

**Subject:** Re: PMCSA methamphetamine report

**Date:** Sunday, 15 April 2018 at 10:26:09 AM New Zealand Standard Time

**From:** Jeff Fowles

**To:** Anne Bardsley

**CC:** Felicia Low

Dear Dr Bardsley,

Thank you for the opportunity to review the report, and to be acknowledged as such. I would be pleased to be included in your list of reviewers.

Please refer to me as:

Dr Jeff Fowles, Tox-Logic Consulting, Santa Rosa, CA, USA

Best regards

Jeff

Sent from my iPhone

On Apr 14, 2018, at 2:23 PM, Anne Bardsley <

Dear Dr Fowles,

I am writing again to ask whether we can acknowledge your review of our report. The acknowledgments section is currently worded as follows:

### **Acknowledgments**

This work has benefitted from cooperation and expert advice from a number of national and international researchers and agencies. In New Zealand this included the National Drug Intelligence Bureau, the Institute for Environmental Science and Research (ESR), the Ministry of Health, Massey University School of Health Sciences, Housing New Zealand, the Ministry of Business, Innovation and Employment, the National Poisons Centre, the New Zealand Drug Foundation, the Real Estate Authority, the Auckland Regional Public Health Service, Auckland City Council, and the Auckland Regional Methamphetamine Working Group.

Internationally, advice was received from Dr John Snawder of the US Centers for Disease Control and Prevention (CDC)/National Institute for Occupational Safety and Health (NIOSH), Dr Glenn Morrison of the University of North Carolina Gillings School of Global Public Health, and Dr Jackie Wright of Flinders University College of Science and Engineering, Adelaide, Australia.

Research, analysis and writing was carried out by Dr Anne Bardsley and Dr Felicia Low of the Office of the Prime Minister's Chief Science Advisor.

We would like to thank the following reviewers who provided comments on the report:

- Dr Nicholas Kim, Massey University, Wellington, NZ
- Dr Adam Pomerleau, National Poisons Centre, Dunedin, NZ
- Dr Leo Schep, Dunedin School of Medicine, Dunedin, NZ
- Dr John Snawder, CDC/NIOSH, Cincinnati, OH, USA
- Dr Michael van Dyke, Colorado Department of Public Health and Environment, Denver, CO, USA
- Dr Jeff Fowles, [current affiliation]

Special thanks go to Erina Mayo of ESR's Forensic Chemistry Team for invaluable discussions and for facilitating access to ESR data and analysis.

If you are agreeable to having your name listed, can you please send your current affiliation details?

---

Thank you, and regards,  
Anne

Anne Bardsley, PhD  
Research Analyst

---

Office of the Prime Minister's Chief Science Advisor | 85 Park Rd, Grafton | Auckland 1023 New Zealand  
P1

---

**From:** Anne Bardsley <

**Date:** Friday, 13 April 2018 at 2:17 PM

**To:** "jfowles

**Cc:** "sally gilbert"

Chris Nokes

felicia Low <

>, Peter Gluckman

**Subject:** Re: PMCSA methamphetamine report

Dear Dr Fowles,

Thank you for your very helpful comments on our draft report on methamphetamine contamination. It has helped highlight to us areas that could benefit from further explanation or clarification.

We appreciate your and Dr Morgott's viewpoint on the relative merits of the California and the Colorado risk assessments. We do not suggest that a new standard should be developed based on the Colorado health-based reference value. Instead, we have aimed to show how reframing the question of safety ('*At what level of surface contamination might adverse health effects become plausible in the most sensitive individuals?*') could lead to different threshold levels being determined. California's approach is, of course, more precautionary, but part of our brief is to consider what level of caution would be commensurate with the overall risks posed by third-hand exposure, particularly in light of additional data from ESR.

We do note in the report that rodents metabolise methamphetamine much more quickly than humans. At the same time, we've also borne in mind that Colorado did incorporate a 10x safety factor to account for human-animal differences, and that multiple animal studies can give a range of BMDL10s, unlike a single, small, human study that reports on a biological (not adverse) effect. We are aware that children appear to have lower sensitivity than adults to methamphetamine; this makes it unlikely that young infants would be *more* sensitive than adults, but this is conservatively assumed in all assessments. We also appreciate that daily accumulation in humans is theoretically

possible, but it is unclear whether this translates specifically to the low levels involved in third-hand exposures.

