Protocol 30 Classifying Substances as Carcinogenic

May 2018

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Carcinogenic substance" should be added to this list as it is a definition provided in Procedure 8; however, the Procedure 8 definition of a "carcinogenic substance" obviously needs to be revised but unclear how quickly that can happen. Until that time, we assume that a Protocol supersedes a Procedure but perhaps that could be stated here that the Procedure 8 definition substance is no longer valid. Possible solution: Add "carcinogenic substance" to the definitions and then amend Procedure 8. If amendment of Procedure 8 is going to take some time, perhaps state here that the Protocol 30 definition supersedes Procedure 8.	The term "carcinogenic substance" was removed from Procedure 8 once the new CSR definition came in place.
Likely a minor issue but the weight-of-evidence definition in Procedure 8 seems to be a MOE definition. But just to be clear, it is the US EPA weight-of-evidence classification that seems to be the term used in Protocol 30 and so it would probably have been more accurate to use the US EPA definition (i.e., US EPA definitition may not completely match the MOE's Procedure 8 definition). Possible solution: This term could perhaps be removed from this list as it could be confusing. Alternatively, MOE could use the US EPA definition of weight of evidence rather than its own. Finally, MOE could determine that the two definitions are close enough that they do not adjustment.	The ministry agrees that in the context that the term was used it refers to US EPA`s weight-of-evidence classification. The term was removed from Section 1.
For the purposes of the Regulation, a human health risk assessment of a carcinogenic substance at a contaminated site requires that both the non-carcinogenic and carcinogenic effect endpoints of the substance be assessed. Key issues with this statement that both cancer and non-cancer endpoints need evaluation could be further discussed here (or perhaps in TG7) are: • some carcinogenic substances do not have readily available non-carcinogenic TRVs and so it is difficult to	These issues are addressed in TG7.

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evaluate the non-cancer endpoint. A good example is dibenz(a,h)anthracene where a potency factor is available but not a TDI or RfD. And so, it may not be possible to calculate HQ values for some carcinogens. Possible solution: Include a statement here and/or in TG7 that specifies that MOE is aware of such issues and non-carcinogenic endpoints are not required to be evaluated in such cases. • some carcinogenic substances do not have potency factors and instead are treated as threshold substances. Good example examples PCDD/Fs and PCBs both of which are classified as Group 1 by IARC. And so, it may not be appropriate to calculate ILCR estimates for some carcinogens. Possible solution: Include a statement here and/or in TG7 that specifies that ILCRs are not are not required to be evaluated in such cases. • some carcinogenic substances will not have cancer potency estimates available for other reasons. Specifically, IARC is in the business of classifying substances but not in providing potency estimates and, consequently, if IARC has classified a substance as carcinogenic Group 1 or 2A, there can be no assurance that another agency has provided a potency estimate. Thus, it may not be possible to estimate ILCR for some chemicals considered to be carcinogenic substances, Possible solution: Include a statement here and/or in TG7 that MOE is aware of such issues specifies that non-carcinogenic endpoints are not required to be evaluated in such cases. Health Canada has been specifically excluded from this protocol as a source and that is fine. But there could be some confusion in that Health Canada FCSAP Part II: TRVs and Chemical-Specific Factors is a source of toxicological	

