

OFFICE OF THE PRIME MINISTER'S CHIEF SCIENCE ADVISOR

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Methamphetamine contamination in residential properties: Exposures, risk levels, and interpretation of standards

Draft Report

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Table of Contents

1	Background3
	Methamphetamine: therapeutic use to drugof abuse3
	The methamphetamine problem in New Zealand
	Trends in methamphetamine manufacturing4
	Detecting methamphetamine in houses4
	Misunderstandings of hazard, exposure and risk4
	New Zealand guidelines and standards
2	Methamphetamine contam <mark>ination: what's the issue</mark> ?6
	What does methamphetamine contamination really mean?
	How does contamination happen?
	Is contamination different between meth labs and dwellings used for smoking?7
	What does this difference mean for health risks?7
3	Establishing health-based standards for methamphetamine exposure8
	Toxicity assessments
	Estimating passive exposure doses to establish remediation guidelines10
	New Zealand risk assessment11
	The New Zealand standard12
	Comparison of the guidelines
	Alternative calculations of risk levels
4	Are there health risks from passive methamphetamine exposure?
5	
	nd contemination

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Page 1 of 2

Risks in perspective	
Is the current approach in New Zealand commensurat	e with the risk?1
Implications for methamphetamine screening in affects	ed properties1
Problems with field composite screening	<u>1</u>
Recommendations	1
6 Conclusions	1
7 Appendix	2
7.1 Establishing threshold doses for methamphetamin	e2
California: Reference Dose	2
Colorado: Health-based reference value	2
7.2 Why are there so many different remediation guide	eline levels?2
7.3 Conservative assumptions of exposure dose mode	els
Toxicity assessments	2
Exposure assessments	2
7.4 Contamination level at which Colorado's health-ba	sed reference value is reached 2
8 References	2

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Page 2 of 26

1 Background

Methamphetamine: therapeutic use to drug of abuse

Methamphetamine belongs to a class of drugs called stimulants. It is a legally prescribed medication in the United States for the treatment of attention deficit hyperactivity disorder (ADHD), obesity, and narcolepsy. It affects the brain and central nervous system by increasing the amount of dopamine, a chemical associated with pleasure and reward, in the brain.

Because of its stimulant and euphoria-inducing properties, methamphetamine is commonly used as a recreational drug. It is usually smoked from a glass pipe, but it also can be injected, snorted or swallowed. In the short-term, users experience symptoms such as increased heart rate, attention, and wakefulness, agitation, and decreased appetite. Longer-term use results in a constellation of side effects involving physical (weight loss, cardiovascular and organ damage), mental (anxiety and confusion, psychosis), and behavioural (a tendency towards recklessness and violence) aspects [1].

Methamphetamine is highly addictive, so recreational use in most cases leads to continual drug-seeking behaviour and drug abuse. Once addicted, abusers require repeated and ever-increasing doses to achieve a 'high'. Addicts often turn to crime to support their habit. There is a significant criminal activity associated with importing or manufacturing and selling the drug. These factors further percelulate the problem in the community.

The methamphetamine problem in New Zealand

Methamphetamine is not used therapeutically in New Zealand; it is classified as a Class A controlled drug under the Misuse of Drugs Act 1975. Due to the sevently of the potential health risks posed by its abuse, and the immense social costs and downstream burden on wider society, particularly the health and law enforcement systems, it carries severe penalties for possession, supply, and manufacture. Possession of as little as 5 grams (a tablespoon) is enough to warrant a conviction for possession for the purpose of sale or supply.

In New Zealand methamphetamine is commonly known as 'P', 'meth', and 'ice'. It is obtained either through smuggling into the country, or by being manufactured locally in clandestine laboratories (so-called 'clan labs' or meth labs) using common household equipment and accessible chemical ingredients.

New Zealand drug use surveys suggest that methamphetamine use and availability are increasing, and that prices are declining [2], Gangs and professional drug dealers appear to have growing involvement in its supply [3]. Remarkably, methamphetamine appears to be more easy to obtain than cannabis throughout the country [4].

While methamphetamine supply seems to be plentiful, the number of confirmed meth labs detected has been decreasing in recent years. Seventy-four meth labs were identified in 2016, of which 50 were rental properties and 4 were Housing New Zealand properties [5]. Preliminary data suggest that border seizures of ephedrine, the main precursor used for cooking methamphetamine in New Zealand.^a have declined. This may reflect a preference

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Page 3 of 2

for obtaining fully synthesised methamphetamine from overseas rather than manufacturing locally. Nonetheless, small-scale meth labs are still likely to be active throughout New Zealand. These meth labs may be found in residential dwellings, commercial accommodation, and even vehicles.

Trends in methamphetamine manufacturing

Traditional methamphetamine manufacturing methods involve a range of hazardous (caustic and corrosive) chemicals and solvents. When heated and volatilised during a methamphetamine 'cook', these highly toxic substances contaminate the immediate area and can spread through the dwelling. Exposure to such contaminants, either by being present during the production process (and thus likely inhaling volatile loxins in the air), or by coming in contact with contaminated surfaces, poses a significant health risk.

However, following a number of restrictions on the sale of solvents and certain precursor chemicals, production methods changed in New Zealand. Now the most commonly used methods do not use solvents, and the reaction is mostly performed by distillation with water in contained vessels that do not emit furnes. The primary contaminant associated with this manufacturing method is methamphetamine itselffed.

Detecting methamphetamine in houses

Negative perceptions around methamphetamine have extended from societal worries about the drug culture liself, to the effects left behind by its participants, including traces of the drug in houses where it has been smoked. Media coverage of gang involvement in supply, and criminal behaviour and serious health harms following severe methamphetamine abuse, has likely contributed to the overall perception that any contact with methamphetamine is inherently dangerous.

Techniques developed for forensic analysis to identify clandestine meth labs have evolved to a high level of sensitivity that can detect very low levels of the drug and its precursors on surfaces, to aid in the investigation of lilicit drug production activity. These techniques have increasingly been used in New Zealand to detect methamphetamine in houses, regardless of whether or not criminal manufacturing activity is suspected, and an industry of operators that test and remediate contaminated dwellings has flourished. This industry is currently unregulated [including light-production-level industry in the support of th

The extensive publicity surrounding methamphetamine contamination, fuelled by industry claims of the high health risks posed by living in dwellings where residues of the drug can be detected, has led to considerable alarm especially amongst tenants, landlords, and potential home buyers and property investors. Evidence of contamination is placed in Land Information Memorandum (LIM) reports, which impacts on property values. Outrage over the possibility of innocent parties being put at risk by the irresponsible and illegal actions of others is compounded by a lack of knowledge about the effects of chronic low-level exposure, and an assumption that the presence of any level of residue would have adverse health effects.

Misunderstandings of hazard, exposure and risk

Concerns around the methamphetamine contamination issue in New Zealand appear to be particularly large compared to other jurisdictions, and likely stem from misunderstandings about the concepts of hazard, exposure and risk.

