

To: Kathryn Guyton[GuytonK@iarc.fr]; Rusyn, Ivan[IRusyn@cvm.tamu.edu]
From: Martin, Matt
Sent: Thur 1/22/2015 2:21:21 PM
Subject: Mono 112 Section 4.3 (Generic)
Monograph 112 Section 4.3.docx

Hi Kate and Ivan,

Attached is an early draft of the section 4.3 which at this point is fairly generic to chemical.

I am imagining that once the details of the analysis are ironed out and figures generated we will also be able to provide a chemical-specific summary and conclusion (of sorts).

I figured I would send this early draft to get feedback.

In talking with a few folks around NCCT here is some of the feedback I received:

1. A bit simplistic and all encompassing – maybe focus down the assay space (essentially include assays/targets we have good evidence for linkage)
2. Reduce/Group by gene and/or gene family prior to analysis (reducing bias for targets with many assays vs ones with limited; also reduces impacts of single false positives)
3. Although it is understood that a relative assessment is not what is being sought, we still need to put these individual chemicals in relative space (relative to other chemicals and relative potencies and efficacies across assays for a given chemical) to even begin to provide context and understanding of the results.
4. Reduce assays based on association (statistical) with cancer outcomes or classifications (i.e., run statistical analysis comparing each assay or group of assays to rodent tumor findings and to the iarc classifications) and use the resulting assay set to provide insight to what associated targets each chemical hits.

I figured I would throw most of the thoughts/ideas at you for digestion.... I think #2 is a good idea and will help in communicating this to the rest of the group as we would be talking about biology rather than specific assays (e.g., androgen receptor antagonism vs tox21_ar_bla_antagonist etcetcetc)...

I am also working on pulling together a similar generic structure for the “other adverse outcomes” section using ToxRefDB (I think that is what you want from that section?).

Matt

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