Again, with respect to third-hand exposure levels, the data on the consequences of prenatal exposure are not straightforward to interpret as they involve much higher doses. Indeed, one of the papers you referred us to (the IDEAL study, involving NZ children - Chakraborty et al, 2015) concludes that prenatal exposure does not affect visual cortex function, an area of the brain thought to be particularly sensitive to abnormal neurodevelopment. Those children had prenatal meth exposure verified by meconium testing, and were assessed for global perception functions at 4.5 years of age. A separate assessment of the IDEAL study cohort observed subtle effects on fine-motor performance at 1 year (mostly in heavily exposed individuals) that mostly resolved by 3 years of age (see Smith LM, et al. *Motor and cognitive outcomes through three years of age in children exposed to prenatal methamphetamine*. *Neurotoxicology and Teratology*. 2011;33(1):176-84).

We will clarify the wording as relates to your points 3 and 6, and will reinsert discussion (inadvertently omitted from previous drafts) noting that *absence of evidence of an effect* does not equate to *evidence of absence of an effect*. We also wish to emphasise that 15 µg/100 cm<sup>2</sup> is not a proposed alternative standard, and will endeavour to make this clearer. This level is discussed for its potential utility in initial screening assessments, and is based on the availability of rapid tests with this level of sensitivity that could identify the specific areas where further testing and cleanup may be needed. We are comfortable with the statement that the risks from third-hand methamphetamine exposure below this level are very low, and enforcing a lower level of detection and remediation across the board is not warranted given what we know about patterns of methamphetamine manufacture and use in New Zealand.

Once again, thank you for your input. In view of your time and effort, **please let us know if you are happy to be listed as one of the peer reviewers for our report?**

Kind regards,  
Anne Bardsley and Felicia Low, on behalf of Sir Peter Gluckman

Office of the Prime Minister's Chief Science Advisor | 85 Park Rd, Grafton | Auckland 1023 New Zealand  
Ph:

---

**From:** "[sally\\_gilbert](#)"  
**Date:** Wednesday, 11 April 2018 at 4:45 PM  
**To:** Anne Bardsley <[anne.bardsley@pmcsa.govt.nz](#)>  
**Cc:** "[sally\\_gilbert](#)" <[sally.gilbert@pmcsa.govt.nz](#)>, Arati Walia <[arati.walia@pmcsa.govt.nz](#)>  
<[sally.gilbert@pmcsa.govt.nz](#)>  
<[arati.walia@pmcsa.govt.nz](#)>  
<[sally.gilbert@pmcsa.govt.nz](#)>  
**Subject:** Re: PMCSA methamphetamine report

Dear Anne

Many thanks for the opportunity to provide comment on the methamphetamine report. In my view, the findings provide useful context and reassurance that the current clean up levels in NZS 8510:2017 protect public health, including the most vulnerable people (pregnant women, foetuses, and infants). However, the report argues that the clean up levels are overly precautionary and may create unwarranted public concern and incur unnecessary decontamination costs. If the report is finalised in its current form, it may require a review of the NZS 8510:2017

I have sought advice from ESR (Chris Nokes and Jeff Fowles) and from Matt Allen, our representative on the Standards Committee. In the interest of time, I have attached Jeff's comments on the report. I consider that Jeff has provided a very considered assessment of the report, despite the tight timeframe for responding. As you know, Jeff is a very experienced toxicologist and I hope you find his comments helpful.

In addition, Chris Nokes has advised that Erina Mayo, ESR forensic scientist on the Standards New Zealand Committee, is happy with the content in relation to the discussions she has had with you and the references made to the Clan Lab's work.

