

**BenchMark Toxicology Services**  
Empowering Through Knowledge

**Report to the Hamilton City Council on the Potential  
Risks of a Spraying programme Using Foray 48B.**

Review and Evaluation of Health Risk Assessment and Health Surveillance Reports  
and Concerns Expressed by Community Groups

Prepared for

**Hamilton City Council**

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## **Report to Hamilton Council on the potential health risks of a spraying programme using Foray 48B**

Hamilton City Council has requested BenchMark Toxicology Services Pty Ltd for an independent review of the potential health risk of a spraying programme using Foray 48B to control an infestation of Gypsy Moth based on the following brief.

MAF is to undertake an aerial spraying programme in the Hamilton area with Foray 48B (*Bacillus thuringiensis*) to eradicate Asian Gypsy Moth. There is considerable opposition from residents to the spraying programme and Hamilton City Council has resolved:

1. "Council accepts that there is sufficient evidence of potential harmful health effects, on a significant portion of Hamilton residents, of aerial spraying to warrant the Council conducting an urgent, independent, professional assessment of the health risks of the proposal, and,
2. Council request the Chief Executive to engage (with cost recovery to be sought from MAF) an appropriate independent professional person to conduct a preliminary and urgent health risk assessment into the proposed MAF aerial spraying programme, and provide advice to Council as to:
  - a. Means of abatement of the risk that could be undertaken, and"
  - b. Whether "removal" of the aerial spraying programme is necessary to reduce the health risk to a level sufficient to ensure the Council's duty of care under the Health Act 1956 is fulfilled"

The brief comprises:

- A. Review all current documentation including the Health Risk Assessments and give your interpretation of the level and nature, as you understand it, of the public health risks.
- B. Review the current health precautions being undertaken and give your opinion on the need for additional or a different approach
- C. Undertake this in a way, which gives effect to the above Council resolution.

Hamilton City Council or the relevant authority in New Zealand will provide all documents to be reviewed and no additional literature search is required.

Based on the information provided, BenchMark Toxicology will provide Hamilton Council with a comprehensive report outlining:

- Toxicological properties and hazards of Foray 48B
- Likely health risks and the conditions under which they may manifest
- An evaluation of the risk assessment and the risk management proposed by MAF to reduce or eliminate any risks
- An evaluation of the criticisms of the health risk assessments (if appropriate documents are available)
- Recommendation on whether additional risk management measures are required
- Recommendation to Hamilton City Council on whether or not a health nuisance exists which is "injurious or offensive to health" within the context of the interpretation provided by you.

### **Overview**

A list of the documents that have been provided to BenchMark Toxicology Services is provided in Appendix A, Part I. In addition, a number of other

documents, including press releases, that were provided are listed in Appendix A, Part B. These have been perused, but not analysed in depth and have not been referenced in the document.

All documents listed in Appendix A Part I were summarised. Some were additionally reviewed in depth, others less so, particularly those dealing in areas outside the expertise of BenchMark Toxicology Services (eg, medical issues, sovereign issues). The latter were summarised and comments provided where appropriate only.

The detailed summaries and assessment are attached at Appendix B, together with additional references used in the evaluation.

Appendix C outlines calculations and assumptions made to estimate exposure from aerial spraying of Foray 48B, taking three different approaches.

The following sections address each of the areas on which BenchMark Toxicology Services was requested to report. Overall BenchMark Toxicology Services considers that the spraying of Foray 48B insecticide does not pose an unacceptable risk to the community. Hence the following considerations, include recommendations to Hamilton Council on risk management options should the spraying go ahead.

### **Toxicological properties and hazards of Foray 48B**

The toxicological data base on *bacillus thuringiensis subsp. Kurstaki* or the formulation of Foray 48B is not extensive. The data provided (MAF, 1995) included single and short-term human and animal studies on Foray 48B. Additional data were identified in other documents listed in Appendix A.

There were no chronic, reproductive, genotoxic or carcinogenicity studies.

The pesticide has been used widely for several decades and reports of adverse reactions in the literature are scant.

Foray 48B is unscheduled. The Foray 48B product did not trigger any of the thresholds for classification or scheduling under the Toxic Substances Act in New Zealand.

The results of experimental data in animals and human and of environmental studies in humans suggest that irritation of the skin, mucous membranes and eyes is the most important hazardous property of Foray 48B. Foray 48B does not appear to be a skin sensitiser.

Sedation was reported the first day after dermal application in rats at 2500 mg/kg body weight. The significance of this is unclear and it does not appear to occur in humans nor after oral dosing in rats.

Although Foray 38B formulation contains viable spores of *bacillus thuringiensis subsp. Kurstaki* and they have been shown to colonise human tissues, the bacterium is not pathogenic to humans. Infection, therefore is not considered to be a hazardous characteristic of Foray 48B.

Given its hazard profile, it would be expected that irritation might trigger responses in asthmatics. Studies on this sensitive subgroup exposed to aerial spraying indicate that asthmatics are not affected at the concentrations generated during the spraying.

The risk assessments conducted in conjunction with spraying programmes in Auckland (Jenner Consultants, 1996; ARPHS, 2003), additionally identified that some of the inert components and components of the spent broth may trigger allergic reaction at sufficiently high doses in people who might have developed hypersensitivities to the chemicals from food and cosmetics.

This sensitive subgroup was identified in the Auckland programme and comprised 0.34 per 1000 people of which 0.27 per 1000 were described as having the highest severity. For the population in the area to be sprayed in Hamilton (30,600), these equate to 10 and 8 individuals respectively.

The amounts of the inert components in the formulation were not quantified, although they should be known. With respect to the spent culture broth, its composition is unlikely to have been characterised. The consideration by ARPMS that it might contain food allergenic components is sensible and precautionary, but likely speculative.

The threshold for hypersensitivity is expected to be lower than for adverse reactions such as irritation. Notwithstanding, oral tolerable intakes have been established for the chemicals that were identified by the community groups as having these properties (JECFA, 1996, see Appendix B for reference). In addition, ARPMS (2003) concludes that exposure in the spray to the inert ingredient in the Foray 48B formulation that was considered to have these properties was estimated to be less than the tolerable intake.

WHO (1994) defines a Tolerable Intake as an estimate of the intake of a substance that over a lifetime is without appreciable health risk. It is expressed in mg/kg/day (examples are the Acceptable Daily Intake, Tolerable Daily Intake, Tolerable Weekly Intake, Reference Dose, Reference Concentration, Virtually Safe Dose and Risk [acceptable] Specific Dose). In essence a Tolerable Intake is an estimate of a safe dose for the particular substance.

### **Likely health risks and the conditions under which they may manifest**

Irritation is the major hazard presented by Foray 48B. It has been reported at relatively high concentrations in both animal and human studies. In human studies it has been reported after accidental spillage on the face and in workers spraying Foray 48B on the ground. The former exposure situation is not relevant to spraying programmes in general, except in cases of accidental spillage. The latter occurred at air concentrations of Foray 48B which were about three orders of magnitude higher than the levels to which the community in a spray area is likely to be exposed.

BenchMark Toxicology Services considers that it is highly unlikely that the components of sprayed Foray 48B, individually or together, will cause irritation.

The threshold for hypersensitivity is likely to be lower than for other systemic effects or effects such as irritation. BenchMark Toxicology services has not reviewed the individual inert components in Foray 48B. However, estimates of exposure suggest daily doses of the ingredients of Foray 48B in sub microgram range per unit body weight. These are well below oral Tolerable Intakes for the substances identified by the community, which are in the milligram range, and likely to fall within the Tolerable Intakes for inhalation and dermal exposure.

BenchMark Toxicology Services considers that it is very unlikely that the components of sprayed Foray 48B, individually or together, will trigger hypersensitivity reactions at the amounts to which sensitive people are likely to be exposed.

### **An evaluation of the risk assessment and the risk management proposed by MAF to reduce or eliminate any risks**

The assessments undertaken in conjunction with the spraying programmes in Auckland were semi-quantitative health risk assessments. They did not attempt to quantify a dose or a concentration of Foray 48B to which residents in the areas being sprayed would be exposed or had been exposed.

The assessments were comprehensive and thorough. Despite the criticisms levelled at them, it is the view of BenchMark Toxicology that they were sufficiently robust and of a conservative nature, taking a precautionary rather than pragmatic approach. For example, attempting to identify subgroups in the population who might be at increased risk of adverse effects because of pre-existing conditions, eg people with asthma, hypersensitivity to additives in foods and cosmetics or pre-existing upper respiratory tract ailments.

The qualitative conclusion that the doses to which residents might be exposed would be unlikely to cause any adverse effects was justified and is supported by the low exposure doses estimated by BenchMark Toxicology Services (see Appendix C).

Notwithstanding, appropriate processes were put in place to cater for possible eventuality that an adverse reaction might occur, including identifying and relocating people at risk.

In follow up studies during and after the spraying programme services were made available to the community to report any effects from or concerns they had about the spraying programme. Although a number of health effects and concerns were reported, analysis of the information gathered overall did not reveal any causal link between Foray 48B and the effects reported.

The spraying however, was associated with instances of situational stress (0.54 per 1000) and some of the actions taken to prevent people from being sprayed might have contributed to this.

Concern about future manifestations of adverse effects because of exposure to Foray 48B spray was the most reported concern. A voluntary register has been established for people to note their concerns for future reference.

#### **An evaluation of the criticisms of the health risk assessments (if appropriate documents are available)**

The risk assessment was severely criticised by community groups and their representatives. Principally because of the poor data base for Foray 48B, the inability of Government to release commercial in confidence information, inexact estimates of exposure, no certainty in the outcome and the influence of personal values or biases of the risk assessors. The critics, however, were unwilling or unable to offer alternatives on how to do the risk assessment better.

Health risk assessment is not a precise science. It relies on the available information, with default or reasoned assumptions to fill the gaps, established methodologies and expert judgement in the decision-making. Transparency and accountability in the use of information, judgement and other processes in the assessment is extremely important. In addition to clear and comprehensive documentation, consultation and stakeholder participation, the use of agreed approaches to risk assessment (for example, enHealth 2002<sup>1</sup>) helps achieve transparency and accountability. Criteria on how to establish causality are part of the process.

In the end decisions will include an assessment of the strength and weight of the evidence, which by its very nature requires the exercise of judgement. Inevitably, this will reflect the values of the individuals concerned. This does not necessarily reflect a lack of objectivity and is not sufficient argument by itself to dismiss a risk assessment.

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<sup>1</sup> EnHealth Council (2002). [Environmental Health Risk Assessment - Guidelines for assessing human health risks from environmental hazards](#). (Accessed 29 October 2003)

Moreover, it needs to be emphasised that the outcomes of risk assessment are not the only factor considered in the overall decision-making. It is one of a number of tools used to inform the process.

The criticism is consistent with an adversarial position, focusing on the areas of greatest uncertainty. Generally the scientific consideration was limited to discussions of the hazardous properties of the formulation and its components, the imprecise nature of the exposure assessment and attempts to discredit established and agreed scientific principles and methodologies by raising the spectre of the unknown or unknowable (multiple chemical interactions, multiple chemical sensitivities, obscure scientific theories).

