Fortnightly meeting 30th April 2019

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Contents

1 Basic Inhalation Investigation

1.1 Limit to inhalation studies

We are interested in generating inhalation-based TTC values; therefore, we need to filter for inhalation studies.
I'm going to start by getting a general sense of the number of studies that fit with the basic criteria we used for the oral, chronic TTC values and then focus down.
I'm going to start off by using these filtering criteria:

- Test species: Rat, mouse, other rodents, or rabbit
- Route of exposure: Inhalation

As we can see there a total of 28,772 POD values present in ToxVal that meet our basic criteria. These PODs cover 3,103 unique chemicals.

1.2 Filter out acute and subacute studies

Now we are filtering based upon:

- Test species: Rat, mouse, other rodents, or rabbit
- Route of exposure: Inhalation
- Study duration: subchronic, chronic, reproductive, developmental, and multigeneration

By filtering out the acute and subacute studies as well we drop down to 7,102 POD values covering 817 unique chemicals.

1.3 POD types

However, we still don't know what the types of POD are that we have in this dataset. So let's have a look:

Table 1: Count of each inhalation POD type

POD Type	Count
noael	2702
noaec	2110
noel	532
loael	463
loaec	303
rfc	234
lel	220
nel	220
noec	92
bmdl	56
loec	49
undefined	42
loel	32
bmcl	23
concentration level	13
bmcl10	3
noael/loael	2
bmdl10	2
lec	1
matc	1
mtd	1
lc100	1

As we can see above, there are 15 different types of POD present for this filtered set.
The three most prevalent are for NO(A)ELs, NO(A)ECs, and NOELs. The fact NO(A)ELs and NOELs are two of the top three PODs present is good because, based upon our previous work, they are what we're after. Also having NO(A)ECs at the top is good because concentrations are, typically, used when discussing inhalation studies.

Whilst this tells us the total number of each type of POD present in the filtered ToxVal set, it doesn't tell us about the number of unique chemicals that are covered by the NO(A)EL/NOEL studies.

By filtering for only those studies that are measure either a NO(A)EL or NOEL, we find out there are 3,234 studies with either NO(A)EL or NOEL data covering 629 unique chemicals.

However, if we add NO(A)EC PODs into the mix, there are 5,436 studies with either a NO(A)EL, NOEL, NO(A)EC, or NOEC value. These 5,436 studies cover 760 unique chemicals. Given the number of NO(A)EC values, would it be a good idea either to convert the NO(A)ELs/NOELs to NO(A)ECs or vice-verse?

1.4 Filtering for only NO(A)EL and NOEL POD studies

Now we know how many studies measure a NO(A)EL/NOEL we can start to look at the units these PODs are measured in. To do this we need to filter for those studies that measure NO(A)EL or NOEL values and see what the breakdown of POD units are. So we are now filtering based upon:

- Test species: Rat, mouse, other rodents, or rabbit
- Route of exposure: Inhalation
- Study duration: subchronic, chronic, reproductive, developmental, and multigeneration
- POD type: NO(A)EL or NOEL

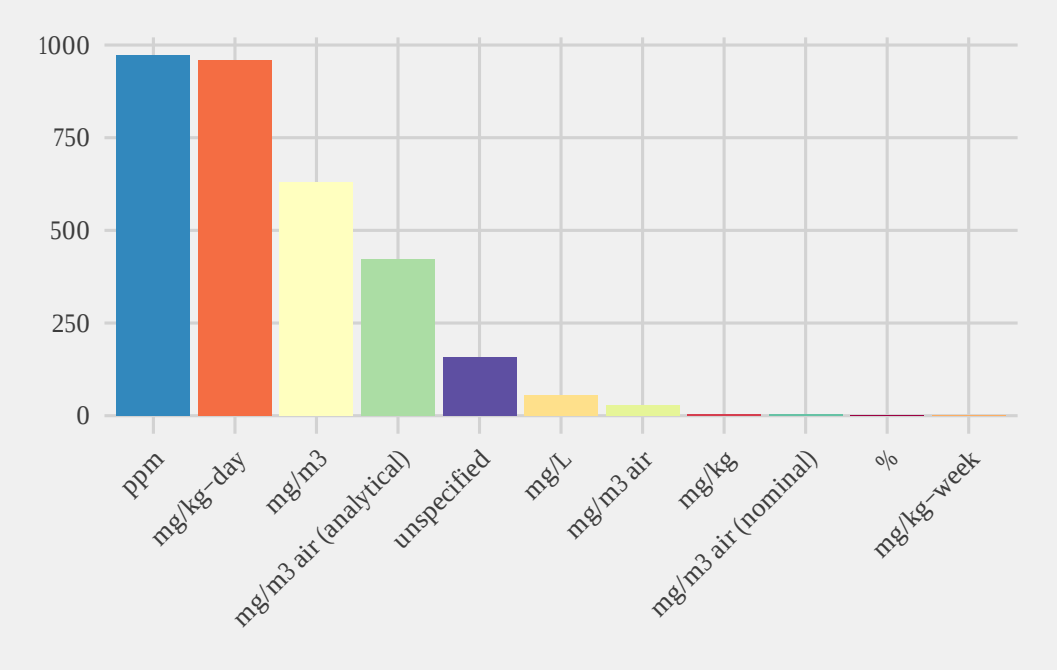

Figure 1: Count of NOEL or NO(A)EL studies each POD unit is measured in

As we can see in Figure 1. above, the majority of these studies are measured in terms of either ppm or mg/kg-day. Therefore, if we can convert from one to the other (maybe from ppm to mg/kg-day via mg/m^3) then we will roughly double our sample size. We could also add in quite a few more POD values if we convert from mg/m^3 or mg/m^3 analytical air to ppm or mg/kg-day, what do you think?