*Matt has advised that "I find it hard to disagree with pretty much anything in the report. However the issue of the 1.5 level not being ideally universally applied was of course something [the Standards Committee] discussed with the ideal of having a split for houses with just smoking versus suspected clan labs BUT... what objective criteria can be set to determine what category a house falls into.... I can't comment on the composite sample issues- I deferred to the ESR rep on the standards committee on that issue."*

I would add that the advice we received was that trying to determine what was a lab and what was a property where meth had been used is highly problematic and risked home owners and residents defaulting to the clan lab standards as a precautionary measure. This is also why levels were provided for non-habitable spaces - to prevent people applying the 1.5 to every space in the house, even attics and basements...

I hope this is helpful. If you wish to discuss Jeff's comments further with him, please feel free to contact Chris to arrange further discussions (if you have lost their contact details I am happy to re-send them).

Kind regards - Sally

Sally Gilbert  
Manager  
Environmental and Border Health  
Public Health  
Protection Regulation and Assurance  
Ministry of Health

<http://www.health.govt.nz>

---

From: [sally.gilbert@health.govt.nz](mailto:sally.gilbert@health.govt.nz)  
To: "Sally Gilbert" <[sally.gilbert@health.govt.nz](mailto:sally.gilbert@health.govt.nz)>  
Date: 10/04/2018 02:20 p.m.  
Subject: PMCSA methamphetamine report

**Subject:** from Jeff Fowles

**Date:** Tuesday, 20 March 2018 at 9:12:49 AM New Zealand Daylight Time

**From:** Anne Bardsley

**To:** Felicia Low

---

**From:** Jeff Fowles <jeff.fowles@ecdc.govt.nz>

**Date:** Tuesday, 20 March 2018 at 8:02 AM

**To:** Anne Bardsley <anne.bardsley@ecdc.govt.nz>

**Cc:** "Chris.Nokes"

**Subject:** Re: Prime Minister's Chief Science Advisor's report on methamphetamine exposure risks in residential properties

Dear Dr Bardsley,

Thank you for your email queries on the subject of our methamphetamine residue risk assessment.

I believe my colleague Chris Nokes has provided you with a letter that ESR sent regarding the issue of heavy metals and that in the initial writing up of the report, I had included as a precaution the recommendation to screen houses for lead and mercury since there had been one historical case of mercuric chloride found in a NZ meth lab. Subsequent conversations with forensics experts clarified that the finding of Hg in this single case was felt to be coincidental and not related to meth manufacture (no further details were provided to me about why the mercury was there). Thus, from a production method standpoint, there is no justification to include metals as a separate analytical requirement. However, in my professional judgement, given the general lack of attention to occupational or personal safety in such settings, home laboratories could easily end up being contaminated with various metals stemming from broken thermometers, lighting fixtures, or just old decadent equipment. But, rather than making a rigid requirement for a metals test in each laboratory, it makes sense to leave the need to conduct additional testing up to the professional judgement of the independent forensic investigator.

Regarding the selection of appropriate reference dose, I would like to ensure that you are aware of the peer review comments from Dr David Morgott (Pennsport Consulting) who strongly supported the California value over the Colorado number due to the use of repeated dose data in humans vs rats. The elimination half life of methamphetamine is 70 min in rats vs 12 hours in humans, which is a very large difference that impacted our choice to not use the Colorado rodent-based value.

Best regards

Jeff Fowles

Sent from my iPhone

On Mar 18, 2018, at 12:01 PM, Chris Nokes <chris.nokes@ecdc.govt.nz>

Hi Jeff

I should also have said that my sending this letter to Anne should not prevent you from adding further comment if you wish in explanation of why you considered the recommendation necessary.



around the dangers of 'third-hand' exposure to low-level methamphetamine residues (not chemicals from manufacture). Do you know of any documentation of health effects from the levels of exposure people might encounter from living in houses where it has previously been smoked? Have any instances of reported effects been confirmed as being related to low-level, indirect methamphetamine exposure (aside from those encountered in active or recently active labs)? I am unaware of any such notifications in New Zealand, where there is a particularly heightened perception of the risks around this issue.