These approaches, though challenging and demanding of accountability, are non-discriminating and do not add value to the process of informing the stakeholders about the possible risks of chemical use. Instead they tend to divide and entrench a sense of fear and anxiety in the community that can be much more damaging than any low probability risks of what can be considered trivial reactions (for example in the case of Foray 48B, mild, transient and reversible irritation).

BenchMark Toxicology Services is not suggesting that the concerns that people had or the health effects that they have reported during the spraying programmes in Auckland are imaginary or insignificant. On the contrary, there is a reasonable probability that some of the reactions were in some way connected to the aerial spraying. All health effects, whether related to the spraying or not, are important and need to be addressed.

What cannot be demonstrated by established scientific principles is that it is the Foray 48B or its components that have caused the effects – would these effects have been reported if a control substance (eg, water) had been sprayed instead of Foray 48B? Answering this question is particularly problematic in this case, because Foray 48B has such a low toxicological profile and the application rate is low.

The critics of the health risk assessment and medical surveillance do not accept this outcome.

Critics argued that not being able to prove causality scientifically does not mean that the effects are not there. Benchmark Toxicology agrees that the absence of proof does not necessarily mean absence of adverse effects.

There are many limitations in experimental animal studies and epidemiological, environmental and other human studies that might prevent identifying a particular cause and effect relationship. These need to be identified and acknowledged in the risk assessment process as part of the transparency and accountability.

Further they argued that the absence of scientific evidence for causality is not proof the adverse health effects were not caused by the spray. The expectation for proof that a substance does not cause adverse health effects is unreasonable. It is logically, hence scientifically, impossible to prove a negative proposition. There is no limit, to the number of experiments with negative results that would need to be performed to exclude the possibility that the next experiment would not have shown an effect. Similarly, the expectation of certainty of outcome, either from science in general or the risk assessment process in particular, is unreasonable.

The agreed scientific approach is to assess the weight and strength of both positive and negative evidence and reach a consensus by expert judgement.

What is relevant in the criticism by the PAM Community Coalition and important from their community based study is the feeling in the community (not an

exclusive list) of being disenfranchised, not kept informed or having inconsistencies/contradictions in the information, being concerned for their children being sprayed at schools and their education, not being involved in decision making, being patronised, having their lives disrupted, incurring financial loss and an apparent inability or unwillingness of government or authorities to listen to and act on their concerns.

These can readily be addressed and it is recommended that the recommendations by ESR (2003) be implemented as well as a comprehensive environmental monitoring programme to be able to assess exposure more reliably.

**Recommendation on whether additional risk management measures are required**

The measures put in place during the Auckland spraying programme are generally considered appropriate. Advice to stay indoors during the spraying is still valid, provided traffic in and out of dwellings is kept to a minimum.

Risk communication and public involvement needs to be reviewed and strengthened. The community needs to be kept fully informed in the most efficient way to empower their lives.

A monitoring programme should be put in place to assess exposure more reliably similar to the one used in Canada where viable spores were measured. The method should be validated as a reliable index of Foray 48B exposure by establishing a relationship between the spore concentration in the products used and the concentration of the ingredients. The measure of viable spores in the environment during the spraying can then be related to the concentration of Foray and its ingredients.

Processes should be put in place to ensure timely responses to community demands for social and health professional support.

In cases where, there is serious concerns that a reaction might have been triggered by the Foray 48B, additional investigations to define exposure further should be instituted. Cultures of mucous membrane swabs may be used, although they do not appear to be a good measure to quantify exposure. Time and resources did not permit BenchMark Toxicology Services to undertake additional research to recommend additional methods for monitoring exposure.

**Recommendation to Hamilton City Council on whether or not a health nuisance exists which is "injurious or offensive to health" within the context of the interpretation provided by you.**

This review by BenchMark Toxicology has identified that the most important hazardous property of Foray 48B is irritation. Irritation occurs at high exposure doses such as accidental splashing or in the process of ground spraying, as well as in animal studies.

Based on the estimates of exposure calculated by BenchMark Toxicology Services and its understanding of the mechanisms underlying irritation, the risk of the sprayed Foray 48B or its components causing irritation (other than in an accidental spillage) would be extremely low. Thus it is considered that in this context, a health nuisance does not exist which is "injurious or offensive to health".

Jenner Consultants (1996) and ARPHS (2003) have identified that the formulation contains other ingredients, which are also used in other commercial products such as food and cosmetics, to which some members of the community may be sensitised because of prior exposure. There may be circumstances during the spraying programme when hypersensitivity reactions will be triggered, but it will

be extremely difficult to establish the causative agent. This appeared to be the experience with the spraying programme in Auckland and is likely to be even more difficult with the smaller number of people estimated to be exposed in Hamilton (30,600 with 8-10 estimated to be hypersensitive).

Oral Tolerable Intakes have been established for some of chemicals that were identified by the community as having hypersensitivity hazardous characteristics. Whether those chemicals are the same as the inert ingredients in Foray 48B is not known. However, with respect to the ingredients assessed by ARPHS (2003), they conclude that the levels to which the community would be exposed are likely to be lower than the Tolerable Intakes.

The estimated exposures are very low (sub microgram range; see Appendix C). Taking into account the biological mechanisms of hypersensitivity and the reactions of sensitised individuals, the threshold for the effect would be lower than for other systemic effects or irritation and would vary widely between individuals. Therefore there is more uncertainty about predictions of adverse effects from the available information.

BenchMark Toxicology Services is reasonably confident, however, that the predicted levels of exposure will not trigger hypersensitivity reaction.

Notwithstanding, the estimated 10 individuals at high risk should be assessed and if necessary given the option of relocating to a spray free area to avoid exposure completely.

If relocation is not an option, appropriate management measures should be put in place so that if a reaction occurs, prompt intervention can prevent any progress to a more serious condition.

Based on the risk assessment, the high probability of difficulties in establishing a cause and effect relationship between the spray and any reactions and the management options that can be put in place to deal with any eventuality of hypersensitive reactions, BenchMark Toxicology Services considers that a health nuisance does not exist which is "injurious or offensive to health".

## APPENDIX A

### Part I

List of documents provided by and reviewed for the Hamilton City Council.

- Aer'aqua Medicines Ltd (2001). Health Surveillance following Operation Ever Green: A programme to eradicate the white-spotted tussock moth from the eastern suburbs of Auckland. Report to the Ministry of Agriculture and Forestry May 2001.
- Anonymous (2003). Review of: Watts M. Painted Apple Moth eradication programme: health risks and effects.
- [ARPHS] Auckland Regional Public Health Service (2003). 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. Auckland Regional Public Health Service, October 2003.
- Blackmore H (2003a). Painted Apple Moth Era Painted Apple Moth Project eradication Campaign West Auckland. Draft Interim report of the Community-based Health and Incident Monitoring of the Aerial Spray Programme. January-December 2002.
- Blackmore H (2003b). Foray 48B aerial spray campaigns. Public Health Critical Information – September 2003
- [ERMA] Environmental Risk Management Authority (2002). Decision: Application HSR02044. 14 November 2002.
- ESR (2003). Commentary to MoH on report titled: "Draft Interim report of the Community-based Health and Incident Monitoring of the Aerial Spray Programme. January-December 2002. Author: Hana Blackmore
- Jenner Consultants (1996). Health Risk Assessment of Btk (*Bacillus thuringiensis var. kurstaki*) 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, Jenner Consultants, 4 September 1996.
- [MAF] Ministry of Agriculture and Forestry (1995). Foray 48B Toxicological assessment 1995.
- [MAF] Ministry of Agriculture and Forestry (2003a). MAF Biosecurity Painted Apple Moth Project. PAM Health Service Reporting. Month of August 2003.
- [MAF] Ministry of Agriculture and Forestry (2003b). MAF Biosecurity Painted Apple Moth Project. Health Monitoring Strategy. Version 3, August 2003.
- [MAF] Ministry of Agriculture and Forestry (2003c). Gypsy Moth response Hamilton. Operating Plan. October 2003 Version 4.
- Pearce M, Habbick B, Williams J, Eastman M and Newman M (2002). The effects of aerial spraying with *bacillus thuringiensis kurstaki* on children with asthma. Canadian Journal of Public Health 93 (1): 21 – 25.
- Petrie K, Thomas M and Broadbent E (2003). Symptom complaints following aerial spraying with Biological insecticide Foray 48B. New Zealand Medical Journal 116 (1170): 354.
- Teschke K, Chow T, Bartlet K, van Netten C, Leung V and Ross A (2000). Airborne Exposures to *Bacillus thuringiensis var. kurstaki* During Gypsy Moth Eradication *Final Report to the Capital Health Region* May 2000.

Watts M (2003). Painted Apple Moth Eradication Programme: Health risks and Effects.

## Part II

Documents sighted by BenchMark Toxicology Services but not necessarily accessed or reviewed.

Anonymous. A series of pages with various sections entitled:

- Health effects of aerial spraying of Foray 48B.
- Environmental effects of aerial spraying of Foray 48B.
- Aerial application of Foray 48B.
- Alternative eradication methods

Axys Environmental Consulting (2003). Assessment of Environmental and Human Health Effects from Proposed Application of Foray 48B in Waskesiu, Prince Albert National Park of Canada (2003).

Blackmore H (2002). Open letter to all parents, schools and childcare establishments in the painted Apple Moth aerial spraying zone in West Auckland.

Blackmore H (2002). Exposure risk for schools during the Painted Apple Moth (PAM) aerial spraying programme.

Blackmore & Watts (2003). Additional notes on the inert ingredients of Foray 48B. Attached to a media release dated 4 May 2003.

CC-PAM (2003) – Damning evidence of adverse health effects –CC-PAM releases an Interim report of the community based health and incident monitoring and associated press releases from [www.moth.co.nz/homepage.htm](http://www.moth.co.nz/homepage.htm)

Correspondence between Swarbric Dickson and Hamilton City Council dated August 2003 and September 2003.

Correspondence between Tony Banks and Hamilton City Council dated September 2003 and October 2003.

Fleming, Graeme (2003). Health Act 1956 – Asian Gypsy Moth Spray. Memo to Chief Executive Officer, Hamilton City Council, September 2003.

No Spray Zone (2003). Information on Pesticides.  
[www.nosprayzone.org/pesticides/index.html](http://www.nosprayzone.org/pesticides/index.html).

MAF. Information about Gypsy Moth in Hamilton

Sharov *et al.* (2002). Evaluation of preventive treatment in low-density Gypsy Moth Populations Using Pheromone Traps. *J Econ Entomol* 95(6): 1205 – 1215 (provided by councilor Macpherson).

Washington State Department of Health (2001). Report of Health Surveillance Activities. Aerial Spraying for Asian Gypsy Moth – May 2000 Seattle, WA July 2001

WSDA 2002 Gypsy Moth Program Summary Report

## APPENDIX B

This appendix comprises the summaries and evaluations of the documents reviewed by BenchMark Toxicology Services. The documents have been listed in alphabetical order; the order does not reflect their significance or relevance to the review.