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information that is cited in TG7 and this Health Canada document may provide cancer potency factors that are not required to be considered (e.g., phenanthrene). Possible solution: There could be some benefit to specifically state that MOE is aware of this and this is the intention of the protocol (but it may be obvious enough without this	
Although we cannot be certain as the specific details on the methods of Omnibus standard development have not been released, it would seem that there is some potential that certain substances were not treated as carcinogens in the development approach would be flagged as carcinogens in the HHRA approach. Although the supporting information for criteria development is not yet available but the lead (Pb) scenario (see below) is an example of the potential disconnects that are likely unanticipated and will only come about when risk assessors start using the new guidance Possible solution: Ensure that this "3.1, 3.2 or 3.3 approach" is consistent with the Omnibus standard approach (i.e., it would be awkward if this approach triggered a different classification than was used to develop standards). Nevertheless, if there are examples where a different approach in risk assessment vs standard development is preferred, this protocol could state that is the intention (i.e., to prevent some from using the rationale that they used the standard assessment classification)	The standards derivation methods for ministry-derived standards do not contradict Protocol 30 for any substance other than lead. In the case of lead an alternative approach was used reflective of the non-threshold effects (i.e. the exposure term was adjusted to reflect lifetime exposure). The ministry recognizes that standards that were adopted from US EPA Regional Screening Levels may in some cases contradict Protocol 30, which may be addressed in the future.
Related to the above issue is lead (Pb). IARC considers lead to be Group 2A but few agencies consider Pb to be carcinogenic and it seems unlikely that the MOE used a cancer potency factor approach to develop the IL standard for Pb or for the other land uses. With that said, California EPA (see: https://oehha.ca.gov/chemicals/lead-and-lead-compounds) has oral and inhalation cancer potency factors for Pb (none of the other agencies cited in TG7 have recommended slope factors). And so it would seem possible	The ministry did not consider carcinogenicity in its standards development and does not currently require risk assessors to evaluate lead as a carcinogenic substance. Although IARC has listed lead as a Group 2A carcinogen, there is no consensus on the issue among jurisdictions and science indicates that the human evidence is inadequate. Lead will be re-evaluated when pertinent information becomes available. The current risk assessment requirements are clarified in TG7. See also the previous comment.

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that some could consider that Protocol 30 is stating risk assessments need to consider Pb as a carcinogen due to the IARC classification and then use the CalEPA potency factor even though it would seem that Omnibus standards did not. We give this example for Pb but there are bound to be other chemicals that will have a similar issue. Possible solution: MOE should examine this issue and provide risk assessors with guidance that state the preferred approach. It would seem that if the cancer designation was available at the time the Omnibus standards were developed but not used by the MOE, that the HHRA should not be required to evaluate the substance as a carcinogen. Alternatively, if that is not the case, the MOE could state that such substances are required to be evaluated as carcinogens if that is the intention. Either way, it is recommended that this issue should be clarified	
Is it important to MOE that the source of the selected TRV is the same as the source of the carcinogen classification? Currently, it would seem that Protocol 30 could direct a risk assessor to use a classification from US EPA/IARC/CCME and then use a TRV that is not from the same source. This would definitely occur with any IARC classification (since IARC does not provide potency estimates) but could also occur with other sources. Is that a problem? Possible solution: It is recommended that MOE evaluate this issue. If MOE has no problem with such an approach, the text of Protocol 30 is fine; however, if that is not the intention, the text would need to be revised to prevent this interpretation	It is the ministry's intention that Protocol 30 is used for determining whether or not a substance should be considered a carcinogen under the CSR, whereas the TRV selection should follow the hierarchy as available in TG7.
Because the US EPA approach is a bit complex (i.e., risk assessors need to be able to use pre- and post-2005 guidance, a bit more context might be useful. Possible solution: Consider some introductory text such as the following: *In providing cancer potency information, US EPA has typically provided a descriptor that classifies the*	More context was provided and the sections following were re-named and re-organized for clarity (see response following).

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likelihood of a substance may be a carcinogen to people. Since 2005, US EPA has used a classification scheme that describes carcinogenic potential using a weight-of-evidence descriptor; however, prior to 2005, an alphanumeric descriptor system was used. Although new evaluations use the US EPA (2005) classification system, there are numerous carcinogens on the US EPA IRIS database that are still only evaluated under the older system. In the case that a weight-of-evidence evaluation using the US EPA (2005) classification system is not available, the US EPA alphanumeric descriptor should be used. Consequently, the following two approaches need to be considered.	
Rename section as "*3.1.1 US EPA Weight-of-Evidence Evaluation Descriptor*" Rename section as "*3.1.2 US EPA Alphanumeric Classification Descriptor*"	The two sections were renamed to Weight-of-Evidence Descriptors and Alphanumeric Descriptors; the US EPA 1996 descriptor "known/likely carcinogen" was moved into Section 3.1.1.
Likely a minor issue but we could not verify that "known or likely human carcinogen" was a previous US EPA category. Entirely possible that it was but we could not find it. Possible solution: This is likely a minor issue but MOE could determine if they have information that supports this and if not, remove bullet (a)	This was the 1996 category. On the IRIS website few chemicals can still be found with this classification.
US EPA (2005) does discuss the issue that some chemicals may have multiple classifications on page 2-58 of their document. Not sure if this is likely to be an issue but it could be discussed in this protocol. Essentially, it is stating that some classifications may be different for: 1) the same chemical for different routes of exposure; and 2) the same chemical for different dose rates or air concentrations. Possible solution: Although it will apply to only a limited number of chemicals	This is correct. The risk assessment approach should follow the approach taken in standards derivation, which is that a carcinogen needs to be carcinogenic by the exposure pathway evaluated, as stated in TG7.