Dr Sally Gilbert from the NZ Ministry of Health suggested that it may be useful to speak to you directly about these issues, and I would welcome the opportunity to do so. Please let me know if you are amenable to a phone call (possibly next week?), and if so, the phone number and best time to reach you.

Kind regards,  
Anne

Anne Bardsley, PhD  
Research Analyst

Office of the Prime Minister's Chief Science Advisor | 85 Park Rd, Grafton | Auckland 1023 New Zealand

---

**From:** Chris Nokes ·  
**Date:** Thursday, 1 March 2018 at 11:28 AM  
**To:** Anne Bardsley ·  
**Cc:** "[sally gilbert](#)", [David G. ...](#), [Kevan Walsh](#) ·, [Felicia Low](#)  
**Subject:** RE: Prime Minister's Chief Science Advisor's report on methamphetamine exposure risks in residential properties

Hi Anne

I've received Jeff Fowles' answers to your questions and identified them in red.

1. Can you clarify why p 25 reports exposure dose for 1-2 year old, at a surface load of 0.1, is 0.021 µg/kg bw/d; but p 41 reports that the dose is 0.015 µg/kg bw/d?

Section 4.3 (p. 25) does seem to cite total exposure from both hard and soft surfaces despite saying that we had eliminated consideration of carpeting. So that is unclear from the wording of the report. The numbers on page 41 are hard floor only which were the basis for the proposed standard. The calculated standard is unaffected.

2. Can you provide further detail on how the recommendation of 1.5 µg/100 cm<sup>2</sup> for carpeted, non-lab houses was arrived at? Is it simply following the OEHHA guideline, i.e. no specific modelling work with NZ data?

We calculated 1.4 ug/100 cm<sup>2</sup> clean up level for hard+carpeted floor scenario. This value was, in our opinion and as I explained during the Standards NZ meeting, practically indistinguishable from the OEHHA value of 1.5. The two methods used gave essentially the same result, which is encouraging. We did use NZ-specific data in place of some standard defaults used in generic risk assessments. This is shown in Table A2 with the Cressey and Horn 2016 citation.

3. Important: Can we assume that the model used gives relatively linear results for the

surface load/exposure dose relationship? That is:

- a. 0.015 µg/kg bw/d dose resulted from surface load of 0.1;
- b. And the RfD of 0.3 was modelled to result from surface load of 2;
- c. Can we reasonably extrapolate this, so the Colorado HBEV of 5 will be reached at a surface load of 33?

**Yes. The calculations are linearly scaleable with surface loading. Changing the MA surface concentration from 0.1 ug/100 cm<sup>2</sup> to 33 ug/100 cm<sup>2</sup> does result in a calculated young child total intake (hard floor only) of around 5 ug/kg-day.**

I hope these answers are satisfactory.

I understand from Kevan Walsh that you would like to contact Jeff directly. Because of time differences and Jeff's other commitments, I suggest you contact him by email first to arrange a convenient time for a call, should it be necessary. His email address is:

Regards  
Chris

---

**From:** Chris Nokes  
**Sent:** Wednesday, 21 February 2018 2:37 p.m.  
**To:** 'Anne Bardsley'  
**Cc:** [sally\\_gilbert](#); Felicia Low <[f](#)>  
**Subject:** RE: Prime Minister's Chief Science Advisor's report on methamphetamine exposure risks in residential properties

Hi Anne

Thanks for your email. I've asked the report's authors for answers to your questions, and will get back you once I hear from them.

Regards  
Chris

<image001.png>

**Chris Nokes** PhD

Science Leader, Risk and Response Group

Institute of Environmental Science and Research Limited (ESR)  
Christchurch Science Centre: 27 Creyke Road, Ilam, Christchurch 8041  
PO Box 29181, Christchurch 8540, New Zealand

[www.esr.govt.nz](#)

<image002.png>



**Subject:** Re: Prime Minister's Chief Science Advisor's report on methamphetamine exposure risks in residential properties

**Date:** Tuesday, 20 March 2018 at 10:07:24 AM New Zealand Daylight Time

**From:** Anne Bardsley

---

**To:** Chris Nokes, jfowles@...  
**CC:** sally\_gilbert@..., Felicia Low, Peter Gluckman

**Attachments:** image001.png, image002.png, image003.png

Many thanks Chris and Jeff (by separate email) for clarifying these issues.