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Page 4 of 26

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^aUse of pseudoephedrine as a precur<mark>sor has n</mark>ot been common in NZ since it was reclassified from a class C to a class B2 controlled drug in 2011, meaning it can only be obtained via prescription.

The risk posed by a hazardous substance (that is, a source of potential harm) depends on how toxic it is, and the level of an individual's exposure and sensitivity to it(Figure 1). For exposure, things to consider include the amount of a substance a person is exposed to, how they are exposed (the route of exposure – for example through the skin, or inhaling or ingesting the substance), and how long they are exposed.

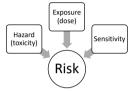


Figure 1: Risk of a hazardous substance is dependent on levels of both environmental exposure and individual sensitivity, as well as the substance's inherent toxicity.

In this context, two interrelated factors have been mostly absent from the discourse on methamphetamine contamination. The first is the level of methamphetamine found in affected dwellings, which dictates how much exposure a person can have by living there and coming in contact with the affected surfaces. There is widespread misperception that any methamphetamine-related activity in a dwelling, no matter how low the level, results in contamination that is a potential health concern. However, generally speaking, the mery presence of methamphetamine does not present a health risk; it only poses a risk if there is a realistic route and duration of exposure, and the doses are high enough throughout this exposure to have a physiological effect.

The second factor is whether the dwelling had been used for methamphetamine manufacture (which may also involve smoking) or for smoking alone. This distinction is about what hazards may be present. Dwellings used for manufacture, depending on the process used, may pose risks from a number of hazardous chemicals and by-products of production of the drug. In contrast, with smoking the potential hazard is methamphetamine itself, residues of which may be deposited on surfaces near where the activity occurred. The risk will be based on whether the levels are high enough to result in physiological effects (and what those effects are) in individuals exposed to them through skin contact or ingestion via hand-to-mouth transfer from contaminated surfaces. These issues are expanded upon in sections 2, 3 and 4.

New Zealand guidelines and standards

Because of the known, risks of exposure to traditional methamphetamine manufacturing chemicals and solvents, guidelines have been developed internationally around cleaning of contaminated premises after a meth lab has been discovered. These guidelines use the detection of methamphetamine below a specified low level after remediation as a signal that other contaminants have been sufficiently cleaned away.

In New Zealand, prior to June 2017, the threshold of residue levels at which a dwelling was considered to be 'contaminated' and thus require clean-up, was based on the 2010 Ministry

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Page 5 of 2

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Just an FYI that there may be one possible exception to this in an Australian document, where I suspect the testing industry has not gone feral in the same way as NZ's has. The document (not sure of its status) is the 2011 one ralled:

Clandestine Drug Laboratory Remediation Guidelines, attributed to the Australian Crime Commission

Although the document title is definitely about labs, some of the content seems to argue that smoking is as bad and the same rules should apply when it comes to meth residues:

Studies have also established that smoking methylamphetamine will likewise contaminate the inside surfaces of buildings with methylamphetamine. Regardless, the presence of methylamphetamine on inside surfaces at a level of greater than 0.5 micrograms (µg) per 100 methylamphetamine on inside surfaces at a

This document can be hard to get because of website restructuring. The link here should lead to it:

https://www.homeaffairs.gov.au/crime/Documents/cland estine-drug-laboratory-remediationguidelines.pdf#search=Clandestine%20%20%20Drug% 20%20%20Laboratory%20%20Remediation%20% 20Guidelines

I think much of the Australian tox guidance has gone through as largely unchallenged recommendations. It seems to heavily on the opinion of Jackie Wright of Environmental Risk Sciences Pty Ltd. Shethey seem to have had a lot to do with the Australian numbers and were also origin of the first N2 O.5 value, which was taken from a draft report (for which I could find no peer review).

of Health Guidelines for the remediation of clandestine methamphetamine laboratory sites[6]. The guideline's cut-off value was 0.5 µg of methamphetamine per 100 cm² surface area, which was derived directly from an Australian assessment for meth labs[7], and is considered to be very conservative – there is no evidence that chronic exposure to methamphetamine at levels several times higher than this will lead to adverse health effects. Nonetheless, this guideline provided a benchmark that was then used by the methamphetamine testing industry to signal that testing and remediation was necessary, and led to the belief that even low levels of methamphetamine were potentially dangerous. It began to be used to test large numbers of houses for any traces of methamphetamine. Despite the clean-up guidelines applying specifically to former meth labs, these types of properties became conflated with properties unlikely to have been used for manufacture, leading to much confusion.

This threshold resulted in numerous properties testing positive for methamphetamine. The efforts of Housing New Zealand to test for methamphetamine and remediate properties exceeding the guideline, incurring large expenses and resulting in removal of numerous properties available for habitation, have received intense media scrutiny. Emotive stories, such as of tenants being evicted or of young families feeling unable to move into newly purchased properties following detection of methamphetamine residues, have also been reported. Fears aroused by the messagesthat any detectable level of methamphetamine presented a risk that needed to be remediated may have led to reporting of health affects believed to be attributed to methamphetamine contamination.

A New Zealand Standard released in June 2017[8] adopted a higher – but still conservative – clean-up <u>guideline levelof 1.5 µg/100 cm²</u>, without distinguishing between former meth labs and non-meth labs. At the time of writing, this standard has not yet been cited in an Act or Regulation, and is therefore not yet legally enforceable. The higher level of methamphetamine allowable in the new standard has meant that a considerable number of properties that were previously designated as needing remediation were now considered safe to occupy. However, this does not mean that levels above the standard's threshold are necessarily *unsafe*. In fact, detecting levels above this should not be a cause for alarm, unless other factors suggest that methamphetamine manufacturing activity has taken place within the dwelling. This report aims to explain this distinction more thoroughly.

2 Methamphetamine contamination: what's the issue?

What does methamphetamine contamination really mean?

In this report, the term 'contamination' is used to refer to the presence of methamphetamine as a non-natural substance. It is not intended to imply that levels are high, or, importantly, that any health risk is posed

In New Zealand, the term 'methamphetamine contamination' has been taken well beyond its use in other countries. Where in other places the concern is primarily about what is left behind after methamphetamine has been manufactured in a dwelling, here the issue has been taken more broadly to concern all levels of detectable methamphetamine.

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Page 6 of 26

How does contamination happen?

Methamphetamine residue can be deposited on surfaces within dwellings in areas where the drug has been 'cooked' or smoked. Some surfaces may be more contaminated than others, depending on how close they were to the activity, and how frequently the activity was carried out. Methamphetamine residues can be detected on surfaces only at trace levels by assays that report levels generally in the range of 0.01–1,000 μg of methamphetamine per 100 cm² surface area (ref 25, cited in [9]).

Is contamination different between meth labs and dwellings used for smoking?

Manufacture and smoking have different implications for health risks, because while both result in surface contamination by methamphetamine, the former activity potentially involves additional risks posed by residues of other hazardous chemicals used in the manufacturing process. The specific range (and levels) of additional contaminants that may be present in the dwelling depends on the method of manufacture and rigour of the process [10], and toxicity assessments on these contaminants have been made [7].