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(e.g., nickel), it is recommended that MOE should Consider whether these multiple classifications by US EPA are applicable (we think they ae reasonable) and then if so, include the mention. Or if they are not MOE's intention, that could be stated too	
Likely a minor issue but we think the CCME avoids the terms "carcinogenic" and "possibly carcinogenic" in stating these are the carcinogenic PAHs of concern. Instead, CCME states that their scheme is adopted on the WHO approach and order of magnitude cancer potency factor (see page 120 of the CCME document). Possible solution: This is likely a minor issue but MOE could determine if they have information that supports this and if not, remove these terms	On page 24-25 of the document cited, it reads, "*CCME has provisionally defined the carcinogenic PAHs of interest to […], as well as the possible or known carcinogens chrysene and benzo[j]fluoranthene."* The comment is correct in that CCME does not assign classes, but has used a description such as that used in Protocol 30.
This wording could lead some to interpret that HHRAs need to only consider the PAHs in Table 1 as the carcinogens (we don't think is necessarily the intent and instead it would seem that these Table 1 PAHs need consideration plus any others triggered by US EPA and IARC systems). In other words, we are not sure that it will be entirely clear that risk assessments will need to evaluate all PAHs in Table 1 plus any other PAHs that are accordingly classified in Sections 3.1 and 3.2. Currently, the list in Table 1 is accurate but as US EPA and WHO continue to evaluate, there is the possibility that a PAH could be added to the list and so Table 1 should not be construed as the only PAHs that need to be evaluated in the future and instead the risk assessor should stay on top of this issue. Possible solution: More clearly state that in addition to the Table 1 PAHs, HHRAs need to check the US EPA and IARC classifications (currently it would seem that no other PAHs would be triggered but that could change with time as US EPA and IARC re-do their assessments from time to time)	The intent is to only evaluate the PAHs listed in Table 1. If new evidence becomes available the substance should be included; the ministry will update Protocol 30 as necessary.
Even though CCME is being cited as the source of classification, it would seem that TG7 states that Health	This is clarified in TG7.

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Canada slope factors and PEFs should be preferentially used. Although they seem to be the same PEFs for the PAHs that are considered carcinogens, Table 7 provides a bunch of other PEFs and so it could create confusion if a person does not figure out that a protocol is supposed to supersede guidance. Possible solution: This could probably addressed in TG7 but it could still be noted here that CCME, US EPA and IARC are only a source of classification and not the source of TRVs.	
On page 2 of Draft TG7, it is stated that Table 7 of Health Canada PQRA should be the source of PAH PEFs. Health Canada PQRA Table 7 provides PEFs for a great number of PAHs that are not listed in Table 1 of Protocol 30 and so it could create confusion if a person does not figure out that a protocol is supposed to supersede guidance. Possible solution: This could probably addressed in TG7 but it could be noted here as well	This is clarified in TG7.
CCME updates their values periodically and so if CCME has a new document say in 2018 or 2019, should the risk assessment amend this list? Possible solution: Include a clause that the risk assessor should also check and use more recent CCME reports if available	It is good practice to check more recent documents once they become available. However, the ministry intends to update Protocol 30 as necessary.
Is there is a way to not cite documents 2 to 4? These are potentially problematic in that they are awkwardly just earlier versions of document 1 and the hyperlinks do not seem to provide these earlier versions of the document. Possible solution: Remove documents 2 to 4 from the reference list. Alternatively, provide hyperlinks to the actual documents	The reference to the ‘Review Draft of 1999’ was removed and the remaining links were updated to link directly to the actual documents.