We are still at a loss to demonstrate any health effects from third-hand exposure aside from anecdotal stories - I have yet to find any that have been verified as related to (or even evidence of absorption of) methamphetamine itself. We will be discussing this issue again tomorrow with representatives from the Auckland DHB, who record claims of health effects related to meth houses (these may be clan-lab related, and as far as I am aware none have been verified or notified to the Ministry of Health). There is of course more on the effects of other contaminant from clan labs that have used older production methods, which as far as I can tell have been mostly phased out in NZ in favour of contained, solvent-free methods (Parr bombs).

We will continue to note the need for forensic expertise in determining what other chemicals might be present when a lab is discovered, but would like to give a realistic, evidence-based explanation of the risks in NZ - i.e.:

- *likelihood* and *consequence* of encountering other chemicals when there is no evidence of, or reason to suspect a lab, and
- effects of low-level exposure to methamphetamine in the absence of other chemicals (the more likely situation in NZ).

We intend to explain the derivation of the 1.5 µg/100 cm<sup>2</sup> (and the earlier 0.5 µg/100 cm<sup>2</sup>) guidelines as protective against the worst-case scenario, but have been asked by many stakeholders if we can help them understand how, when (and if!) this should be operationalised in different situations.

The perception of the risk has been hugely elevated in NZ, based largely on here-say and fears stoked by a burgeoning methamphetamine testing and remediation industry. Having this level as a screening level for composite swabs throughout a house essentially means that detection of a very low level of methamphetamine (i.e. possibly one swab at 1.5 and the rest negative – or all below 1.5 but pooling to bring the level up to or above this) triggers another round of testing to determine where cleaning needs to be done. This also means that the house is permanently noted as being “contaminated”, and in the past, Housing NZ (social housing) tenants have been evicted in order to remediate houses – situations where the risks to these families from being removed from their homes are often far higher than those posed by possible exposure to low levels of meth on their walls and floors.

I am not aware of such an exaggerated situation around methamphetamine testing and remediation in other countries – this appears to be unique to NZ at present, and so requires a unique approach to the risk perception issue and explanation of health risk levels.

My thinking from interpreting the risk assessments and the rest of the literature, in light of the NZ situation, is that for houses where a lab is not suspected, a less sensitive screening methodology that would give an instant presence/absence of reasonable levels of methamphetamine (possibly >10-15 µg/100 cm<sup>2</sup>) would be more appropriate for an initial screen. This would identify the areas where actual contamination was present, and then these areas could be re-screened and a more targeted remediation plan put in place. (Note – ESR has confirmed with me that in their forensic investigations, in absence of other signs, they do not consider that a lab was present if levels are <30 µg/100 cm<sup>2</sup>).

If you have any further thoughts about this I would very much appreciate your insight and perspective.

Kind regards,  
Anne

Anne Bardsley, PhD  
Research Analyst

Office of the Prime Minister's Chief Science Advisor | 85 Park Rd, Grafton | Auckland 1023 New Zealand  
[www.pmc.govt.nz](http://www.pmc.govt.nz)

---

**From:** Chris Nokes <[chris.nokes@ecsr.govt.nz](mailto:chris.nokes@ecsr.govt.nz)>  
**Date:** Tuesday, 20 March 2018 at 8:18 AM  
**To:** Anne Bardsley <[a.bardsley@auckland.ac.nz](mailto:a.bardsley@auckland.ac.nz)>  
**Cc:** "sally\_gilbert@ecsr.govt.nz" <[sally\\_gilbert@ecsr.govt.nz](mailto:sally_gilbert@ecsr.govt.nz)>; "John Fowles" <[jfowles1@ecsr.govt.nz](mailto:jfowles1@ecsr.govt.nz)>  
**Subject:** RE: Prime Minister's Chief Science Advisor's report on methamphetamine exposure risks in residential properties

Hello Anne

I've attached a copy of a letter to the Ministry of Health on the topic of heavy metals, which may throw further light on the matter. I sent the letter soon after the report was originally prepared, following discussions with our forensic colleagues.