It is important to note that in New Zealand, methamphetamine has long been manufactured mostly using small, purpose built metal cylinders, and involving solvent-free methods [9]. Various chemical reactions that occur during manufacture are contained within this sealed pressure vessel, which, unlike traditional glassware setups, prevents the release of associated fumes and contaminants. This method of manufacture only releases methamphetamine and very small amounts of various by-products during the later phases of the manufacturing process [9]

Nevertheless, manufacture in general results in greater contamination levels for methamphetamine than smoking alone [11]. Experiments involving simulated *smoking* of methamphetamine found that contamination levels decline markedly over a few days [9, 12]. Samples taken soon after a <u>simulated</u> smoking' <u>session</u> estimate that a single session may result in levels lower than 0.1 µg/100 cm², and multiple sessions, 1.5–5.1 µg/100 cm²[11]. These levels were calculated using conservative measurements, and are likely to overestimate levels arising in practice.

Methamphetamine levels that are observed in known-former meth labs are substantially higher than these. Forensic work by the Institute for Environmental Science and Research (ESR) suggests that levels of methamphetamine can be assessed against an 'excessive' threshold that is indicative of manufacturing activity[9]. A US study has reported levels typically higher than 25 μg/100 cm²(13), and New Zealand ESR data from 136 meth labs found an average level of 54 μg/100 cm², with about 25% of samples exceeding 30 μg/100 cm²(9]. The ESR data suggests that in a 20 m² room, a level of 30 μg/100 cm² would require around 1,500 smoke sessions. Hence, levels around or exceeding 30 μg/100 cm² are regarded as strongly suggestive of manufacturing activity.

What does this difference mean for health risks?

Although it is not possible to conclusively determine whether a dwelling had been used for manufacture or only for smoking based solely from the methamphetamine levels found, it is reasonably straightforward to determine the health risks involved. Assuming that the same

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Page 7 of 2

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"It is important to note that in recent years, the preferred means of methamphetamine manufacture in New Zealand has become a solvent-free method that relies on small, purpose built metal cylinders."

level of methamphetamine residue has been found in two different dwellings – one used only for manufacture, and the other only for smoking – then the health risk posed by methamphetamine tiself is the same in both dwellings

In theory, a former meth lab may potentially have other contaminants that contribute to the health risk. In cases where there are signs of traditional manufacturing activity, these may be of concern if high levels of methamphetamine contamination indicate that cleaning has not been done. However, since methamphetamine levels are considered a marker for the levels of other potential contaminants, a former meth lab containing low levels of methamphetamine is also likely to contain low levels of other associated substances. Furthermore, the manufacturing methods most often used in New Zealand now mostly involve solvent-free distillation in sealed vessels that minimise contaminant spread, although methamphetamine (and low levels of minor by-products) is released in the salting out phase. The use of highly toxic substances such as lead and mercury has not been recorded in New Zealandf91.

Hence from a health risk perspective, ifmethamphetamine levels are low, it is likely to be immaterial whether a dwelling was used as a meth lab or not. The relevance of distinguishing between the two types of dwellings is mostly relevant for forensic and law enforcement purposes.

3 Establishing health-based standards for methamphetamine exposure

A health-based risk assessment is a process used to estimate the nature and probability of adverse health effects in people who may be exposed to chemicals in the environment. Such assessments start with a toxicological characterisation of the substance to establish whether it has the potential to cause harm (is it a hazard?), and if so, under what circumstances. This involves determining the numerical relationship between exposure to the substance and any resulting health effects, known as a dose-response assessment. After this, exposure assessments are conducted to identify the extent to which the exposure actually occurs. All of this information feeds into a risk characterisation, which forms a conclusion about the nature and the size of the risk, and whether additional risk management measures are needed.

Toxicity assessments

We know that methamphetamine has the potential to cause harm (as do most chemicals if the exposure is high enough) – but at what doses or exposures would this occur? The aim of a toxicity assessment is to establish the relationship between an adverse effect of a substance (the harm it causes) and the dose (the exposure level) at which it takes place. Then, a threshold dose can be calculated to indicate the dose that would have either no effect on human health, or represent the lowest dose at which an effect might be observed. This difference in how the threshold dose is defined is important, as it can lead to very different thresholds being calculated.

Toxicity assessments on methamphetamine have been undertaken independently by the US states of California[15] and Colorado[16, 17], for the purpose of establishing a risk-based remediation standard for methamphetamine. California developed a "Reference Dose" (RD).

Page 8 of 26

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^b Further New Zealand data are available from ref [14] which reports levels from 20 suspected clan labs, although interpretation is limited by most sites having been cleaned prior to sampling.

which is a formal toxicological measure that estimates the amount of a substance that humans (including children and other sensitive groups) can be exposed to daily, over their lifetime. without any harmful effects. Because there are no data to suggest that low doses of methamphetamine are toxic in humans, the assessment was based on a single clinical study of methamphetamine used as a weight control therapy in pregnant women in order to have a starting point from which to measure any dose effects[18]. The lowest dose that exhibited any effect in this study was 5.000 ug per day (equivalent to 80 ug/kg body weight/day for the average woman). Incorporating a large safety factor to ensure that there would be no possibility of an effect in even the most sensitive individual, the RfD was calculated to be 0.3 ug/kg body weight/day[15]. It means that an individual who may be especially sensitive to methamphetamine, such as a small child (10 kg) or a woman of childbearing age (70 kg), can respectively consume 3 µg or 21 µg of methamphetamine every day for the rest of their

In contrast, Colorado developed a health-based reference value, which indicates the lowest dose that humans (including children and other sensitive groups) can be exposed to at which the first onset of any adverse health effect may occur. This value is distinct from a RfD. which by definition is more conservative. The reference value was calculated, based on a number of animal toxicology studies, as5-70 µg/kg body weight/day (it is expressed as a range to reflect the different results from the body of studies assessed)[16, 17].Calculating from the more conservative end of this range, the lowest dose at which there is a potential for an adverse effectwould be 55 up of methamphetamine daily for a child, or 345 up daily for

A comparison of the two assessments, summarised in Table 1, and further described in Appendix 7.1, shows that the California-derived reference dose is more conservative than the Colorado health-based reference value by a factor of between 17 and 233 (depending on which end of the range - 5 or 70 µg/kg body weight/day - is taken). This means that Colorado's assessment allows for at least 17 times the amount of methamphetamine a sensitive individual can be exposed to before possible onset of a health effect. This marked difference mainly reflects the difference in how safety has been defined (i.e. level with no appreciable risk vs lowest level at first possible adverse effect), and these definitions have in turn been informed by very different types of studies (one primary human study vs multiple animal studies). It is therefore not possible to give primacy to one assessment over the other, but it should be emphasised that both assessments incorporate very conservative assumptions and a very large (~300-fold) safety factor.