**Aer'aqua Medicine Ltd (2001). Health Surveillance following Operation Ever Green: A programme to eradicate the white-spotted tussock moth from the eastern suburbs of Auckland. Report to the Ministry of Agriculture and Forestry May 2001.**

This document is a comprehensive report of the White Spotted Tussock Moth Spraying Programme – Operation Evergreen - in Auckland's eastern suburbs in 1996 and the subsequent health surveillance programme.

Three hundred and seventy five individuals, including a few reports by medical practitioners, reported various concerns.

Fear of unspecified future disease was the most frequently reported single concern, followed by headache and upper respiratory symptoms. Concerns were reported for nearly all organs systems. Follow up of the reported concerns through various processes did not identify any significant disease attributable to the spraying. General Medical Practitioners in the area were asked to inform the Medical Officer of Health about any health problems which they thought might be associated with the spraying. Neither systematic problems nor individual reports were reported after 1997.

Based on two sentinel medical practices, no adverse pattern of illness were found.

A voluntary register of individual exposed to the spray has been compiled and placed in the National Archives.

Overall the report concludes:

*"A comprehensive health surveillance programme has examined health outcomes for a period of two years afterwards (after Operation Ever Green) - 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 to MAF 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 was well supported and has been placed in the National Archives (Auckland Regional Office) to assist with any future health studies." (italics added)*

The findings of the study are consistent with the health risk assessment and the outcomes of overseas studies.

**Anonymous (2003). Review of: Watts M. Painted Apple Moth eradication programme: health risks and effects.**

This is a review and assessment of Watts (2003) document – it is not evaluated.

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**[ARPHS] Auckland Regional Public Health Service (2003). 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. Auckland Regional Public Health Service, October 2003.**

This report summarises Foray 48B as a brown liquid, with a pungent odour sometimes likened to yeast, having a pH of around 4 and containing 2% *Bacillus thuringiensis subsp. kurstaki* spores, about 20% spent culture, about 20% inert ingredients and 50% water.

The culture broth is described as including soy meal, corn (maize) starch and fishmeal, with other micronutrients added. The spent culture broth is predicted to contain breakdown products of these ingredients, bacterial waste products and dead bacteria. ARPHS (2003) considers "that the spent culture material is likely to be the main source of potential serious reactions to the spray." in people with known severe food allergies. The measures put in place for the PAM project to handle this issue are appropriate if spraying goes ahead in Hamilton.

ARPHS (2003) describe the inert ingredients as "These ingredients are included preservatives, dispersants, sticking agents and a pH regulator. With one exception, these ingredients are on the US EPA's list 4B of allowable ingredients in pesticides, categorised as "generally regarded as safe". The other ingredient (a preservative) is on List 3, and in wide use. None of the ingredients are on Lists 1 or 2, which include known hazardous materials. The ingredients are approved in NZ by Medsafe and NZFSA for use in a variety of food, medicines and cosmetics."

Further they point out that one preservative may be a dermal irritant at high enough concentrations and two other ingredients that can be sensitisers with sufficient exposure. However, the concentrations at which they are found would lead to exposures considerably lower than FAO/WHO (JECFA) Acceptable Daily Intakes.

Benchmark Toxicology Services has not had access to the formulation details for Foray 48B. However, based on the standard practices of establishing Tolerable Intakes such as the Acceptable Daily Intakes set by JECFA, all known adverse effects are taken into consideration.

WHO (1994) defines a tolerable intake as an estimate of the intake of a substance that over a lifetime is without appreciable health risk. It is expressed in mg/kg/day (examples are the Acceptable Daily Intake, Tolerable Daily Intake, Tolerable Weekly Intake, Reference Dose, Reference Concentration, Virtually Safe Dose and Risk (acceptable) Specific Dose). In essence a tolerable intake is an estimate of a safe dose for the particular substance.

Thus the conclusions by ARPHS (2003) that the effects are unlikely to occur at the likely exposure doses are justified. Nonetheless, for the PAM campaign the PAM Health Service took a precautionary approach, offering people with reactions to preservatives to contact them for advice.

Should the spray programme go ahead in Hamilton a similar approach is recommended.

ARPHS (2003) analyses the health concerns and effects related to Foray 48B based on the information from the surveillance reports from Operation Evergreen, three NZ HRA and HRA undertaken in North America, WHO reports, published literature and clinical information from the PAM Health Service. The following conditions were identified as being of concern: asthma and respiratory conditions, congenital hypothyroidism, thyroid disease, infection, gastrointestinal effects,

irritation, allergies and related diseases, headaches and constitutional symptoms, situational stress, pregnancy and miscarriages and endocrine disruption.

Whilst concerns were raised or reported about these conditions and some mild, transient irritation of mucosa, skin and eyes was predicted, there was no evidence for a causal association with the spraying of Foray 48B. This is consistent with overseas research (Capital Health Region Office of the Medical Health Officer, 2001).

There were about 10 people who notified the PAM Health Service as having food or non-food product allergies who had symptoms considered to have a temporal association to possible Foray exposure.

The PAM Health Service reports that 70/269 people with support plans suffered from situational stress. Whilst this may be caused by the spraying programme and the disruption to their lives, it is not a consequence of Foray 48B itself and is likely to occur in other relocation circumstances without fear of being poisoned.

ARPHS (2003) further attempts to predict the number of people from Hamilton who may be concerned or report these same conditions based on the studies carried with previous spraying programmes. The major differences between the programmes in Auckland and Hamilton are the size of the population likely to be exposed (30,600 in Hamilton), different population characteristics and behaviour, and different spraying schedules.

The document by ARPHS (2003) also includes précis of studies some of which were different from those in the toxicological profile provided on Foray 48B (MAF, 1995). These included animal studies of up to 5 months duration with active or formulated product, experimental studies in human volunteers with formulated *bacillus thuringiensis subsp. Kurstaki* containing 3,000,000,000 viable spores/gram (up to one gram in capsules for 5 days), environmental studies associated with aerial spraying programmes and occupational studies in field spray operators. No adverse effects were reported except in one occupational study (attributed to Nelson *et al.*, 1992, as quoted in WHO, 1999, which appears to be the same study quoted by Teschke *et al.*, 2000, except that the maximum spore concentration reported for air differed by a factor of about two) and in two case reports attributed to Green *et al.* (1990) and Samples & Buettner (1983) as quoted in Siegel (2001).

In the occupational study operators experienced chapped lips, dry skin, eye irritation and nasal drip and stuffiness. The symptoms were transient and usually occurred during the beginning of a spray run when *bacillus thuringiensis subsp. Kurstaki* spray concentrations were increased. Nearly all workers exposed to high levels were culture positive, with some remaining culture positive up to 40 days. The monitored concentration of *bacillus thuringiensis subsp. Kurstaki* spores in air were said to range up to 7,200,000/m<sup>3</sup> (Teschke *et al.*, 2000 quote 18,500,000 CFU/m<sup>3</sup>).

The case reports related to a worker being splashed in the face and eyes with the commercial product and developing dermatitis, severe itching, burning, swelling and erythema, with conjunctival injection and a farmer who developed corneal ulcers after accidental splashing of the product on his face.

### **Assessment**

The report by ARPHS (2003) is a comprehensive analysis of the likely outcomes in people who might be exposed to Foray 48B during the aerial spraying programme. Consistent with previous assessments, it generally takes a precautionary approach in identifying individuals in the community who might be at increased risk of reacting to any of the components of Foray 48B and putting management measures in place that would reduce or avoid coming in contact

with the aerosol spray, as well as measure in place to manage individuals who might be exposed.

There is an associated risk of situational stress, the acceptability of which needs to be considered. For example the impact of a low probability of adverse reaction to the spray needs to be weighed against the seriousness or the impact of the more likely situational stress.

**Blackmore H (2003a). Painted Apple Moth Era Painted Apple Moth Project eradication Campaign West Auckland. Draft Interim report of the Community-based Health and Incident Monitoring of the Aerial Spray Programme. January-December 2002.**

The following is given in the introduction as the reasons for the study:

*"There has been considerable community concern from the first aerial spray that adverse health effects have been trivialised, discounted or dismissed, while the social and economic impacts on the community are simply not acknowledged in any form.*

*The Painted Apple Moth Community Coalition (CC-PAM) was formed in June 2001 in response to the news that the eradication programme was moving onto an aerial spraying footing. The community-based group was designed to enable public participation and input into the decision-making process, and ensure health protection was a prime consideration.*

*When the group became aware that the same problems experienced in the Tussock Moth campaign of under recording and devaluation of health effects were occurring, CC-PAM in conjunction with the then established Community Advisory Group (CAG), re-introduced the WSTM community-run health and incident reporting system.*

*This interim health and incident report is the first outcome of that undertaking. It presents the community's experience to date. It does not attempt to determine plausibility of effects, or prove causal relationships between the spray and presented symptoms. The report simply accepts, summarises and presents the actual events, effects and patterns of symptoms as experienced and reported by the community." (Italics added)*

A total of 1397 people reported spray-related incidences, of which 315 reported symptoms. The document comprehensively reports a range of health related symptoms, generally annotated against specific statements in the "Health Risk Assessment (HRA)", presumably conducted prior to the start of the spraying programme. The HRA could not be clearly identified but appeared to be the one conducted by the Auckland Regional Public Health Service.

The document also reports cases of social and economic disruption as well as cases of frustration about choice, participation, communication, and generally the way individuals felt treated by officials. These issues need to be addressed as well as the health issues as they can impact on the well being of the community.

Generally the health conditions were similar to those reported in other studies, except that in this case they were presented as extracts of notes written by the individuals concerned at or about the time they felt affected.

Whilst the author claims in the introduction that the study "does not attempt to determine plausibility of effects, or prove causal relationships between the spray and presented symptoms" the tone of the document tends toward causal statements and specific contradiction of the HRA and the health studies.

Consistent for this type of study there are neither statistical analyses of the results nor use of controls (either pre exposure for the same group or comparison with matched control groups from non-spray areas). Thus causation and even

association is difficult to assess. Notwithstanding, the report describes a variety of effects and conditions that were reported to occur at the time of, or subsequent to, the spraying.

BenchMark Toxicology Services concurs with the ESR review of this document and their recommendations (ESR, 2003).

In addition, any studies undertaken in conjunction with any future spraying programmes should include appropriate monitoring of air concentrations of Foray 48B.

**Blackmore H (2003b). Foray 48B aerial spray campaigns. Public Health Critical Information – September 2003.**

This document appears to be a memo comprising 24 dot points and signed by Hana Blackmore for CC-PAM.

Benchmark Toxicology Services is unable to comment on dot points 1 – 5 because they relate to internal issues in New Zealand, are not related to toxicology and risk assessment and are outside the agreed scope of works, and dot points 8 - 14, 16, 17, 23 and 24 because BenchMark Toxicology Services has not been provided a list of inert ingredients, the issues raised relate to internal operations in New Zealand and relate to professional issues, such as what information should be provided to GPs.

**Dot Point 6** refers to a cluster of thyroid abnormality that was investigated by the health authorities. Benchmark Toxicology Services is satisfied that the analysis and explanation of this case by ARPHS (2003) was adequate and concurs with their conclusions that a link with the spray is not considered plausible based on the lack of temporal relationship. Benchmark Toxicology Services is unable to comment on the medical opinions expressed in the ARPHS report.