Regards  
Chris

---

**From:** Anne Bardsley [mailto:[a.bardsley@auckland.ac.nz](mailto:a.bardsley@auckland.ac.nz)]  
**Sent:** Friday, 16 March 2018 4:10 p.m.  
**To:** jfowles1@ecsr.govt.nz  
**Cc:** Chris Nokes <[chris.nokes@ecsr.govt.nz](mailto:chris.nokes@ecsr.govt.nz)>; sally\_gilbert@ecsr.govt.nz  
**Subject:** FW: Prime Minister's Chief Science Advisor's report on methamphetamine exposure risks in residential properties

Dear Dr Fowles,

I received your contact email from Dr Chris Nokes at ESR, following discussions we have been having around methamphetamine contamination in houses and health risks to occupants. You have kindly provided answers to some previous questions we had regarding your 2016 report '*Review of Remediation Standards for Clandestine Methamphetamine Laboratories: Risk Assessment recommendations for a New Zealand Standard*'.

My colleague Dr Felicia Low and I have a couple of additional questions we hope you can answer.

Firstly, your report states that the guideline for carpeted houses was based on a calculation of a maximum surface load of  $1.4 \mu\text{g}/100 \text{ cm}^2$ , and in response to our earlier questions, you indicated that the calculations are linearly scalable with surface loadings. Based on this, we would like to confirm whether we can again assume a linear scalability and do a similar extrapolation from the Colorado HBEV - i.e.:

7 November 2016

Environmental and Border Health  
Public Health  
Ministry of Health  
PO Box 5013  
WELLINGTON 6145

Attention: Paul Prendergast

Dear Paul

**Methamphetamine laboratory remediation standard review: relevance of the recommendation to survey for heavy metals**

I write to clarify the recommendation to survey methamphetamine laboratories for heavy metals, particularly lead and mercury, made in ESR's report: *Review of Remediation Standards for Clandestine Methamphetamine Laboratories: Risk Assessment recommendations for a New Zealand Standard (7 October 2016)*.

Following discussions with ESR's Clandestine Laboratory experts we now understand that, to date, methods for producing methamphetamine in New Zealand have not used lead or mercury. The one reported finding of mercuric chloride in a New Zealand laboratory, mentioned in the report, was not associated with methamphetamine production. For this reason, undertaking heavy metals surveys of methamphetamine laboratories should be unnecessary.

However, the likely absence of heavy metals reflects current practice and manufacturing trends. Any future changes in precursor availability may result in changes in the manufacturing process. Consequently, we suggest, as a matter of general public health precaution, that the need for heavy metal surveys be kept in mind should forensic services find evidence of the introduction of production methods that may include heavy metals.

To be clear, **the proposals for remediation standards for methamphetamine levels in the report (Section 5) are unaffected by the above discussion.**

Yours sincerely

Dr Chris Nokes  
Science Leader, Risk and Response Group



J. Fowles, Ph.D.  
Tox-Logic Consulting  
Santa Rosa, CA

09 April, 2018

**Comments on draft report entitled: Methamphetamine contamination in residential properties:  
Exposures, risk, levels, and interpretation of standards, by Professor Sir Peter Gluckman**

Comments:

- 1) This draft report makes the assertion, in several places, that no evidence exists for the toxicity of MA at the low doses that result from the residue levels contained in the proposed MA standard. While this is true on face value, it is also misleading. A common misconception in public health or in toxicological risk assessment, is that *'Lack of evidence equates to evidence of absence'*. The MA standard is derived to protect infants and toddlers' developing nervous systems from potential low dose effects of MA. Since there have been no studies on post-natally exposed infants and toddlers with low doses of MA, it stands to reason that there would be no (direct) evidence, since any effect would be subtle, likely non-specific, and behavioural in nature. Thus, the only possible data source for "evidence" would arise from clinical case reports or notifications of injury as a result of chemical contamination of the environment. However, since we are not talking about acute life-threatening poisonings, or overt effects like seizures, it is highly unlikely that a parent would think to associate a toddler's restless sleep patterns, nervousness, or behavioural change with exposure to a residual contamination of the walls of their home, much less notify a doctor or local health authorities about it.