Table 1: Summary of methamphetamine toxicity assessments									
	California (OEHHA)	Colorado (CDPHE)							
Measure of toxicity	Reference dose	Health-based reference value							
Definition	The dose at or below which adverse health effects are unlikely to occur	Lowest dose at which an adverse effect may occur							
Study population and effects Calculated dose (µg/kg body weight/day)	women	Developmental and reproductive toxicity in laboratory animals 5–70							

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These values can also be placed in perspective by comparison with the recommended doses for therapeutic purposes(Figure 2). Treatment of children six years and older for ADHD symptoms begins at 5,000 µg and increases to about 20,000–25,000 µg daily, while treatment of adults for obesity involves 5,000 µg per meal over a few weeks. As with most medications, therapeutic use of methamphetamine may involve side effects such as headaches and appetite loss, though it is not known how common these effects are[19].

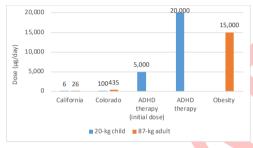


Figure 2: Comparison of maximum daily intakes derived from the California and Colorado guidelines with therapeutic daily doses for ADHD treatment in a six-year-old child or for obesity treatment in an adult. The lower end of the recommended ADHD therapy dose (20,000 ug/day) for a six-year-old child is shown. Obesity treatment dose assumes that three meals are consumed daily.

Estimating passive exposure doses to establish remediation guidelines

This section briefly describes how various jurisdictions have estimated the exposure doses of sensitive individuals to methamphetamine in remediated dwellings, and how these estimates were used to establish remediation guidelines. It is important to note that all the quidelines (except the New Zealand ESR report[20], as discussed later) have considered methamphetamine residues only in former meth labs, and that residues arising from smoking alone have not been considered.

Each agency used different mathematical models to estimate methamphetamine exposure doses. The models take numerous factors into account, such as the type of surface containing the residue (hard floors or carpets), the way exposure to residues might occur (through skin on hands and body, or through ingestion from a child's 'mouthing' activity with toys and fingers), and how frequently the dermal contact or mouthing activity might occurin scenarios that assume maximum possible exposure. Where such data were not available best estimates from a conservative standpoint were used.

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make the case or imply that traces in houses are as

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bad. See comment N4.)

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- California found that, in order not to exceed their previously determined Reference Dose of 0.3 µg/kg body weight/day for a child aged 1–2 years old, the surface concentration of methamphetamine should be no higher than 1.5 µg/100 cm²[21].⁵
- Colorado analysed 3 proposed remediation standards: 0.05, 0.1, and 0.5 µg/100 cm².
 Their modelling found that for an infant, a 6-year-old child, and a woman of childbearing age, a standard of 0.5 µg/100 cm² led to exposure doses well below the health-based reference value of \$5.000-70,000 µg/kg body weight/day,⁴
- In Australia, the government adopted a value of 0.5 μg/100 cm² as a clean-up guideline[22] – this was based on a risk assessment report that modelled estimated doses against California's Reference Dose [7].*

New Zealandrisk assessment

In 2010, the New Zealand Ministry of Health published a remediation guideline of **0.5** µg/100 cm² for former meth lab dwellings [6]. This was directly taken from the Australian risk assessment report in lieu of a separate assessment.

A 2016 ESR report[20]* commissioned by the Ministry of Health has since proposed a New Zealand-specific set of remediation standards. It estimated the total exposure doses for a young child and for an adult woman (through whom a fetus may become exposed). It also modelled the exposure doses in houses with and without carpets. In order not to exceed the California Reference Dose, the following clean-up levels were recommended:

- 2 μg/100 cm² for non-carpeted dwellings that have not been used for manufacture.
- 1.5 µg/100 cm² for carpeted houses not used for methamphetamine manufacture.
 The level is lower because carpeted floors lead to higher exposure doses.⁹

Although in theory the above guidelines are appropriate for remediated houses regardless of whether they had been used for manufacture or smoking, the report acknowledges that former meth labs carry an additional risk of additional contaminants that may have been undetected or not adequately removed during clean-up. Therefore, as a precautionary measure, the report recommended the considerably more conservative guideline of 0.5 µg/100 cm² for dwellings previously used for methamphetamine manufacture.

The rationale is that lower levels of methamphetamine are likely to indicate lower levels of other chemicals. Thus, this lower level should not be interpreted as methamphetamine per se posing a greater risk in a former meth lab. In theory, and according to the report's

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Page 11 of 2

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guidelines, a test result showing a level of 0.5–2.0 µg/100 cm² in a known former meth lab would be considered to pose no safety risk from methamphetamine itself.^h

The New Zealand standard

In June 2017, Standards New Zealand published a standard on the testing and decontamination of methamphetamine-contaminated properties (NZS 8510:2017). The standard does not focus on risk assessment or health effects, but the selection of a clean-up level was informed by the 2016 ESR report. On the basis of this report and public submissions, a single remediation level of 1.5 μ g/100 cm² was chosen, irrespective of whether the dwelling had been used for manufacture or smoking, or whether carpets are present or not!

Table 2 summarises the chosen remediation values by each agency.

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Table 2: Guidelines for maximum methamphetamine levels in remediated dwellings. All except for NZ Standards are risk-based assessments. Note that Australia and ESR based their assessments on California's more conservative reference dose.

			California	Colorado	Australia	NZ (ESR)	NZ Standards
	Former meth lab		1.5	0.5	0.5	0.5	
Guideline	Non- meth lab Carpeted Non- carpeted	Carpeted	-	-	-	1.5	1.5 (3.8 for
(μg/100 cm²)		-	-	-	2.0 (3.8* for adult	low-use areas)	

^{*} This value is higher than that for young children due to greater body weight and an assumed absence of exposure via oral ingestion.

Comparison of the guidelines

Despite the variation in recommended remediation levels (Appendix 7.2), all of the described guidelines (except the New Zealand standards) are risk-based, meaning they take into account the toxicity of methamphetamine as well as the potential levels of exposure to it.

Page 12 of 26

^cThe model also showed that the most important factor in determining overall exposure dose was the fraction of methamphetamine that is transferred from surface to skin.

d Remediation standards higher than 0.5 μg/100 cm² were not assessed.

^e This guideline is more conservative than that adopted by California, despite use of the same Reference Dose. The risk assessment report attributed this to use of a less complex model to estimate exposure doses, as well as use of more conservative estimates.

This report provided an up-to-date review of the scientific and 'grey' literature on methamphetamine, evaluated the remediation guidelines from other jurisdictions, and presented modelling work estimating exposures for the New Zealand population. It differs from other assessments by providing guidelines for both non-carpeted and carpeted dwellings, and also distinguishing between dwellings previously used by methamphetamine smokers or by methamphetamine manufacturers.

⁹ California also include carpeting in their model, but only the single guideline of 1.5 µg/100 cm² is provided.