**Dot point 15** appears to refer to the document by Watts (2003), which is reviewed elsewhere in this document.

The statement that there is "*evidence of no known safe level of inhalation*" for benzoic acid is somewhat misleading as it can be interpreted, and in the experience of BenchMark Toxicology Services has been interpreted, as there being no safe level for the chemical. This is not the case. The study to which Dr Watts (2003) refers reported effects at all doses tested. It cannot be inferred from these results that there is no safe dose for benzoic acid by inhalation (see critique of Watts, 2003).

**Dot Point 17** argues that the hazardous properties of propylene glycol will manifest under all conditions. This is scientifically implausible given that Tolerable Intakes for propylene glycol have been established by JECFA (Acceptable Daily Intake of 25 mg/kg/day), the US Environment Protection Agency (an Oral Reference Dose of 5 mg/kg/day and an inhalational Reference Dose of 0.86 µg/kg/day) (US EPA, 2002) and the Agency for Toxic Substances and Disease Registry (ATSDR, 1997) (a Minimal Risk Level of 2 mg/kg/day). This is one case that illustrates higher toxicity by inhalation, probably because of higher bioavailability) by inhalation than by ingestion. The exposure estimates by BenchMark Toxicology Services (Appendix C) suggest that these tolerable intakes would not be exceeded.

**Dot Points 18-19** relate to supposed deficiencies in the estimates of exposure in the health risk assessment. The 1996 HRA (See above) was a qualitative risk assessment and did not attempt to quantify exposure. These issues are not relevant if the approach taken in Appendix C is adopted.

**Dot Point 20** appears to be referring to the findings of Teschke et al. (2000) reviewed below. BenchMark Toxicology Services confirms that Teschke et al.

(2000) reported particle size in the respirable range. However, if one assumes that all of the spray droplets reach the lungs and the components absorbed then the size of the droplets becomes immaterial (see Appendix C).

**Dot Point 21** also seems to refer to Watts (2003). Watts did not attempt to quantify exposure; the assessment is purely qualitative. As shown in Appendix C, the highest possible exposure for residents it is at least 40 times lower than the lowest exposed worker.

**[ERMA] Environmental Risk Management Authority (2002). Decision: Application HSR02044. 14 November 2002.**

This document provides the decision maker's reasons to allow importation of BACTUR 48LC, a product with the same active ingredient as Foray 48B.

**Jenner Consultants (1996). Health Risk Assessment of Btk (*Bacillus thuringiensis var. kurstaki*) 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, Jenner Consultants, 4 September 1996.**

The report states the following as the proposed objectives:

1. To clarify and document who are the population exposed to the proposed Ministry of Forestry eradication programme for white spotted tussock moth in eastern Auckland.
2. To appraise the operational plan for the eradication programme in the Auckland Eastern suburbs in terms of possible health impacts.

To provide in the report an assessment of the likely significance to health of:

- human exposure to BTK;
  - public exposure to various components of the formulation Foray 48B, where these components are already known to the Ministries of Health and Forestry, and in the light of existing information about their effects;
  - physical effects to the public from the spray programme;
3. To make appropriate input to the final operational programme so that, where any potential health impacts are identified, these may be minimised.

Certain aspects of this document are not directly relevant to the Hamilton eradication programme and are not considered further. These include:

- The spray programme
- Demographics
- Exposure population characteristics.

### **Biological hazard**

The document takes a conservative approach in concluding that *bacillus thuringiensis kurstaki* could cause human disease by infection on theoretical grounds although the evidence is lacking.

### **Chemical hazard**

Foray 48B comprises the active ingredient *bacillus thuringiensis kurstaki*, residues of the culture medium used to grow the active ingredient and a number of inert

ingredients. Jenner Consultants (1996) claim that sufficient proprietary information has been made available to ascertain that the inert ingredients in Foray 48B are included in Group 4 of the US Environment Protection Agency (EPA) list 4 classification as materials which are generally recognised as safe (GRAS). Materials on the GRAS list are approved for use without the requirement for toxicological studies for each product submission for registration or use.

The risk assessment concludes (page 28) that "Overall, the inert ingredients contained in Foray 48B are of low toxicity although the possibility exists that some individuals may be hypersensitive to these components as a result of previous exposures in food, cosmetics and pharmaceutical agents. However, the proposed exposure route is such that hypersensitivity reactions are considered most unlikely due to the very small amount of the compound to which vulnerable people will be exposed."

The list of inert ingredients and their concentration in the end use product was not provided to BenchMark Toxicology Services for review.

The acute toxicity studies in animals submitted in support of the registration of Foray 48B (MAF, 1995) suggest that the product is of low toxicity, non sensitising, although may be slightly irritating to the eyes and skin.

The conclusion that some individuals may be hypersensitive to the ingredients from previous exposures through foods, medicines or cosmetics is a conservative approach that identifies a possible group at high risk. While it may be difficult to determine if a hypersensitivity reaction is caused by exposure to Foray 48B or some other agent, the important issue is to increase awareness and medical vigilance so that any incidence involving hypersensitivity, no matter what the trigger, can be managed accordingly if required.

Jenner Consultants (1996) reviewed information from occupational studies, case reports of accidental spillage, medical consultations and hospital admissions in conjunction with Foray spraying in Vancouver. They concluded that the studies suggest that skin and eye irritation may occur in exposed populations, particularly at high levels occupational exposure. However, there was no clear evidence of increased effects in people from the spray area in Vancouver compared with people outside the spray area, although the symptoms reported to doctors and hospital could be consistent with the effects of Foray 48B.

The risk assessment devotes considerable space to analysing the different types of exposure that might arise because of different activities and locations, however, it does not attempt to quantify exposure. It acknowledges that it is difficult to know with any certainty the extent of exposure. This is reasonable given the area of the spray programme and the different activities likely to be undertaken by the residents, workers, and visitors.

### **Assessment**

The document is a comprehensive review of Foray 48B and its known toxicological and adverse reaction profile. It is a qualitative risk assessment that concludes that some of the effects seen at high doses in animal studies and in occupational exposures are unlikely to be seen at the relatively low and infrequent doses to which residents may be exposed.

It suggests that groups that have been identified as having a potentially higher risk of suffering ill effects as a consequence of exposure should avoid exposure, for example by staying inside dwellings during spraying. Staying inside building, however, may minimise, but not prevent exposure completely. Teschke (2000) reported that indoor levels of CFU/m<sup>3</sup> (indicative of Foray 48B concentrations) increased with time and tended to persist. Interpretation of their findings is confounded by the observation that levels inside dwellings may have been

influenced by monitoring staff entering and leaving the building. However, keeping the doors and windows closed may minimise the amount of spray moving indoors.

The basis for Jenner Consultants (1996) concluding that Foray 48B would not have any effects on pregnant women could not be identified. The toxicological document reviewed by Benchmark Toxicology Services (MAF, 1995) did not include any reproductive, developmental or teratogenic animal studies.

**[MAF] Ministry of Agriculture and Forestry (1995). Foray 48B Toxicological assessment**

Foray 48B contains 10,600 IU of potency per mg which is equivalent to 2.2% of active proteins of *bacillus thuringiensis subsp. Kurstaki*.

The following acute toxicity tests using Foray 48B FC formulation were described:

- Oral in rats– no effects noted at 5000 mg/kg
- Shaved dorsal skin of rats – 2500 mg/kg sedation on day of treatment no other effects. Small wounds on exposed surface
- Dermal in rats - 2500 mg/kg sedation on first day no other signs of toxicity
- Inhalation for 4 h 6.81 mg/L no effects noted over 14 days
- Rabbits shave dorsal skin 4 h under occlusion, slight skin reactions in one rabbit but overall classed as non-irritant
- Instillation of 0.1 mL into conjunctival sac of eye of rabbits – classed as moderately irritating to the eyes. Non-sensitising

Slight irritation of the skin and moderate irritation of the eyes was also shown with the technical grade active constituent.

Human studies after spraying in Vancouver showed no link between spraying and health effects. Noted high levels temporary discomfort, but can be prevented by simple use of precautions.

Subchronic, chronic, reproductive, genotoxic and carcinogenicity studies were not described.

**[MAF] Ministry of Agriculture and Forestry (2003a). MAF Biosecurity Painted Apple Moth Project. PAM Health Service Monthly Reporting. Month of August 2003.**

This is a monthly report of the Health Support part of the two health initiatives established during the PAM Project (the other is Health Monitoring).

The cumulative number of new residents with health concerns (from 30 December to 31 August) is 3371 of which 1251 have been assessed by a doctor and 628 have been assigned to Practical support Plans. No new cases were added for the month of August 2003.

**[MAF] Ministry of Agriculture and Forestry (2003c). Gypsy Moth response Hamilton. Operating Plan. October 2003 Version 4.**

This document provides a comprehensive description of the biology and pest status of Gypsy Moth, the development of the strategy and goals, key roles and responsibilities, relevant legislation, programme components of both ground and aerial operations and contingency actions.

Of relevance to this review the aerial spray operations will cover an area of 1250 hectares and were to begin on 6 October with a maximum of 8 sprays planned at 5-7 days interval. It is estimated that the 1250 hectares that need treatment will take about 4-5 hours to spray.

The aerial spray must aim to deliver:

- At least 10 drops/cm<sup>2</sup>. This works out at around an average of 0.5 ml of product per square metre.
- Droplet size to be 120 microns (within the 100 to 150 micron size and minimises droplets of less than 50 microns).
- Application rate to be between 5 and 7 litres/hectare (average 5.5 mL/hectare) by the final spray and reflecting the increase in leaf surface as the leaves expand in the spring.
- The minimal height at which the planes may fly is 45 m.

A total of 55,132 L of Foray 48B is estimated to be needed for the entire operation.

Appropriate safety measures for users and a description of the spray decision criteria have been outlined in the document.

While the document describes monitoring of the efficacy of the programme, it does not outline any monitoring to assess the levels of Foray 48B in the environment during and after each spraying event. This needs to be addressed.

Should the spray programme go ahead in Hamilton, a monitoring programme should be devised to collect information of the extent of exposure of residents in the spray area.

**[MAF] Ministry of Agriculture and Forestry (2003b). MAF Biosecurity Painted Apple Moth Project. Health Monitoring Strategy. Version 3 August 2003**

The purpose of this document is to define the strategies for meeting the health monitoring needs of people potentially affected by the PAM Eradication Operation.

Components of the strategy need to be prioritised by the Health Advisory Group.

There are two human health related initiatives within the context of the PAM Eradication Operation. Health Monitoring and Health Support. The approach to 'Health Support' is addressed elsewhere.

BenchMark Toxicology Services assumes that the health monitoring activities outlined in this document will be put in place with any spray programme with Foray 48B in Hamilton.

The purpose of the health monitoring activities is given as:

To determine the safety of the eradication programme, which exposes a residential community to aerial applications of Foray 48B. This will supposedly be done by:

- Medical Assessment as appropriate to ensure that any individual adverse health events associated with the spraying programme are investigated and a clear diagnosis obtained wherever possible.
- Surveillance to investigate whether there may be an epidemiological relationship between health status and the spraying programme, ie,
  - Monitor whether there is any alteration in the pattern of relevant health status outcomes among the community exposed to the spraying,
  - Select these health status outcomes taking into account community concerns and recent knowledge of *bacillus thuringiensis subsp. Kurstaki* use
  - Determine whether any altered patterns of outcomes are associated with the use of Foray 48B.