Commented [FL1]: Will acknowledge this

This use of standard conservative default assumptions in the face of uncertainty is not unusual in toxicological risk assessment. The exception to the rule lies in the case of a vast and robust data base that exists from which to derive precise risk based values, such as in the case of blood lead or mercury levels, having decades of studies and thousands of human subjects followed longitudinally. Methamphetamine residue exposures have nothing even remotely approaching such a data base. Therapeutic histories of MA use in adults and older children do not provide a comfortable basis to assume that very young infants would not be more susceptible to neurological effects.

Commented [FL2]: Since children appear to have lower sensitivity than adults, it is unlikely that young infants would be *more* sensitive than adults, but this is conservatively assumed anyway

- 2) The report appears to take no position on the qualitatively different starting points of departure used by the states of California and Colorado for their respective toxicological risk assessment (human vs rat), and concludes that they are equally valid since the same margin of safety (300) is applied in both instances. However, as discussed in the ESR 2016 report and confirmed by peer review, the rat is not recommended as a suitable experimental basis for quantitative risk assessment, due to the clearly greater sensitivity of humans to MA.

Commented [FL3]: •Colorado incorporated a 10x buffer to account for human-animal differences.  
•Multiple animal studies can give a range of BMDL10s, unlike the single, small human study.

*"Foremost among these is the large species-dependent disparity in sensitivity to the drug, with laboratory animals (particularly rats and mice) generally being much less sensitive to MA than humans. For example, in characterizing the cognitive effects of postnatal exposure to MA in mice, Acevedo et al. (2007) utilized a daily dose of 5 mg/kg. In an adult human, this would be equivalent to a total dose of 300-350 mg, which would be potentially life-threatening. In addition, the pharmacokinetics of MA in laboratory animals and humans differ substantially. As Cho et al. (2001) point out, the elimination half-life of MA is 70 minutes in rats and 12 hours in humans. Thus, these data alone support the use of the 10X safety factor to account for the extrapolation of toxicity data from the results of studies conducted in animals for use in the application to humans.." (ESR, 2016).*

Dr David Morgott, an experienced toxicologist and risk assessor echoed these concerns in his peer-review comments of the ESR report:

*"In my opinion, the only technically supportable value that should be used in the exposure analysis is the value of 0.3 µg/kg-day proposed by OEHHA. This value should be used to the exclusion of all others because it is based on the results obtained in a repeated-dose study with humans. A comparison of the blood half-life values for methamphetamine in rats and humans produced t<sub>1/2</sub> values of 70 min and 12 hrs, respectively. <sup>1</sup> This is a very large difference and indicates a potential for day-to-day accumulation in humans, but not in rats. Since it takes 5-6 half-lives for a substance to be eliminated from the body to an appreciable extent, daily administration to humans will result in an increased body burden on each successive day of the exposure regimen. In contrast, elimination from rats will only require about 7 hrs, which is a short enough time interval to prevent day-to-day accumulation from occurring. As such, the body burdens achieved in rats are not representative of those that will be found in humans following repeated administration, and any RfD that is based on the results from a study rats should be abandoned in favor of those based on human data."*

**Commented [FL4]:** Agree with theory, though unclear if this translates to situation of third-hand exposure in practice.

The current report later tabulates the various rodent studies. However, the sheer number of rat studies does not outweigh the fact that the rat is known to be less sensitive to MA than humans, nor the fact that no studies account for the complete lack of data on human infants and toddlers.

3) It is not a correct statement in Table 2 that the NZ standard is the only non-risk based assessment. The ESR 2016 report is a human health risk assessment, using deterministic values as applied in a standard risk assessment context.

**Commented [FL5]:** Our intended meaning was that NZ Standards did not fully adopt ESR's risk-based recommended guidelines; instead their selection of a single level of 1.5 was based on procedural reasons, rather than any further risk assessments. But can amend wording to clarify.