The ESR report proposed that screening for lead and mercury, which are heavy metals that can accumulate in the body, should be undertaken in dwellings formerly used as clan labs. However as current manufacturing methods in New Zealand do not use these components[9], they are no longer considered to pose a risk unless deemed otherwise by a forensic investigator (J Fowles, report co-author, pers comm, 20 March 2018), or unless production methods change to include these components (C Nokes, ESR, pers comm, 20 March 2018).

The purpose of this standard was to provide best practice guidelines to accurately sample and effectively decontaminate affected dwellings, and to ensure that methods for testing are reliable. The wider aim was to ensure that a dwelling previously used to manufacture or smoke methamphetamine is safe for subsequent occupants.

The reasons for adopting a single level, in contrast ESR's four recommendations for specific situations, are discussed in the Standards document [8]. They generally relate to practicability, for example that not all clan labs can be easily identified, and that sampling of carpet may itself be a destructive process.

There are two important points to be noted about all of the remediation guidelines as a whole. First, from a health perspective, none should be interpreted as a specific 'threshold' that if exceeded – and particularly by a small margin – is likely to result in an adverse effect. The second point is that all ofthe guidelines can be considered to be very conservative as they are deliberately based on factors assuming 'worst case' scenarios that are unlikely to reflect a real-world situation (Appendix 7.3). It should also be noted that methamphetamine does not accumulate in the body,' and animal studies suggest that the effects in the brain from single or short-term exposure to a high dose are reversible [25].

Alternative calculations of risk levels

The ESR report calculated clean-up guidelines based on the level at which the California RID would not be exceeded. However, the ESR exposure data can also be scaled up to calculate the maximum residue level at which Colorado's health-based reference value will not be exceeded. This calculation gives a maximum acceptable contamination level of 33 µg/100 cm² for dwellings without carpets, and 23 µg/100 cm² for carpeted dwellings." These figures indicate levels above which an adverse health effect may be observed; in other words, lower levels are unlikely to have health impacts. Notably, these figures are 15–22 times as high as that adopted by Standards New Zealand.

A similar exercise extrapolating the calculated contamination level based on Colorado's exposure data and their own health-based reference value can likewise be performed (Appendix 7.4).

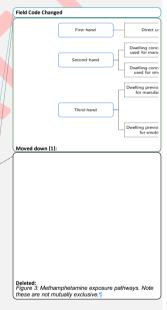
4 Are there health risks from passive methamphetamine exposure?

The health risks posed by methamphetamine depend primarily on the type and level of exposure (). The adverse effects of first-hand exposure — that is, its abuse involving large doses over a prolonged period, are well documented. In New Zealand, the number of hospitalisations attributed to methamphetamine abuse has risen dramatically between 2012 and 2016, from 51 cases to 262[5].

There are also reports of ill-health associated with second-hand exposure via residing in a dwelling concurrently or previously used as a clan lab [26, 27]. The drug can be detected in hair of exposed children [28], in whom behavioural problems are common [26], although the latter finding may be confounded by other social factors. Less is known about the effects of

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Page 13 of 2



breathing in smoke arising from methamphetamine use, and the US National Institute on Drug Abuse notes that available evidence for negativehealth effects of second-hand exposure is currently lacking[29].

In contrast, there are almost no known data relating to third-hand exposure situations, which affect a greater majority of the population — that is, non-users living in dwellings (whether remediated or not) that had been previously used only for smoking of methamphetamine (). To the best of our knowledge there is currently no available evidence in the scientific or grey literature that low-level methamphetamine exposure, involving levels that may be encountered from skin contact or oral ingestion of residues on household surfaces, posse a health risk in humans. Realistic scenarios of exposure through contact with surface residues, even for toddlers who often put their hands in their mouths, do not suggest that levels would reach close to a threshold where adverse effects would be observed.

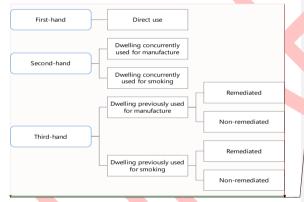


Figure 3: Methamphetamine exposure pathways. Note these are not mutually exclusive

Under the Health Act 1956, "poisoning arising from chemical contamination of environment" is a notifiable disease(30). This includes methamphetamine poisoning. Since 2013 a national register monitoring diseases, injuries and illnesses from hazardous substances has been maintained." Between 2014 and 2016, twocases of food poisoning (from the same

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Page 14 of 26

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^k The time taken for half of an orally ingested dose of 10–20 mg methamphetamine to be cleared from the body (the half-life – used in pharmacology to indicate how quickly a drug is eliminated) is about 10 hours [23], Within 24 hours, about 70% of the dose is excreted in urine [24].

J Fowles, pers comm via C Nokes, 1 March 2018.

[&]quot;ESR's exposure data show that at a contamination level of 0.1 µg/100 cm²in non-carpeted dwellings, the total exposure dose for a young child is 0.015 µg/kg body weight/day. This relationship was scaled up in a linear manner such that a dose of 0.3 µg/kg body weight/day (i.e. California's RID) would be reached at the ESR guideline of 2 µg/100 cm². Further extrapolation to a dose of 5 µg/kg body weight/day (Colorado's health-based reference value) results in a value of 33 µg/100 cm². The ESR analysis found that in a carpeted dwelling a child would reach the California RID at a contamination level of 1.4 µg/100 cm² (J Fowles, pers commvia C Nokes, 1 March 2018). Extrapolating this level in a similar manner, using Colorado's reference value, results in a value of 23 µg/100 cm².

ⁿ This surveillance system is undertaken by Environmental Health Indicators New Zealand (EHINZ), Massey University, on behalf of the Ministry of Health.

household) were attributed to methamphetamine intake via a contaminated container [31].^o

No other confirmed cases have been reported.

The Ministry of Health also notes that there have been no recorded cases in New Zealand of poisoning or injury arising from residing in dwellings that had been previously used for manufacture or use of methamphetamine. While there have been some anecdotal reports of minor ill effects associated with such dwellings, as publicised in the media, there are no reports on whether these cases have received a formal medical diagnosis, or had their causes attributed. Furthermore, the reported symptoms (e.g. asthma, skin rashse) are diverse and generally not known to be physiological effects of methamphetamine. The contribution of other common factors known to affect health, such as dampness and mould, or other chemical exposures in houses, has not been examined and may be equally or more likely explanations of the diverse symptoms claimed. Reporting of such effects to public health services appears to have declined following the introduction of the new standard (NZS8510:2017),⁹ with its higher 'contamination threshold' for a property requiring cleaning. This suggests that a significant proportion of the reports prior to this were based mainly on the perception that low levels of methamphetamine were dangerous.