The document identifies health status outcome that will be included in the surveillance and provides a description of how each will be examined including an analysis of the strengths and weaknesses, contribution to the body of knowledge, cost and priority to be assigned.

Birth weight, gestational age, measles and meningococcal disease are excluded from the epidemiological study because they were adequately addressed by the operation Evergreen Health Surveillance.

Benchmark Toxicology is unable to comment on the methodological veracity of the surveillance (outside its area of expertise), nor on the adequacy of the identified sources from which the data will be gathered (no knowledge of health collection data in New Zealand).

Notwithstanding, the health outcomes to be studied are comprehensive and cover the conditions about which the community has expressed concern or current literature suggests that they may be associated with spraying of Foray 48B.

The document, however, should be rewritten as a proposal specifically for the Hamilton spraying programme and made available to the community. It provides useful information that may influence the expectations about the outcomes such programmes can deliver.

**Pearce, M, Habbick, B, Williams, J, Eastman M and Newman M (2002). The effects of aerial spraying with *bacillus thuringiensis kurstaki* on children with asthma. Canadian Journal of Public Health 93 (1): 21 – 25.**

A North American Gypsy Moth infestation in Southern Vancouver Island was treated with areal application of Foray 48B. Three applications were made at 10-day intervals at 61-metre altitude and design rate of application of 4 L per hectare. The objective of the study was to determine if the application of the pesticide was associated with an increase in symptoms or change in Peak Expiratory Flow rate of children with asthma living within the spray zone. Children with asthma were considered a potentially high-risk group, because of previous suggestions that people with hypersensitivity may be at increased risk during spraying.

A pre/post matched pairs cohort design was used. Children living in the spray area (19 males and 10 females) were matched with children outside the spray zone (19 males and 10 females). Thirty-eight children refused or withdrew from the study. Peak respiratory Flow Rates (as a measure of lung function), asthma symptoms and non-asthma symptoms were recorded in diaries.

The study found no evidence of adverse effects in children with asthma as a consequence of the aerial spraying. This is consistent with the findings of other studies (Capital Health Region Office of the Medical Health Officer, 2001).

Exposure was confirmed using Kromecote cards (used to measure droplets deposition), although not quantified, outside the residences and nasal swabs of the subjects. Culturable airborne *bacillus thuringiensis kurstaki* concentrations were published separately.

**Petrie K, Thomas M and Broadbent E (2003). Symptom complaints following aerial spraying with Biological insecticide Foray 48B. New Zealand Medical Journal 116 (1170): 354.**

Petrie *et al.* (2003) investigated the effects of aerial spraying of Foray 48B on self reported symptom complaints, health perceptions, and visits to healthcare providers in the PAM Project. The participants were residents within the most intensively sprayed area of the initial MAF spray zone in West Auckland. Base line data were gathered by questionnaire from 292 participants at the end of October 2001 10 weeks prior to the first spray in the presence of a research

assistant in the participant's home. At the end of March 2002, after the area had been sprayed on three occasions, participants were sent a follow up questionnaire and asked to repeat the symptoms checklist and self rated health items. Sixty two percent (181) of the initial participants responded to the postal questionnaire after the spraying, ie, 111 of the original participants did not complete the study. Petrie *et al.* (2003) identified this as a limitation of the study.

Statistically significant increases in the reporting frequency of symptoms were found. Petrie *et al.* (2003) suggested that these indicated three broad types of effects: neuropsychiatric responses (sleep problems, difficulty concentrating and dizziness), upper respiratory tract irritation (irritated throat and itchy nose) and gastrointestinal disturbance (stomach discomfort, gas discomfort and diarrhoea). There was also a 65% increase in the frequency of reporting of chronic eye irritation, but was not statistically significantly different ( $p = 0.07$ ). There was no increase in the reported visits to medical practitioners or alternative healthcare provider. In addition, 70% of respondents felt that their own health had not been affected by the spraying and 50% felt that the health of their children had not been affected. Less than 10% (in each group) felt that their health or the health of their children had been moderately, quite a bit or extremely affected. About 20% reported that their and their children's health had been affected a bit.

There were no significant differences in the responses for asthmatics or people with other allergies. This is consistent with studies conducted in British Columbia (Pearce *et al.*, 2002).

Petrie *et al.* (2003) attribute the significant increases in neuropsychiatric symptoms to sleep disturbance (early morning low flying aircraft and increased anxiety because of the spraying), the upper respiratory tract symptoms to the local irritant effects of the spray, and the gastrointestinal symptoms to the *bacillus thuringiensis subsp. Kurstaki* enterotoxin or the bacterium itself germinating from the spores and colonising the gastrointestinal tract.

While the explanations offered for neuropsychiatric symptoms and irritation seem plausible, the explanation for the gastrointestinal symptoms is not. The evidence does not support the claim that *bacillus thuringiensis subsp. Kurstaki* is pathogenic, even though it has been isolated in exposed people during and after exposure to Foray 48B (Jensen *et al.*, 2002).

Petrie *et al.* (2003) identify a number of limitations of their study. They suggest that it is likely that people who perceived themselves as being affected by the spraying would have been more inclined to respond. This is a confounding factor in these types of studies

Further they state that they cannot conclude that the increase in reporting of symptoms was a direct result of the spraying programme nor can they exclude the possibility that severe health effects had occurred in a very small proportion of the people exposed to the spray. The latter is not consistent with their observation that there was no increase in reported visits to health practitioners, although they claim that the follow up period may have been too short.

The material Safety Data Sheet and literature on Foray 48B end use product formulations suggest that it is a mild irritant of mucous membranes, skin and eyes. Thus it is possible that individuals exposed to the spray aerosol may have suffered transient irritation if they were exposed to sufficiently high doses of aerosol. Petrie *et al.* (2003) discount increased levels of pollen during summer contributing to the upper respiratory tract irritation based on the pattern of symptoms (no significant increase in eye irritation, wheezing and coughing). However, they recommend the use of a control group without spray exposure in future studies to help resolve this issue.

Their conclusion that the results of this study do suggest that aerial spraying with Foray 48B is associated with some adverse health consequences reflects the findings of the study. However, the study lacks convincing argument and evidence that the adverse health effects that were reported were caused by Foray 48B itself.

Overall the results of this study do not provide any additional evidence that would progress the issue of a causal relationship between the effects reported and exposure to Foray 48B.

**Teschke K, Chow T, Bartlet K, van Netten C, Leung V and Ross A (2000). Airborne Exposures to *Bacillus thuringiensis* var. *kurstaki* During Gypsy Moth Eradication Final Report to the Capital Health Region May 2000.**

This was a comprehensive study of environmental levels of Foray 48B after aerial application in British Columbia. Spore levels (measured in Colony Forming Units, CFU) outside homes in the sprayed areas during and up to three hours after spraying ranged from less than 10 CFU/m<sup>3</sup> up to 1600 CFU/m<sup>3</sup>, with an arithmetic mean of 739 CFU/m<sup>3</sup>. Concentrations inside homes ranged from less than 10 CFU/m<sup>3</sup> to 627 CFU/m<sup>3</sup>, with an arithmetic mean of 159 CFU/m<sup>3</sup>. Initially levels inside homes were lower than outside. The concentrations of spores in air outside decreased at a faster rate than inside dwellings. Teschke et al. (2000) estimated that the half-life of spores in the environment was 2.4 days, which is longer than determined in laboratory studies.

Teschke *et al.* (2000) refer to levels of spores published in the literature of up to 11,000CFU/m<sup>3</sup> during applications by spraying. They also quote Noble *et al.* (1992) who reported that workers applying Foray 48B by ground application were exposed to spore concentrations of between 200,000 and 18,500,000 CFU/m<sup>3</sup> (by personal exposure monitoring).

Teschke *et al.* (2000) further reported that the aerodynamic diameter of the droplets measured on spray collected using an Andersen sampler ranged between 4.3 and 7.3 microns (respirable size), whereas the diameter of drops collected on Kromecote cards ranged between 50 and 150 microns. The explanation for the smaller diameter spray droplets was that they were generated after spraying, did not precipitate out of the air as fast as larger sized droplets and the aerodynamic diameter can be measured in samples collected using the Andersen sampler. The estimates of diameter on Kromecote cards was from the mark left on the cards by the droplets and may or may not be the same as the aerodynamic diameter.

Notwithstanding the information indicates that the spray mist consists of a range of particles from less than 10 microns and possibly up to the size generated from the spray equipment. However, there is no measure of the proportion of different size particles.

The approximate time for droplets of 1, 5 and 10 microns diameter to reach the ground from the plane flying at 61 m altitude was estimated to be 20 days, 1 day and 5 h respectively, and indeed may not settle because the wind velocities may be higher than their falling velocity.

In the absence of wind, the droplets measured after aerial spraying would take around one day to settle, longer in windy conditions. Therefore, exposure to the spray would occur over a longer period than the time taken to apply the spray.

Teschke et al. (2000) concluded that overall, Kromecote card densities were not good predictors of airborne exposures to *Bacillus thuringiensis* subsp. *Kurstaki*.

Teschke et al. (2000) also analysed Foray 48B to identify its components both in the field and in the laboratory. Table 1 from their publication is reproduced in total below, except for the retention times and the measure of fit for the identification. As can be seen a variety of substances were identified some of

which are listed in the US EPA lists of inert ingredients Generally Regarded as Safe (GRAS).

These may or may not be the so-called inert ingredients that the manufactures add to Foray 48B for a variety of reason (stabilisers, surfactants, etc.). Some of them may be products of the fermentation process used to produce *bacillus thuringiensis subsp. Kurstaki*.

Moreover, Teschke et al. (2000) did not quantify the components; hence their use in risk assessment is limited.

Some of these substances may possess hazardous properties as demonstrated by adverse effects in animal studies at experimentally toxic doses as listed in the Painted Apple Moth Community Coalition (CC-PAM) press release of 23 May 2003 (<http://www.moth.co.nz/homepage.htm>). However, at lower doses or lower concentrations they do not exert the same or other adverse effects as evidenced by inclusion in the US EPA GRAS list, eg. benzoic acid for which the Joint FAO/WHO Committee on Food Additives (JECFA) has also set an Acceptable Daily Intake of 5 mg/kg body weight per day).

