75.2
Maori	21	13.7	8.8
Pacific	4	15.9	8.9
Asian	5	8.1	
Other or not specified	1	7.4	7.1

10 Annexes

These Annexes include reports produced in New Zealand, technical materials and a small number of papers requested by reviewers. Other papers referred to in the HRAs and other reports are readily available through libraries (particularly university libraries) and internet services. Major health risk assessment reports from North America are available on the internet, and are referred to in the NZ Health Risk Assessments.

1 *Health Risk Assessment of the 2002 Aerial Spray Eradication Programme for the Painted Apple Moth in Some Western Suburbs of Auckland: a Report to the Ministry of Agriculture and Forestry. Public Health Service, Auckland District Health Board, March 2002*

2 *Health Surveillance following Operation Ever Green: A programme to eradicate the white-spotted tussock moth from eastern suburbs of Auckland, May 2001, Aer'aqua® Medicine Ltd (formerly Jenner Consultants Ltd). (also available on the MAF website)*

3 *Health Risk Assessment of the Proposed 1997-1998 Control Programme for the White-Spotted Tussock Moth in the Eastern Suburbs of Auckland, Report to the Ministry of Forestry, Public Health Protection Service, Auckland Healthcare Ltd, September 1997*

4 *Health Risk Assessment of* Btk *spraying in Auckland's Eastern Suburbs to Eradicate White-Spotted Tussock Moth (*Orgyia thyellina*). Report to the Ministry of Health and the Ministry of Forestry, commissioned by the Northern Regional Health Authority, North Health, 4 September 1996 (ISBN 0-473-05908-8), with Addendum*

5 *Clarification of issues raised in "Our Case Against moth Spraying" – 1998. (needs clearance from MAF as not previously published)*

6 *Report of Health Surveillance Activities, Aerial Spraying for Asian Gypsy Moth – May 2000, Seattle, WA. Washington State Department fo Health, Environmental Health Programs – (www.doh.wa.gov/ehp/pest.htm accessed October 2003)*

7 *Human Health Surveillance During the Aerial Spraying for Control of North American Gypsy Moth on Southern Vancouver Island, British Columbia, 1999*

8 *Pearce M, Habbick B, Williams J, Eastman M, Newman M. The effects of aerial spraying with Bacillus thuringiensis Kurstaki on children with asthma. Can J Public Health. 2002 Jan-Feb;93(1):21-5.*