Again this is focussed on the number of studies/POD values we have for the filtered set, but it says nothing of the number of unique chemicals present in the set.

If we look at just the studies which measure the NO(A)EL/NOEL in terms of ppm, we can see that there are 303 chemicals.

However, if we consider those studies that measure their POD in terms of ppm, mg/kg-day, or mg/m^3 (including mg/m^3 air (analytical)):

Then we can see that there are 609 unique chemicals, with 2,983 associated studies.

If we add the NO(A)EC and NOEC values that are measured in one of these units there are 609 unique chemicals, with 2,983 POD values.

Below (Figure 2), is a bar chart of the breakdown of each POD unit used in a study with a NOEL, NO(A)EL, NOEC, or NO(A)EL value reported.

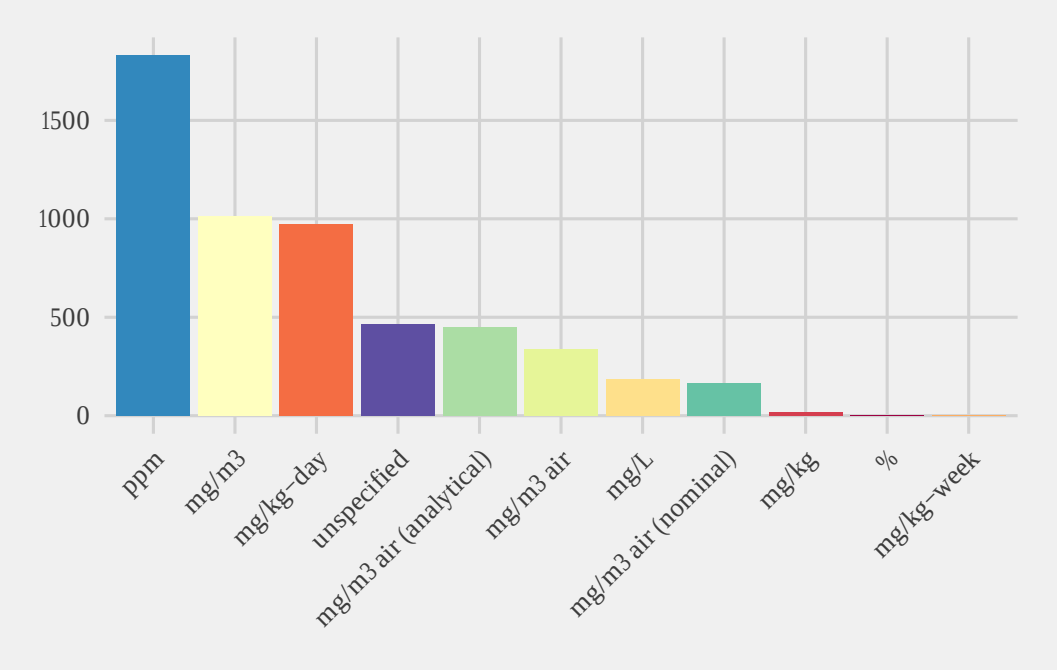

Figure 2: Count of NOEL, NO(A)EL, NOEC, or NO(A)EC studies each POD unit is measured in

1.5 Study criteria I think might be best

Therefore, I feel like it may be best if we take studies that fit these criteria:

- Test species: Rat, mouse, other rodents, or rabbit
- Route of exposure: Inhalation
- Study duration: subchronic, chronic, reproductive, developmental, and multigeneration
- POD type: NO(A)EL, NOEL, NO(A)EC, and NOEC
- POD units: ppm, mg/kg-day, mg/m^3, and maybe mg/m^3 air (analytical)

Whilst having multiple POD units means we're going to have to do a bit more work on the front end to get them all to be the same, I think the benefit of the additional chemicals it will allow us to include will be of benefit.

How would you feel about also including the chemicals present in the Escher et al inhalation TTC paper? I don't know if there are overlaps between to two datasets or not, it's more a question I'm throwing out there.

The Tluczkiewicz et al (2016) paper also uses the LOEC and an extrapolation of 3 to estimate a NOEL for chemicals that don't have a NOEL already defined, we could may be give this a try if we don't have enough information.

2 Extra information that might be of interest

2.1 Comparison of POD units across all POD types

Now we know the types and numbers of PODs present in ToxVal for inhalation studies, let's have a look at the spread of units for these PODs.

Table 2: Count of each inhalation POD type

POD Type	Count
ppm	2550
mg/m3	1592
mg/kg-day	1144
unspecified	475
mg/m3 air (analytical)	447
mg/m3 air	384
mg/L	312
mg/m3 air (nominal)	175
mg/kg	18
mg/kg-week	1

The above table shows the breakdown of POD units present for inhalation studies in ToxVal that fit out filtering rules. However, they cover all 22 POD types in the previous table.

The fact there are more studies measured in ppm is also good for us. This is because the other 3-4 articles I've seen that have tried to calculate TTC values for inhalation studies have put their TTC values in terms of ppm.

Additionally, there are another 2598 studies with PODs using some variation of mg/m^3. Although, I'm not too sure of the conversions needed to get mg/m^3 air into mg/m^3 units.

For those studies using straight mg/m^3, if we can get the MW for each chemical then it shouldn't be too difficult to convert the mg/m^3 into ppm units, which will provide us with another 1592 POD values that we can take into account.