**Table 1:** Summary of volatile compounds in Foray 48B, identified by GC/MS  
**Solid-phase micro-extraction sampler at 37°C**

Compound	CAS Number	GRAS List
thietane	287-27-4	
acetic acid, 2-propenyl ester	591-87-7	
2-butanone, 4-acetyloxy)	10150-87-5	
acetic acid, anhydride	108-24-7	4B
1,5-hexanediene-3,4-diol, 2,5-dimethy	4723-10-8	
sydnone, 3-(phenylmethyl)	16844-42-1	
2 methyl-2,3-pentanediol	7795-80-44	
phosphine, trimethyl	594-09-2	
2 methyl-2,3-pentanediol	7795-80-44	
2 methyl-2,3-pentanediol	7795-80-44	
phosphine, trimethyl	594-09-2	
cyclotrisiloxane, hexamethyl	541-05-9	
disiloxane derivative	18420-09-2	
cyclotetrasiloxane, octamethyl	556-67-2	3
5-hexen-2-one, 5-methyl	3240-09-3	
2,4-hexadienedioic acid	505-70-4	
cyclopentasiloxane, decamethyl	541-02-6	3
benzoic acid	65-85-0	4B
cyclohexasiloxane, dodecamethyl	540-76-6	
trisiloxane	3555-47-3	3
butylated hydroxy toluene	128-37-0	3
phenyl amine - silane derivative	10538-85-9	

***Solid-phase micro-extraction sampler at 23°C***

<b>Compound</b>	<b>CAS Number</b>	<b>Grass List</b>
acetic acid, mercapto -,methyl ester	236-48-2	
acetic acid, 2-propenyl ester	591-87-7	
ethylene diamine	107-15-3	3
ethanol, 2-(1methylethoxy)-	109-59-1	
2-heptanone, 3-hydroxy-3-methyl	13757-91-0	
2 methyl-2,3-pentenediol	7795-80-44	
phosphine, trimethyl	594-09-2	
ether, sec-butyl isopropyl	18641-81-1	
cyclotrisiloxane, hexamethyl	541-05-9	
disiloxane derivative	1438-82-0	
cyclotetrasiloxane, octamethyl	556-67-2	3
1-propanesulfonyl chloride	10147-36-1	
cyclopentasiloxane, decamethyl	541-02-6	3
benzoic acid	65-85-0	4B
cyclohexasiloxane, dodecamethyl	540-76-6	
trisiloxane	3555-47-3	3
butylated hydroxy toluene	128-37-0	3
phenyl amine . silane derivative	10538-85-9	
cyclohexasiloxane, dodecamethyl	540-97-6	

***Charcoal tube***

<b>Compound</b>	<b>CAS Number</b>	<b>Grass List</b>
penta siloxane, dodecamethyl	141-63-9	
benzoic acid, siloxane derivative	10586-16-0	
cyclohexasiloxane, dodecamethyl	540-97-6	
cyclohexasiloxane, dodecamethyl	540-97-6	
trisiloxane derivative	3555-47-3	3
additional siloxane derivatives		

**Alcohol extract of bulk Foray 48B sample**

<b>Compound</b>	<b>CAS Number</b>	<b>Grass List</b>
ethanol, 1-methoxy-,acetate	4382-77-8	
benzoic acid	65-85-0	4B
galacticol	608-66-2	

***Toluene extract of bulk Foray 48B sample***

Compound	CAS Number	Grass List
Chloroform	67-66-3	
2-hydroxy pyridine	142-08-5	
benzoic acid	65-85-0	4B
benzoic acid, 2-hydroxy-,phenyl ester	118-55-8	

CAS

Chemical Abstract Service

GRAS The US Environmental Protection Agency lists inert ingredients, which might be used in pesticides. The lists have the following meanings:

3 Inert ingredients of unknown toxicity.

4B Inert ingredients with sufficient data to substantiate that they can be used safely in pesticide products.

**Watts M (2003). Painted Apple Moth Eradication Programme: Health risks and Effects.**

In the first three dot points under scope of the document Watts (2003) states:

*"This document has been produced at the request of Stop Aerial Spraying after advice received from Sir Geoffrey Palmer.*

*It relates to the Ministry of Agriculture and Forestry's (MAF's) aerial spraying campaign over parts of West Auckland to eradicate the Painted Apple Moth (PAM).*

*In particular it addresses the adverse health effects apparently experienced by members of the community exposed to the aerially applied insecticide Foray 48b."* (Italics added)

The document was produced after studying various risk assessments prepared for MAF, health reports and papers from the published literature, with the primary document used being the Kalemba *et al.* (2002) HRA document (not reviewed here).

The report is a rather acerbic critique of the Kalemba *et al.* (2002) document on aspects of both principle and practice of toxicology and risk assessment.

Watts (2003) identifies a number of flaws in the risk assessment as listed in the executive summary (italics added).

1. *Failure to take heed of the symptoms previously reported by exposed communities because no link could be proven (e.g. Operation evergreen in East Auckland 1996-7*

In undertaking a health risk assessment one would consider any known adverse effects caused by a particular substance and would also include monitoring of any effects or condition about which a community may have expressed concerns. However, professional judgement needs to be exercised to assign priorities and resources to the most important issues.

The recommended monitoring for the Hamilton programme, should it go ahead, should include all conditions and effects considered previously, whether or not a causal link with Foray 48B was established.

On page 7 of the report Watts (2003) states 'This HRA acknowledges reports, during and after the 1996/97 spray programme, of "minor eye, throat and skin irritations and headaches", but concluded "we found no evidence of a causal association with Foray 48B spray" (p v). Note that a lack of evidence of causal

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association is *not* evidence that there is no link. It is not proof that the effects did not occur as a result of the spray.' (Italics added).

It is not possible to prove that an effect did not occur as a result of the spray by scientific investigation because it entails proving a negative. Logically that is not possible.

2. *An assessment of exposure that differs significantly from the actual exposure: the assessment assumed that people would be exposed only once per spray event, when in fact some people have been directly exposed up to six times per day, together with ongoing exposure to residual spray in homes and work places*

BenchMark Toxicology Services is not aware that any of the risk assessments undertaken prior to the spraying programmes attempted to quantify exposure in terms of daily doses internalized by exposed individuals. Dr Watts does not provide any measure of exposure other than to say that the risk assessment has underestimated it for a number of people. This is addressed by the exposure assessment undertaken by BenchMark Toxicology Services (see Appendix C).

3. *Failure to characterise the risk of inhalation of the chemical components of the spray, relying only on data for dermal contact and ingestion, when it is known that some chemical are many times more toxic by inhalation;*
4. *In particular, failure to identify the inhalation risk for one of the ingredients, benzoic acid: whilst benzoic acid is regarded as being of low toxicity when ingested, except to those people allergic to it, there is no known safe level of exposure by inhalation.*

The bioavailability of chemicals across biological barriers (skin, lung tissue, surface of the gastrointestinal tract) depends on a variety of factors, but principally three: the route of exposure, the chemical form and its chemical properties and the formulation (if any). In the case of inhalational exposure, physical properties of the chemical or formulation will also have an effect (eg, size of respirable particles).

Whilst it is true that bioavailability can be higher through inhalation than through ingestion or on the skin, it does not apply equally to all substances.

Some substances may be absorbed equally completely ie, 100% bioavailability through ingestion or through the lungs; others that require the action of the gastrointestinal contents to turn them into forms that can be absorbed through biological membranes will be absorbed more readily after ingestion than inhalation.

Generally, particles with aerodynamic diameters greater than 10 microns, do not reach the alveoli where absorption occurs. Thus, if the effects are due to systemic absorption of the chemical, particles > 50 microns will be less toxic by inhalation, although they may cause some local effects in the upper respiratory tract. Additionally absorption may occur if the form of the chemical is changed so that it becomes more bioavailable.

The reference doses for propylene glycol set by the US EPA (2002) for chronic exposure are 5 mg/kg/day for oral exposure and 0.00086 mg/kg/day for inhalation exposure (the reasons for the difference could not be ascertained). This may be taken to indicate that that absorption through the lungs is much more efficient than through the gastrointestinal tract. This conclusion holds if the toxic end points on which the reference doses are based are the same systemic effects. Notwithstanding, the exposure estimated in Appendix C clearly indicate that the levels to which residents will be exposed will be less than the reference dose for inhalation set by the US EPA.

Watts (2003) uses the case study of benzoic acid to support the claim that bioavailability can be higher by inhalation than by ingestion, particularly "there is *no known safe level of exposure by inhalation*".

The following is quoted from page 16 of the documents in which Dr Watts quotes from evaluations of benzoic acid by the IPCS (2002) and the EC (2002) (italics added):

*'From the literature it would appear that ingestion poses low risk, but problems may well arise from inhalation.*

*In 2000 the IPCS (p 5) concluded that*

*"as there are no adequate studies available on inhalation exposure, a tolerable concentration for exposure by inhalation cannot be calculated".*

*However two years later the EC (2002, p 10) concluded that*

*"as the rat inhalation studies showed adverse effects at all doses studied, it is not possible to identify a level of inhalation exposure that is without risk".'*

It may be inferred from the quotes that the two organisations reached different conclusions for different reasons. In fact both statements refer to the same study in rats.

The publication to which Watts (2003) refers (current reference EC, 2002b) describes a study in which, rats were exposed to benzoic acid respirable dust at 25, 250 and 1200 mg/m<sup>3</sup> for 6 h per day, 5 days per week for 4 weeks. The only finding at the lowest dose of 25 mg/m<sup>3</sup> was described as "some histopathological lesions were evident". No additional explanation was provided; hence it would not be possible to draw a conclusion from this. For example, the finding at the lowest dose cannot be compared with the finding at higher doses to assess if more severe lesions occurred.

In a separate publication (EC, 2002a) the same results are described as: "At > 25 mg/m<sup>3</sup>, an increased incidence of interstitial inflammatory cell infiltrate and interstitial fibrosis in the trachea and lungs in treated animals compared with controls was seen. Although the number of these microscopic lesions was higher in treated animals than in controls, there was no clear dose dependency for this effect." Except for the > symbol before the concentration, this is quoted *verbatim* (without quotation marks or acknowledgement) from the IPCS reporting of the same study (IPCS, 2000) who correctly use the ≥ symbol before the concentration. Given that there is a difference of 48 times between the lowest dose and the highest dose, the changes observed apparently marginal and there is a lack of a dose dependency, the significance of the effects reported is questionable and in all likelihood the effects are unrelated to treatment with benzoic acid.

Neither the statement by IPCS nor that by EC was meant to imply, nor have toxicologists or health risk assessors interpreted such statement to mean, that there is no safe level of exposure by inhalation. Had the inhalational data base been more extensive and this particular study been sufficiently robust, an estimate of the tolerable intake could have been derived by the standard approach of using the Lowest Adverse Effect Level (LOAEL), rather than the No Observable Adverse Effect Level (NOAEL), with appropriate substance specific adjustment factors.

On this basis, a Tolerable Concentration of 25 µg/m<sup>3</sup> could have been derived using the LOAEL and a chemical specific adjustment factor of 1000 to account for intra and inter species differences and the fact that the LOAEL was used rather than the NOAEL. Based on a respiratory volume of 23 m<sup>3</sup>/day, the total daily intake is 575 µg/kg which equates to a Tolerable Intake for benzoic acid of

8 µg/kg/day for a male adult and 57.5 µg/kg/day for a child. These amounts are higher than the estimated exposures to Foray 48B (Appendix C).

4. *The failure to identify the chemical ingredients in the formulated product so that the assessment can itself be assessed*
5. *Failure to determine the effects of the mixture of chemicals that constitutes Foray 48B, allowing for synergistic or additive effects, as opposed to assessing each chemical as if it were the only chemical to which people would be exposed, when it is known that mixtures can be significantly more toxic*

It is the understanding of BenchMark Toxicology Services that all ingredients in the formulation were identified and considered in the risk assessments. However, the ingredients other than the *bacillus thuringiensis subsp. Kurstaki* were not made public. Hence independent scrutiny has not been possible.