There is currently very limited toxicity data that can inform the assessment of long-term environmental exposures to methamphetamine residues. Methamphetamine is not considered 'toxic' at low doses — if it was, it could not be used as a therapeutic drug for ADHD and obesity. It is not listed in hazardous substances registries such as the ATSDR (Agency for Toxic Substances and Disease Registry), an extensive database run by the US Centers for Disease Control and Prevention (CDC). However, some substances that are not toxic at low doses can accumulate in the body, causing adverse effects over time. Although there are cumulative effects from high-dose, long-term methamphetamine use due to its addictive effects, the chemical itself dose not stay in the body or accumulate to higher levels. Ingested methamphetamine is generally eliminated from the body within about a day. This means that doses or exposures that do not have an effect in the short term are not additive, and theoretically should not lead to any long-term harm.

Indeed, animal studies suggest that chronic low-dose' methamphetamine promotes brain cell development and function [32], and improves outcomes following severe traumatic brain injury [33, 34]. Clinical studies in humans with brain injury, involving multiple doses of 5,000—100,000 µg D-amphetamine (a related drug with similar effects), have not reported any adverse effects associated with the drug itself [35].

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Page 15 of 26

5 Towards an evidential and health risk-based approach for managing potential exposure and contamination

Risk is a combination of the likelihood of a negative event happening (such as coming into contact with a level of methamphetamine that would produce an adverse effect), and the consequence of that event happening (what the effects are, and how serious they are). A risk-based approach to methamphetamine contamination means that actions taken to manage the potential health risks are proportionate to the level of risk.

Risks in perspective

When thinking about how to determine whether a risk is high enough to warrant substantial remediationmeasures, it sometimes helps to compare the risk to other similar risks, and consider how they are dealt with (or not) in society. For example, we do not test for or regulate 'third-hand smoke' residues from cigarettes, which contain carcinogenic polycyclic aromatic hydrocarbons such as benzopyrene, as well as nicotine, which are measurable on indoor surfaces months after the last smoke[36, 37].Similarly, other household hazards such as mould, lead paint and asbestos pose greater health risks than third-hand methamphetamineexposure (at least in a non-meth lab environment).

With regard to methamphetamine 'contamination', there is evidence in some New Zealand communities that methamphetamine can be detected on banknotes[38, 39], and occasionally at levels close to that found in many houses currently testing 'positive' and deemed to be in need of remediation

It is also worth noting that the UK Independent Scientific Committee on Drugs found in 2010 that the overall harm caused by methamphetamine use is far outweighed by that caused by alcohol [401]

Is the current approach in New Zealand commensurate with the risk?

What we know from the preceding discussion is that the likelihood of being exposed to enough methamphetamine on household surfaces to absorb (through the skin or via hand-to-mouth activities) a quantity that would have a physiological effect is extremely low, even in young children. The effects of low-level exposure, if they occur, are likely to be transient – so generally the consequences are also low. Considering the available evidence, the perception of the risk, and the reaction to it in New Zealand, has been disproportionate.

New Zealand appears to be unique with regard to its approach to the issue of methamphetamine contamination of residential properties. While other countries and jurisdictions have also established standards for remediation of premises where methamphetamine clan labs have been identified, these standards are for the most part not used for guiding clean-up of dwellings where no manufacture has taken place. Some states in the US issue only practical guidelines for cleaning a known (former) meth lab, and do not require testing for methamphetamine levels[411].

The international guidelines use methamphetamine as a marker for the presence of other contaminants, recognising that these chemicals and solvents are the main hazards associated with clandestine laboratories. The range and levels of contaminants vary widely among meth labs, making it difficult and costly in practice to test for every single potential contaminant that may remain after clean-up. It is for this reason that an extra conservative

Page 16 of 26

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o Additional details provided by D Read, EHINZ, pers comm, 4 April 2018.

S Gilbert, Ministry of Health, pers comm, 21 Feb 2018. The Ministry has not received any notifications of poisoning arising from chemical contamination of the environment under the Health Act 1956, or of hazardous substances injuries under the HSNO Act due to exposures to methamphetamine contaminated dwellings.

^q D Barnfather and J Whitmore, Auckland Regional Public Health Service, *pers comm*, 21 March 2018.

Rodents are less sensitive than humans to methamphetamine, and therefore higher absolute doses are required to observe health effects. Thus the doses used in these studies are considered to be low in the context of animal research.

guideline is specifically <u>used</u> for former clandestinelabs, where lower levels of remaining methamphetamine are assumed to indicate lower levels of other contaminants. This does not imply that methamphetamine itself poses a greater health risk in former labs.

The trends in methamphetamine manufacturing in New Zealand mean that lab activity is no longer always obvious in a dwelling. But this also means that in general, production methods are cleaner, and the main contaminant associated with any methamphetamine-related activity is the drug itself. Nonetheless, the methamphetamine testing and decontamination industry has promoted the idea that all properties are potentially in danger from methamphetamine contamination.

A study by ESR of ~1,600 New Zealand public sector residential properties that weresuspected to have methamphetamine contamination can provide a general idea of the range of methamphetamine levels that may be found in affected dwellings[9]. Of the total number of properties tested, approximately two thirds showed some detectable methamphetamine 'contamination'. These dwellings by definition represent a biased sample with higher potential for methamphetamine contamination, being rental accommodation and including social housing, and considering that in most cases the landlord or agency had 'reasonable cause' to suspect methamphetamine use. The data are therefore likely to significantly overestimate the extent of the problem in the wider New Zealand housing stock. The data show that out of more than 13,000 surface samples taken, over75% had methamphetamine levels under 1.5 µg/100 cm², and approximately one third were negative. The average level in positive samples was 2.7 µg/100 cm². Thus, smoking-related levels, although generally exceeding the NZ standard clean-up level, are still relatively low.

Less than 1% of the samples in the ESR dataset tested above 30 µg/100 cm², suggesting a low prevalence of properties potentially used for manufacture. Even then, toxic compounds such as lead and mercury that are typically used in traditional production methods have not been found in meth labs in New Zealand.

Implications for methamphetamine screening in affected properties

Given the low probability of encountering excessive levels of methamphetamine in properties where meth lab activity is not suspected, and also considering the very conservative nature of the standards with respect to the risks of adverse effects from third-hand exposure to methamphetamine, a risk-based approach suggests that the guideline of 1.5 µg/100 cm² should not be universally applied.

Remediation is certainly warranted if high levels of methamphetamine are present that are indicative of manufacturing activity or excessive smoking (levels >30 µg/100 cm² signify that manufacture is likely tohave taken place; suggested testing criteria are lower [>15 µg/100 cm² – see Recommendations). Remediation includes removal of all potentially contaminated porous materials or items (furnishings, carpets) and cleaning of the contaminated surfaces, using the NZS 8510:2017 standard as a guide.

Where lower levels are detected, remediation is often not justified. However, as low levels cannot definitively rule out manufacture, remediation down the 1.5 µg/100 cm² standard may be prudent if there is also soundreason to suspect previous clan lab activities. This would only be as a precautionary measure to remove other toxicants that may be present but not measured.

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Page 17 of 26

Commented [N12]: I would be more comfortable with the word very or 'extremely here. One aspect the public and politicians are not good at is getting to grips with the microgram units involved. The units are just discounted. (Here and there it's worth reiterating in this way that the levels are very low. Extremely or would be consistent with introductory text around analytical detection capabilities.)