<sup>1</sup> Cho,A.K., Melega,W.P., Kuczenski,R., and Segal,D.S. (2001). Relevance of pharmacokinetic parameters in animal models of methamphetamine abuse. Synapse 39,161-166.

4) On page 12, the alternative calculation presented uses the Colorado rat-based reference value, which we do not support for reasons explained above.

5) The second paragraph on page 14 once again states that there is no evidence for an adverse effect from residues on surfaces, when in fact there have been no studies to examine this assertion one way or another. The third paragraph uses the lack of MoH notifications of poisoning to bolster the argument that there are no adverse effects from MA residues. For reasons explained above, this is an unlikely source of accurate data on subtle, behavioural health effects.

6) Therapeutic doses of many drugs also carry risks of side effects. Thus, the statement on page 15, paragraph 2, that MA could not be toxic at low doses because it has been approved as a medicine, is not accurate. All pharmaceuticals undergo risk/benefit assessments. There is no benefit to involuntary environmental exposures to MA.

**Commented [FL6]:** Re-reading this, he is certainly going by the strict toxicological definition. We could amend to "MA is not considered to have high intrinsic toxicity" (and omit the low dose), or "not considered to be highly toxic at low doses".

7) The statement on page 16 that "...the effects of low-level exposure... are likely to be transient – so generally the consequences are also low", requires revision. The 2016 assessment assumed daily exposures, not a single exposure. Also, as mentioned in the Cho et al (2001) paper, the half-life of methamphetamine in humans means that daily exposures have the potential to accumulate. Also, *in utero* MA exposures are reported to have associated long-term neurodevelopmental consequences later in life (Smith et al., 2015<sup>1</sup>; Chakraborty et al., 2015)<sup>2</sup>. The kinds of effects that these studies identify include such endpoints as "Global Motion Perception". These are not the sorts of effects that could be easily identified by a typical parent or even a clinician. Again, we do not know if the low dose exposures in post-natally exposed infants or toddlers may be significant in terms of neurodevelopment, or not. There simply are not studies that inform the answer to that question.

**Commented [FL7]:** Indeed, so it is particularly conservative in that respect

**Commented [FL8]:** Negative study

8) I tend to agree with the concern over composite sampling, but this should be the subject of a considered statistical assessment.

9) The conclusions reiterate and intensify the terms "conservative" to "very conservative", and "very large" safety margins. These margins are, in fact, completely in line with many US EPA and other international standards. The magnitude of the margins reflect the data gaps that exist and that are acknowledged.

**Commented [FL9]:** I actually feel comfortable toning it down

10) The mention of the value of 15 ug/100 cm<sup>2</sup> as an alternative level which would not cause health effects, comes subjectively and without any calculated quantitative justification, and thus seems arbitrary.

**Commented [FL10]:** Was my concern. Just need to add more caveats to our discussion

11) The proposed alternative standard of 15 ug/100 cm<sup>2</sup> would place NZ as the highest acceptable MA residue exposures globally. Perhaps this would still be protective, but in any event such a value is not supported by conventional risk assessment parameters, and thus to adopt such a standard would necessitate support for undertaking epidemiological and/or biomonitoring studies for MA exposures and effects in young children reoccupying such houses.

**Commented [FL11]:** Can clarify it's not!

<sup>1</sup>Smith L, Diaz S, LaGasse L, Wouldes T, Derauf C, Newman E, Arria A, Huestis M, Haning W, Strauss A,

---

Della Grotta S, Dansereau L, Neal C, Lester B. 2015. Developmental and behavioral consequences of prenatal methamphetamine exposure: A review of the Infant Development, Environment, and Lifestyle (IDEAL) study. *Neurotoxicology and Teratology* 15, 35-44.

<sup>2</sup>Chakraborty A, Anstice N, Jacobs R, LaGasse L, Lester B, Woules T, and Thompson B. 2015. Prenatal exposure to recreational drugs affects global motion perception in preschool children. *Scientific Reports* 5:16921