Whilst it would be desirable to have all information publicly available, this is a legal, political and commercial issue to be resolved between the New Zealand authorities and the sponsors of the product.

The issue of mixture is also raised with synergistic or additive effects stressed. Equally, inhibitory and antagonistic effects need to be considered. Whilst there are limitations to risk assessment based on individual substances or known formulation of products, it is extremely difficult if not impossible to gather scientific information on the biological behaviour of mixtures, other than for simple mixture consisting of a few (up to 3-5) components or closed bodies (eg, water in lake), that would inform the risk assessment process sensibly. It is not possible to predict the behaviour of complex mixture on a theoretical basis, because of the very large number of permutations that need to be considered.

However, results of studies (single and repeated exposure) conducted with the end use product formulation of Foray 48B have been conducted in animals and the environmental studies in North America and New Zealand were based on exposure to the formulated product. The hazards of the "mixture" have been investigated and taken into account in the risk assessments. All these studies suggest mild irritation as the major hazard of Foray 48B that manifests at high exposure doses.

It seems curious to argue on the one hand that studies should be conducted on mixtures because of the possible interactions between the different components, and on the other hand when such studies show no or minimal effects, to argue that one needs to know the individual components and their hazards.

6. *Failure to determine the effects of ongoing low dose exposure, as opposed to one off exposure to toxic levels, when it is known that this can result in chemical sensitivity.*

Three issues appear inherent in this dot point; firstly, differences between acute and chronic exposure (ongoing), secondly, the shape of dose response curves at low doses; and thirdly chemical sensitivity and its causes.

With respect to acute versus chronic exposure, it is well established that adverse effects can result from chronic doses that are much lower than a single acute dose or doses over a much shorter period. Also the mechanisms of toxicity can be quite different for effects after a single dose and for effects after repeated dosing.

Acute toxicity in animals is generally measured in term of lethality, signs and symptoms of intoxication and postmortem examinations after one dose and observation for 14 days. Acute studies also provide valuable information on choosing doses for repeat dose studies.

Chronic exposure in risk assessment terms is considered to be a lifetime exposure. Hence Tolerable Intakes are expressed as daily doses for a 70-year lifetime. In toxicological terms, chronic exposures are those lasting longer than six months. In this context, exposure over 6 – 8 weeks every 5 – 7 days could not be regarded as chronic, but rather sub chronic. The term ongoing can thus be misleading as it could mean 2 – 3 doses equally as 25,000 daily doses over a lifetime.

Notwithstanding the semantics, animal and human studies of ongoing exposure with the end use formulation suggest that mild irritation is the major effect likely to be seen with exposure to sufficiently high dose of Foray 48B.

Regarding the shape of the dose response curve at low doses, Watts (2003) raises the issue of dose responses that have the appearance of an inverted U and infers that toxic effects could result from exposure to low doses even though no or minimal toxicity occurs at comparatively higher doses.

The only clearly established case in which toxicity decreases with increasing doses is the case of essential elements, for which deficiency causes toxicity hence as the dose increases the toxicity decreases. In this case, excess also causes toxicity, with an amount between the deficiency and the excess at which the biological systems function best, ie, a U shape curve.

Watts (2003) quotes the following on page 21 of the document as evidence for the assertion: '*Colborn et al. (1996, p170) concluded that "neither linear nor always moving in the same direction, the inverted U seems characteristic of hormone systems and it means that they do not conform to the assumptions that underlie classical toxicology—that a biological response always increases with dose."* (Italics added)

It is worth noting that there are vast differences between toxicological and biological responses – the two terms are neither synonymous nor interchangeable, albeit they may have features in common..

Apparently, the reason why this is raised with the respect to Foray 48B is because a component of the formulation may exhibit endocrine activity under some experimental condition and inverted U shaped dose response curves have been shown in a few experiments with hormones or their agonists. This is not compelling evidence or argument that the toxic dose response to Foray 48B at low dose will exhibit the inverted U shape characteristics. It is difficult to envisage how a product such as Foray 48B for which there is no evidence of adverse effects when given to humans or animals in gram quantities can cause adverse or toxic effects when exposure doses are in microgram quantities.

With respect to chemical sensitivity and its causes, it is not clear whether Watts (2003) is referring to chemical sensitisation or the condition known as multiple chemical sensitivity. Benchmark Toxicology Services is unable to comment on the latter as it does not fit conventional toxicological models, but appears to be a medical problem, hence outside its area of expertise. With respect to chemical sensitisation, the data reviewed does not suggest that Foray 48B would cause chemical sensitivity.

Watts (2003) also raises the issue of using occupational data to assess risks to environmental exposures. Benchmark Toxicology Services concurs that workplace exposure standards are not adequate for assessing risk in the community. They are designed for a different purpose, including protection of a more homogenous group than the community in general. However, the result of epidemiological or health studies in the workplace can be used to assess health risk in the broader community provided the differences in the exposure groups are recognised and appropriate measure to address them are instituted.

A number of other issues raised by Watts (2003) have been addressed by Anonymous (2003) and will not be addressed further, except to say that BenchMark Toxicology generally supports the comments by Anonymous (2003).

Overall, Watts (2003) attempts to show that the health risk assessment and the health surveillance undertaken for these projects are inadequate because they do not take a sufficiently conservative approach in assessing the health risks to the most exposed and most sensitive individual in the community and that it does not provide any certainty in the predictions or outcomes. In addition, that value systems can greatly influence the outcomes because adequate amounts and quality of data are seldom available for assessments. The critique is unbalanced, focussing on the areas of greatest uncertainty, but not providing an alternative approach.

Unfortunately the document is adversarial and introduces an opposing value system and bias into the scientific debate that does not add value to the process informing the community, rather it unnecessarily provides grounds for fear and anxiety, the effects of which could be much more serious and debilitating than any theoretical risks of slight and reversible effects by the chemical components of Foray 48B.

Watts (2003) is highly critical of the data and outcomes of the risk assessment – and rightly so. Such processes need to stand up to scrutiny, as transparency and accountability are an extremely important aspect of the risk assessment process and its application. However, the same degree of scrutiny and rigour is not applied to data quoted to support the alternative views expressed in the document.

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## APPENDIX C

### Estimates of exposure

No quantitative estimates of exposure were attempted in any of the risk assessments undertaken in New Zealand for the Foray Spraying programmes.

It would be very difficult to estimate exposure with any degree of precision from aerial spraying of Foray 48B. Even with individuals wearing personal monitors 24 h per day that measured the amounts ingested, inhaled or that landed on uncovered skin, there would be uncertainties about monitoring for the most appropriate substance, degree of absorption through the various routes, and local and systemic effect, just to name a few.

However, it is possible to make broad estimates of what the largest exposure dose would be, given some assumptions about exposed individuals. This will provide an estimate of the worst possible situation and is useful in identifying whether or not there might be cause for alarm.

If the predicted outcome is that the exposure is insufficient to cause any adverse effects, then no further refining of the exposure assessment is required because all individuals are likely to be exposed to less pesticide than was assumed in the calculation.

If the predicted outcome is that the amounts might cause harm, then a better estimate of the exposure would be required to assess whether the amounts to which individuals are likely to be exposed will cause a problem.

### General Assumptions

The following estimates are based on the assumptions that the calculated dose is ingested, inhaled or absorbed through the skin or other organs completely (100% bioavailability), either through each route of exposure individually or through all three routes of exposure combined for each of the 30600 inhabitants estimated in the area to be sprayed.

In addition, initially it is assumed that the estimated dose mass or volume relates to the formulation or each of the individual components.

Estimates will also be derived using the approximate formulation break down provided by ARPHS (2003). Namely, 2% *bacillus thuringiensis subsp. Kurstaki* spores, 20% spent medium, 20% inert ingredients and 50% water.

Other assumptions are outlined in the following tables.

### Case Study 1. Theoretical Estimation of a bolus dose.

Table 1 outlines the estimation of the dose assuming that the amount of Foray 48B to be applied to the 1250 hectare area would be divided equally and given to each resident as a single bolus dose (ie, the total amount of 6875 L to be applied divided by the 30,600 people estimated to be in the area). The doses are estimated for adults and children. Except for local effects, such as irritation, the route of exposure is essentially irrelevant for this exercise.

At an average application rate of 5.5 L/hectare, the application rate is 225 mL per person. Assuming that 1 mL weighs 1 gram, and the applied Foray 48B translates into a bolus dose of 225 g/person every 5 – 7 days, ie 32 – 45 g/day. On a body weight basis the doses are 3.2, 4.5 and 22.5 g/kg for a male adult, female adult and a child, respectively, every 5 – 7 days. This is within the range of the toxicological profile for an unscheduled product of low acute toxicity and LD<sub>50</sub> values greater than 5000 mg/kg (> 5 g/kg).

The estimated doses are up to 225 times higher than the dose of formulated product given orally to 18 volunteers (1 gram each day for 5 days,  $3 \times 10^9$  spores/g) in which there were no adverse effects either at the time of dosing or 4 - 5 weeks later (Fischer and Rosner 1959, reviewed by ARPHS, 2003); up to 45 times higher when expressed on a daily basis over 5 days. These same authors report that 24 g given orally as a single dose to rats had no effects (equivalent to a dose of 50 g/kg for a 500 g rat and 120 g/kg for a 200 g rat).

These estimated amounts are likely to cause irritation.

**Table 1. Theoretical Estimation of a bolus dose of Foray 48B**

			ARPHS Formulation		
			BTK	Inert	Broth
Area of Application	1250 hectares	12,500,000 m <sup>2</sup>	Mg/kg/day		
Rate of Application	5.5 L/hectare	0.55 mL/m <sup>2</sup>			
Frequency of Spray	Every 5 -7 days		2%	20%	20%
Number of Application	8	Max over 8 weeks			
Number of people exposed	30,600	24.48/hectare			
		1/408 m <sup>2</sup>			
Foray 48B/person	225 mL/person	225 g/person*			
Average over 5 days		45 g/person/day*			
Adult Male (70 kg)	3.2 mL/kg	3.2 g/kg*			
		640 mg/kg/day	12.8	128	128
Adult Female (50 kg)	4.5 mL/kg	4.5 g/kg*			
		900 mg/kg/day*	18	180	180
Child (10 kg)	22.5 mL/kg	22.5 g/kg*			
		4.5 g/kg/day	90	900	900

\* 1 mL = 1 g

This is a totally unrealistic exposure scenario as it would be impossible for any individual to be exposed to such amounts of Foray 48B by any route or combination of routes of exposure as a result of the aerial spraying. However, it serves to show that even under such an extreme and unrealistic scenario, the estimated doses are within the same order of magnitude as the single bolus doses that cause no serious toxicity in experimental studies in animals and humans.

For the individual groups of components, the bolus dose averaged over 5 days is estimated to be 12.8, 18 and 90 mg/kg/day for a male adult, female adult and a child, respectively, for *bacillus thuringiensis subsp. Kurstaki* (2% of total), and 128, 180 and 900 mg/kg/day for a male adult, female adult and a child, respectively, each for the inert ingredients and the spent broth fraction (20% of total).