With regard to making screening of properties commensurate with the possible risks, some specific aspects require consideration:

Problems with field composite screening

Combining multiple samples taken throughout a dwelling into a single composite sample, as permitted in NZS 8510:2017, has limited value and does not accurately reflect levels of risk, and depending on how the data are integrated can lead to quite misleading interpretation and false impressions of high exposure. This approach of composite analysis is promoted as a cost-effective option for initial screening, but it is in fact costly because it can falsely impose a requirement for further testing without identifying the areas of potential contamination, nor their levels.

Given the low health risk in properties that were not used as meth labs, if they are to be tested, the initial screening should not involve composite field testing that could produce a false positive result – that is, detecting a level of 1.5 µg/100 cm² (or slightly above) from a composite field sample that adds the readings from all swabs together. Such field composite testing means that every sample can be below the standard, but when combined can raise the overall result, triggering another round of expensive testing.

Recommendations

- Testing for methamphetamine in residential properties should not be the default pathway. Testing is only recommended where meth lab activity is suspected or where very heavy use is suspected.
- Composite field testing that uses a cumulative value to make a yes/no decision against the 1.5 µg/100 cm² standard to determine 'contamination' should not be used.
- There is merit in using tests that rapidly provide a simple positive or negative result in multiple locations for detection of higher levels on site, followed by sensitive testing in targeted to areas that produce a positive signal. For example, NIOSH-validated colourimetric tests are available in the US that detect levels >15 µg/100 cm²(42, 43). In most cases, if methamphetamine is not detected at this level anywhere within a property, there is little cause for concern unless there are other reasons to suspect methamphetamine manufacturing activity.If the screening test shows levels >15 µg/100 cm², then a more thorough assessment should be conducted to determine whether there is an area of high contamination that needs to be remediated.
- Where a former meth lab has been identified, remediation should continue to current quidelines.

6 Conclusions

There is currently no evidence (in either humans or animals) that the levels typically resulting from third-hand exposure to smoking residues on household surfaces can elicit an adverse health effect. Toxicity assessments and exposure dose models used to establish standards for remediation of former meth labs (and which are used in the NZS 8510:2017 to guide remediation for both manufacture and use) have deliberately adopted very conservative assumptions, with very large (~300-fold) safety margins built in.

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Page 18 of 26

commented [N13]: Yes. You may want to double-check what the Standard specifies as regards whether the result should be multiplied by the number of subsamples in the composite (to represent the worst of the sampled areas assuming all but one were clean), and/or how and what area the average of the composite is being taken to represent. Whatever - I think your point is well made. Results I have seen post-standard just show a composite number from several areas, which often does exceed the 1.5. In my experience the testing companies still don't really know what they're doing with composites.

Commented [N14]:

Totally agree. Another link or stakeholder you might want to be aware of here (in case you aren't) is the very small government agency called the Real Estate Authority

https://www.rea.govt.n

They have issued guidance on the request of real estate agents and may want to reconsider what to say in that on the basis of this report.

Their involvement might be one of the faster ways to try to address entrenchment of testing in the New Zealand property market. I think that buyers and sellers, and insurers and banks, and those in the rental market, currently view it as part of 'best practice,' like getting a builder's report.

Taken together, these factors indicate that methamphetamine levels that exceed the NZS 8510:2017 clean-up standard of 1.5 µg/100 cm² should not be regarded as signalling a health risk. Indeed, exposure to methamphetamine levels below 15 µg/100 cm² would be unlikely to give rise to any adverse effects.

Testing for low levels of methamphetamine in residential properties in New Zealand has come at a very high cost. Although promoted as being protective of human health, the actions taken in pursuit of zero risk have been largely disproportionate to the actual health risks. Trade-offs need to be considered, particularly within social housing, where the risk of being in an unstable housing situation is often greater than the risk of exposure to low levels of methamphetamine residues. There have been huge costs to homeowners, landlords, and the state — not only of testing and remediation itself, but the unnecessary stigma of 'contamination', often based on little or no actual risk.

It is crucial that guidelines for mitigation measures are proportionate to the risk posed, and that remediation strategies should be informed by a risk-based approach. This means that, because the risk of encountering methamphetamine on residential surfaces at levels that might cause harm is extremely low, testing is not warranted in most cases. Remediation according to the NZS 8510:2017 standard is appropriate only for identified former meth labs and properties where excessive methamphetamine use, as indicated by high levels of methamphetamine contamination, has been determined.

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Page 19 of 26

7 Appendix

7.1 Establishing threshold doses for methamphetamine

California: Reference Dose

To review the toxicity of methamphetamine, the California Environmental Protection Agency's Office of Environmental Health Hazard Assessment (OEHHA) relied primarily on human studies [15]. From the available literature, a study on pregnant women who were given methamphetamine to control weight gain was used to calculate the Rf0[18]. This is a 1961 placebo-controlled, double-blind study that involved relatively small sample sizes and did not provide statistical analyses. However its findings were corroborated by another similar but smaller study[44]. While weight change does not necessarily reflect an 'adverse' health outcome, it gives an indication of dose levels at which physiological effects can be observed. The drug was given in a sustained release formulation (the same as that used for ADHD therapy), which is thought to best mimic the continuous exposure potentially experienced within a contaminated dwelling

Using the study data, the OEHHA determined that the lowest dose resulting in an observed effect on weight gain was 5,000 µg/day (equivalent to 80 µg/kg body weight/day for the average woman). Guided by other scientific literature on the effects of methamphetamine, the OEHHA further applied widely accepted uncertainty factors to this value, resulting in a reference dose of 0.3 µg/kg body weight/day.

It is important to note that anRfD focuses on absence of potential for harm, and over the long term. Thus, exceeding the dose even over an extended period is unlikely to result in an adverse effect. Furthermore, this level is orders of magnitude lower than the doses that are prescribed for therapeutic purposes (seeFigure 2).

Colorado: Health-based reference value

The Colorado Department of Public Health and Environment (CDPHE) reviewed multiple laboratory animal studies on the developmental and reproductive effects of methamphetamine exposure [16, 17]. They calculated that the dose at which 10% of the effect can be observed is 1,500–20,000 µg/kg body weight/day. After applying conservative uncertainty factors, a health-based reference value of 5–70 µg/kg body weight/day was determined. The lowest end of this range was derived from a single study showing decreased fetal weight in mice (45]. This study intravenously administered 5,000 or 10,000 µg/kg body weight/day methamphetamine to pregnant mice for 3–7 days. Decreased fetal weight was observed in all treatment groups. From this, the CDPHE calculated a benchmark dose level (BMDL) of 1,500 µg/kg body weight /day. Applying a safety factor of 300 yields a value of 5 µg/ka body weight/day.

Figure 4 compares the relative estimated doses for a typical young child and an adult woman that would be reached at the California RfD and Colorado health-based reference value.

For this assessment, the BMDL was taken as the dose associated with the 95% confidence interval around the BMD₁₀ (the dose associated with a 10% effect).

Page 20 of 26

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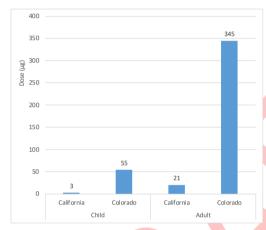


Figure 4: Maximum long-term daily dose of methamphetamine below which adverse events are unlikely to occur (California), or above which an adverse health effect may occur (Colorado), for a 10-kg child and a 70-kg woman.

7.2 Why are there so many different remediation guideline levels?

There are multiple reasons for the considerable variation in remediation guidelines among different agencies.

- Different mathematical models were used to estimate exposure doses: simpler models
 may take fewer factors into account and involve more simplistic calculations; some may
 aim to be especially conservative while others provide better exposure estimations but
 with less of a buffer. Further, the results of modelling can be only as rigorous as the
 quality of the data being input, and each model relies on somewhat different
 assumptions from the lothers.
- There is a substantial difference between the California reference dose and the Colorado health-based exposure value (0.3 vs 5-70 µg/kg body weight/day): this in turn directly impacts on the calculated remediation level.
- Unlike the other models, Colorado did not consider the contribution of carpet residues in
 the exposure calculations. This is because guidelines developed specifically for
 remediating former clan lab dwellings require that carpets be stripped, so it was
 assumed that carpeting in a remediated dwelling would not contain any residues.
 Australia's ERS did find that including soft surfaces led to a two-fold difference in

Page 21 of 26

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exposure, but concluded that this difference was "not considered to be sufficiently great" to warrant a separate quideline.

- The ESR report distinguished between former meth labs and non-meth labs, while others
 did not.
- There are some differences in interpreting the potential for methamphetamine to penetrate materials and re-surface over time.¹

7.3 Conservative assumptions of exposure dose models

Toxicity assessments

- The toxicity measures derived from California and Colorado's assessments incorporate a large uncertainty factor. This provides a safety 'buffer' to account for factors such as differences in sensitivity among different people, uncertainties from extrapolating animal data to humans, and uncertainties posed by incomplete toxicological information. Both assessments used an uncertainty factor of 300. In other words, the values can be multiplied by 300 to obtain the actual dose that was calculated to either not result in any adverse effect, or result in the first sign of an effect.
- Skin contact is the predominant route of exposure in methamphetamine contaminated
 dwellings. However the study that led to the lowest level of Colorado's health-based
 reference value (5 µg/kg body weight/day) involved giving pregnant mice
 methamphetamine intravenously, which also bypasses oral bioavailability and initial
 metabolic breakdown, and so is likely to be highly conservative (see footnote v).

Exposure assessments

- Estimates of exposure levels focused on the most sensitive groups such as crawling/mouthing young children, and adult women of childbearing age in whom a fetus could potentially be exposed.
- The models assumed that exposure levels remain constant after remediation, even though simulated smoking experiments have found that even without intervention, levels of smoke residues decrease significantly over just six days [9]. Other factors are likely to contribute to further decreases over time, e.g. through cleaning, coming into contact with clothes and being laundered out, and each exposure event further reducing the remaining residue levels.
- Colorado's model appears to be especially conservative: it assumes that a child is clad in
 just a nappy, with all its uncovered skin being continuously exposed to contaminated
 surfaces for 12 hours a day.
- For methodological reasons, ESR's model assumed that methamphetamine was 100% bioavailable through oral ingestion, but in practice bioavailability is thought to be 67% (471, This means that about one-third of the drug ingested is not actually absorbed.

Page 22 of 26

¹ The NZ Ministry of Health [6] disagrees with California's assumption that methamphetamine is volatile (evaporates rapidly) and is not a persistent contaminant. It argues that residues may be absorbed in building materials and later re-surface and evaporate, leading to prolonged exposure and at levels higher than indicated by surface testing alone. There is some evidence for this in the literature [46]. However, ESR considers these factors to be of minimal concern for several reasons. For example, the contribution of airborne methamphetamine to overall exposure is low, and over time young children are likely to reduce their exposure though fewer mouthing behaviours, and reduce their effective does due to increasing body weight.

7.4 Contamination level at which Colorado's health-based reference value is reached

Colorado's health-based reference value of 5–70 µg/kg body weight/day is at least 16-fold higher than California's Reference Dose of 0.3 µg/kg body weight/day. Because the Colorado figure is much less conservative, it could be expected that their clean-up level would be much higher than California's guideline of 1.5 µg/100 cm². Yet, their chosen guideline of 0.5 µg/100 cm² is 3-fold lower.

This is because Colorado adopted a 'health protective' approach that simply assessed exposure doses at a range of proposed clean-up levels (0.01, 0.1, and 0.5 μg/100 cm³), and whether any of these levels would result in doses that exceed their health-based reference value. As none of the proposed levels led to an exceedance, the highest level of 0.5 μg/100 cm³ was selected. They did not assess even higher clean-up levels, or calculate the maximumclean-up level at which the health-based reference value would be reached.

However there is expert opinion that such an approach is reasonable [48]. From the Colorado exposure data, it can be calculated that the maximum surface concentration for not exceeding the lowest level of their health-based reference value (5 μg/kg body weight/day) is 13 μg/100 cm². This means that levels exceeding 13 μg/100 cm² may – but would be extremely unlikely to, given the 300-fold safety margin – lead to onset of an adverse effect.

As previously noted, the degree of conservatism of the assumptions used in models of exposure can have a large impact on the calculated guideline. This can be illustrated by recalculating Colorado's exposure data using two modified assumptions: a lower oral bioavailability (from 100% to 67%), and lower skin absorption (from 10% to 3%). Using a lower oral bioavailability alone, or lower skin absorption alone, resulted in a maximum level of about 15 µg/100 cm²; combining both modified variables resulted in further increase of the maximum level to 25 µg/100 cm².

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Page 23 of 26

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Page 24 of 26

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[&]quot; An infant is estimated to be exposed to 0.19 μg/kg body weight/day at a surface level of 0.5 μg/100 cm". Extrapolation of this relationship, which has been determined to be linear [Kim16], shows that exposure to 5 μg/kg body weight/day will result from a surface level of 13.1 μg/100 cm².

^v Because no data for skin absorption of methamphetamine were available, Colorado used 10% as a default value recommended by the US Environmental Protection Agency. It has been suggested, based on data from a 1973 PhD thesis studying the pharmacokinetics of methamphetamine, that the skin absorption could reasonably be assumed to be 3% (L Schep, Dunedin School of Medicine, pers comm, 20 February 2018). California and ESR used a value of 57% based on data from an unpublished draft report (Hui X & Maibach HI (2007) In vitropercutaneous absorption of d-methamphetamine hydrochloride through human skin. Draft Report. Department of Dermatology, University of California, San Francisco).

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Page 25 of 26

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Page 26 of 26