### Case Study 2. Theoretical Estimation of Inhalational exposure

Estimates of doses of Foray 48B by inhalational exposure after spraying are summarised in Table 2. The calculations assume that the pesticide is evenly distributed in an air shed, the dimensions of which are 1250 hectares by 50 m ( $625 \times 10^6 \text{ m}^3$ ). The minimum height at which the plane will fly is 45 m;

therefore, it is reasonable to assume the application will occur on average around 50 m above ground.

The daily exposure dose is estimated to be 253 mg/day, which equates to approximately 3.6, 5 and 25 mg/kg/day for a male adult, female adult and a child, respectively.

If we assume, that an equal amount is ingested or absorbed through the skin, then the daily intake over the spraying period will be three times these amounts, ie, approximately 11, 15 and 75 mg/kg/day for a male adult, female adult and a child, respectively, by inhalation, through ingestion and on the skin.

Thus the highest estimated total daily dose under this scenario is 75 mg/kg/day for a child. This is about 5 times higher than the daily dose ingested by volunteers (14.3 mg/kg/day) in the study above.

The estimates derived under this scenario are more realistic than the estimates of bolus dose. Nonetheless, they are still conservative overestimations of the likely exposure that would occur.

**Table 2. Theoretical Estimation of inhalation exposure after aerial application of Foray 48B**

Area of Application	1250 hectares	
Height of application	50 m	
Volume of air shed	625,000,000 m <sup>3</sup>	
Rate of Application	5.5 L/hectare	
Total volume of Application	6875 L	
Concentration in air		11 x 10 <sup>-6</sup> L/m <sup>3</sup>
		11 µL/m <sup>3</sup> **
		11 mg/m <sup>3</sup> **
Respiratory Volume*	23 m <sup>3</sup> /day <sup>2</sup>	
Exposure Duration	24 h/day	
Intake Foray 48B	Each day	253 mg/day
Adult Male (70 kg)		3.6 mg/kg/day
Adult Female (50 kg)		5 mg/kg/day
Child (10 kg)		25 mg/kg/day

\*: Respiratory volume is less for a child, eg US EPA (2000)<sup>3</sup> uses default value of 8.7 m<sup>3</sup> for a child 1 - 4 years-old, the 23 m<sup>3</sup> is used for all three groups for simplicity.

\*\* : one millilitre = one gram

### Case Study 3. Estimation of Exposure from Environmental Studies

The estimates summarised in Tables 3 and 4 are derived from the environmental monitoring results reported and discussed by Teschke *et al.* (2000) and the viable spore concentration in formulated Foray 48B described by Fischer and Rossner

<sup>2</sup> EnHealth Council (2002). [Environmental Health Risk Assessment - Guidelines for assessing human health risks from environmental hazards](#). (Accessed 29 October 2003)

<sup>3</sup> <http://www.epa.gov/pesticides/op/ddvp/sapresin.pdf> (accessed 29 October 2003).

(1959)<sup>4</sup> as reported by ARPHS (2003). The highest air concentration reported either inside or outside dwellings (1600 CFU/m<sup>3</sup>) was used in the estimate.

The following assumptions were used:

- The viable spores concentration in air is proportional to the concentration of Foray 48B or its constituents (3 x 10<sup>9</sup> CFU/gram)
- The calculation will also be done for spore concentrations of 3 x 10<sup>8</sup> CFU/gram and 3 x 10<sup>7</sup> CFU/m<sup>3</sup>/m<sup>3</sup> (10 - 100 times lower) because the concentrations can vary in different batches and over time relative to the other ingredients
- Exposure to 1600 CFU/m<sup>3</sup> is 24 h/day for the duration of the programme
- 100% of the particles are of respirable size
- Exposure is by inhalation, by ingestion and through the skin
- Bioavailability is 100%. The calculated dose is totally absorbed systemically through each route.

**Table 3. Estimation of exposure to Foray 48B after aerial spraying based on monitoring results of Teschke *et al.* (2000)**

Assumption	Resident	Workers <sup>5</sup>		Worker/Resident	
		High	Low	High	Low
Concentration (CFU/m <sup>3</sup> )	1,600	200,000	18.5 x 10 <sup>6</sup>		
Exposure duration (h)	24	8	8		
Respiratory Volume/24 h	23	23	23		
% Respirable particles	100	100	100		
Daily Intake (CFU/day)	36,800	1.53 x 10 <sup>6</sup>	1.42 x 10 <sup>8</sup>	42	3854

From table 3, it can be seen that each residents would be exposed to approximately 40 times less Foray 48B at 1600 CFU/m<sup>3</sup> than workers exposed to 200,000 CFU/m<sup>3</sup> (the lowest concentration measured during the spray operations). When compared to the highest concentration to which workers were exposed, the exposure margin was over 3800. The irritant effects that were reported by Noble *et al.* (1992) mostly likely occurred at exposure to the higher concentrations; hence they are very unlikely to be reported in residents at these estimated levels of exposure.

For inhalational exposure, residents would need to respire the amount of pesticide formulation in the air for at least 40 days continuously to have a total intake equivalent to that of workers exposed to the lowest concentration during an eight-hour shift.

<sup>4</sup> The only study that was identified in which the dose can be related to both to the number of spores present and the mass of the formulation is the study by Fischer and Rosner (1959) that was reviewed by ARPHS (2003) – 3 x 10<sup>9</sup> viable spores of *bacillus thuringiensis subsp. Kurstaki* per gram of formulation. The concentration of spores in each formulation batch is likely to vary by orders of magnitude, and it is possible that the number of spores in current formulations is lower than at the time of the study. Accordingly the estimates will be calculated using the concentration reported by Fischer and Rosner (1959) and a concentration up to 100 lower.

<sup>5</sup> Noble MA, Riben PD, Cook GJ. (1992) *Microbiological and Epidemiological Surveillance Programme to Monitor the Health Effects of Foray 48B BTK Spray*. Report to the Ministry of Forests, Province of British Columbia. Vancouver: University of British Columbia (as reported by Teschke *et al.* (2000)).

The estimated doses in table 4 are expressed as mass of Foray 48B per unit mass of body weight ( $\mu\text{g}/\text{kg}/\text{day}$ )<sup>6</sup>. The daily intakes by inhalation are estimated to be 0.2, 0.3 and 1.2  $\mu\text{g}/\text{kg}/\text{day}$  for a male adult, a female adult and a child respectively (using a conversion factor of  $3 \times 10^9$  CFU/gram of Foray 48B), and 10 times higher if a conversion factor of  $3 \times 10^8$  CFU/gram of Foray 48B is used to estimate the concentration of the spray. Relative to the sprayers exposed a child would be exposed to a dose 6 and 563 lower than the low and high exposures by workers (assuming all male workers).

**Table 4. Estimated Dose of Foray 48B (ng/kg/day) after aerial spraying**

Assumption	Foray Concentration in air (CFU/g)				
	$3 \times 10^9$			$3 \times 10^8$	$3 \times 10^7$
	Resident High	Worker Low	Worker High		
Daily Intake					
CFU/day $\times 10^3$	36.8	1530	142,000	36.8	36.8
mg/day	0.012	0.51	47	0.12	1.2
$\mu\text{g}/\text{day}$	12	511	47,278	120	1200
Adult ♂ ( $\mu\text{g}/\text{kg}/\text{day}$ ) *	0.2	7	675	2	20
Adult ♀ ( $\mu\text{g}/\text{kg}/\text{day}$ ) *	0.3	10	945	3	30
Child ( $\mu\text{g}/\text{kg}/\text{day}$ ) *	1.2			12	120

\*: Number rounded off

### Inhalation of Propylene Glycol

The community groups identified propylene glycol as a substance of concern. The estimated total inhalational, daily dose of Foray 48B under this scenario for a child (1.2  $\mu\text{g}/\text{kg}/\text{day}$ ) is about the same as the inhalation reference dose ( $R_fD_i$ ) for propylene glycol of 0.86  $\mu\text{g}/\text{kg}/\text{day}$  set by the US EPA (Appendix B, page 12). Hence any polyethylene glycol if present will be well below the tolerable intake.

### Discussion and Conclusions

It is considerably difficult to estimate exposure to Foray 48B from aerial spraying. Benchmark Toxicology Services has estimated exposure doses using three case studies.

In case study 1, it was assumed that the total amount sprayed over the spray area would be equally internalised in its totality by the exposed residents as a single bolus dose. Under these very extremely improbable events the total daily dose is only about 40 times the dose used experimentally in humans by the oral route that was without effect and within the same range of single doses in animals that did not cause overt toxicity.

Thus, even under this most improbable, if not impossible exposure scenario, the amounts of Foray 48B may be sufficient to cause irritation but not other adverse effects.

In case study 2, it was assumed that the spray would be dispersed in an air shed over the spray area within the flight path of the plane and the area to be sprayed and that the complete aerosol would remain suspended and respirable between applications. Under this exposure scenario, the maximum dose for a child by all three routes of administration was 75 mg/kg/day and about 6 times higher than the dose found to have no effect in human studies.

<sup>6</sup>  $\mu\text{g}$  (microgram) is one millionth of a gram ( $10^{-6}$  g)

In case study 3, environmental levels of viable spores of *bacillus thuringiensis subsp. Kurstaki* measured after aerial spraying of Foray 48B in Canada were used to estimate exposure in residents in the spray areas. Using this exposure scenario, a child would be exposed to a maximum dose of about 1 µg/kg/day, a level lower than the concentrations that caused irritation but no other effects in ground sprayers in Canada. If a spore concentration of  $3 \times 10^7$  is used for the calculation of the air concentrations then the highest dose would be 100 µg/kg/day.

Each of the three approaches is progressively less conservative, but overall still far from realistic so that exposure is in all likelihood overestimated considerably. BenchMark Toxicology Services estimates that using more conventional default assumptions normally used for risk assessment would result in dose estimates at least 100 times lower than shown here.

The child (toddler) has been used as the most sensitive receptor and estimates of inhalational exposure are based on the respiratory volumes that are three times higher than the default value used by the US EPA for the same aged child.

Except for case 1 in which exposure was to a bolus dose, exposure to the highest concentration reported or the highest exposure scenario has been considered for community exposure for 24 h/day over the duration of the programme. When comparing the exposures in the community with exposure in workers, the highest levels recorded for exposure of the community have been compared with the lowest exposed workers.

Assumptions of 100% respirable droplets by inhalation and 100 % absorption through the three routes of exposure are also an overestimate.

The estimated doses are applied to Foray 48B formulation and equally to its constituents. Thus exposure to each for the individual constituents would be lower than indicated, probably at least one order of magnitude.

### **Conclusions**

The results indicate overall, that the community in the area to be sprayed is unlikely to be exposed to a sufficiently high amount of Foray 48B, either through inhalation, ingestion or the skin, or a combination of all three routes, that would cause adverse effects on their health. The estimated exposures are too low to cause any irritation of mucous membranes, eyes or the skin which is the only clearly demonstrated hazard of Foray 48B.