Fortnightly meeting 4th June 2019

Mark

4/6/2019

Contents

1 Inhalation TTC

1.1 Phys-chem properties

Profiled the chemicals with QSAR ready SMILES through OPERA to calculate phys-chem properties. These properties are:

- Molecular Weight
- TPSA
- logP
- Melting point
- Boiling point
- Vapour pressure
- Water solubility
- Henry's law
- $\log K_{OA}$
- pKa Acid
- pKa Base
- $LogD_{5.5}$
- $LogD_{7.4}$
- LogOH
- Number of H-bond acceptors
- Number of H-bond donors

1.2 Profiling chemicals using QSAR Toolbox

Ran each of the chemicals with QSAR ready SMILES through the QSAR Toolbox and profiled for:

- Respiratory sensitisation alerts
- Eye/skin irritation exclusion rules
  - based upon physico-chemical cut-offs to ID chemicals that do NOT exhibit eye/skin irritation

- Eye/skin irritation inclusion rules
  - based on structural alerts to ID chemicals with the potential for eye/skin irritation/corrosion

1.2.1 Eye/skin irritation/corrosion inclusion/exclusion rules

- There are 127 unique chemicals with exclusion rules for eye corrosion/irritation
- There are 16 unique chemicals with an inclusion rule for eye corrosion/irritation
- There are 116 unique chemicals with exclusion rules for skin corrosion/irritation
- There are 206 unique chemicals with an inclusion rule for skin corrosion/irritation

I'm not sure how to incorporate the eye/skin irritation incl/excl rules from the Toolbox. I found a table from OASIS that lays out how to use them but the output I have from the Toolbox is different from what they have in their table.

For example, current output says things like "Group C Melting point > 55°C" (I don't know if this means it's not irritating or not corrosive). In the table from OASIS the expected output seems to be "Not corrosive to skin". The table does date back to 2016 so it looks like this hasn't been updated as the output has been updated. Additionally, the inclusion alerts aren't set out as corrosive or irritant either. Therefore, it's going to be more difficult to use the table to categorise the chemicals.

My guess is that if there is an exclusion rule identified then the chemical shouldn't be corrosive or an irritant, irrespective of if there's an inclusion rule.

1.2.2 Respiratory sensitisation alerts

Of the 4703 chemicals profiled for respiratory sensitisation, only 9 chemicals trigger multiple alerts. Of these nine, 4 trigger two different mechanisms (e.g. Michael addition and SN_2).

- Do we only care that a chemical triggers an alert?
- If we can about the type of mechanism, do we only care about the highest level of the alert (e.g. Acylation) or do we also care about the more specific alert (e.g. Di-isocyanate) that is triggered?

1.3 Density plots of minimum ToxVal ppm data converted to mg/m^3

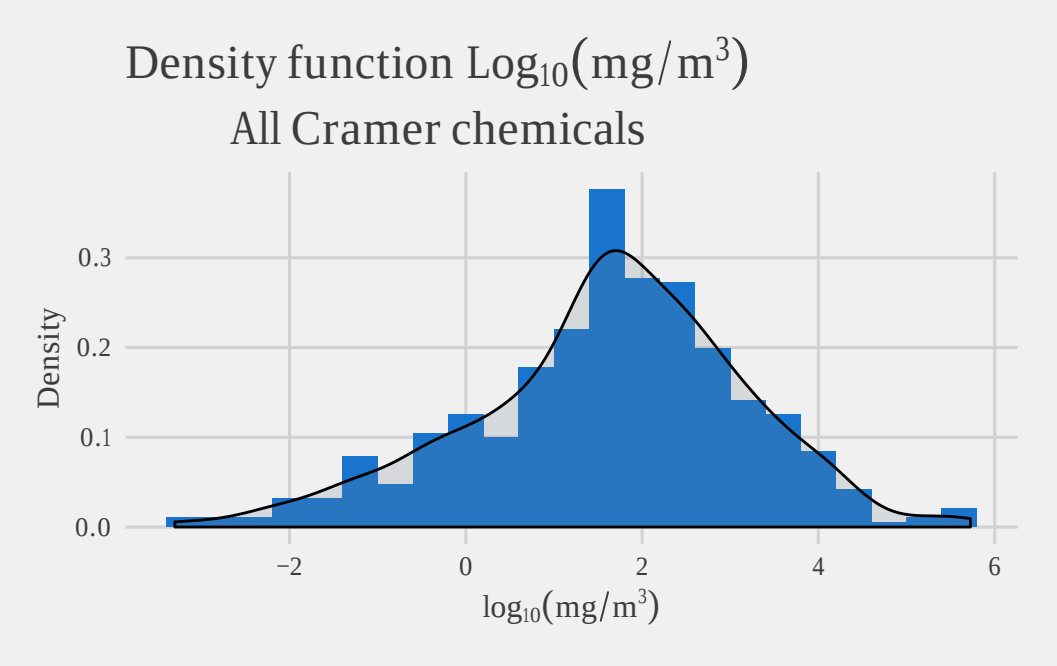


Figure 1: Density plot of minimum toxicity values for all Cramer classes

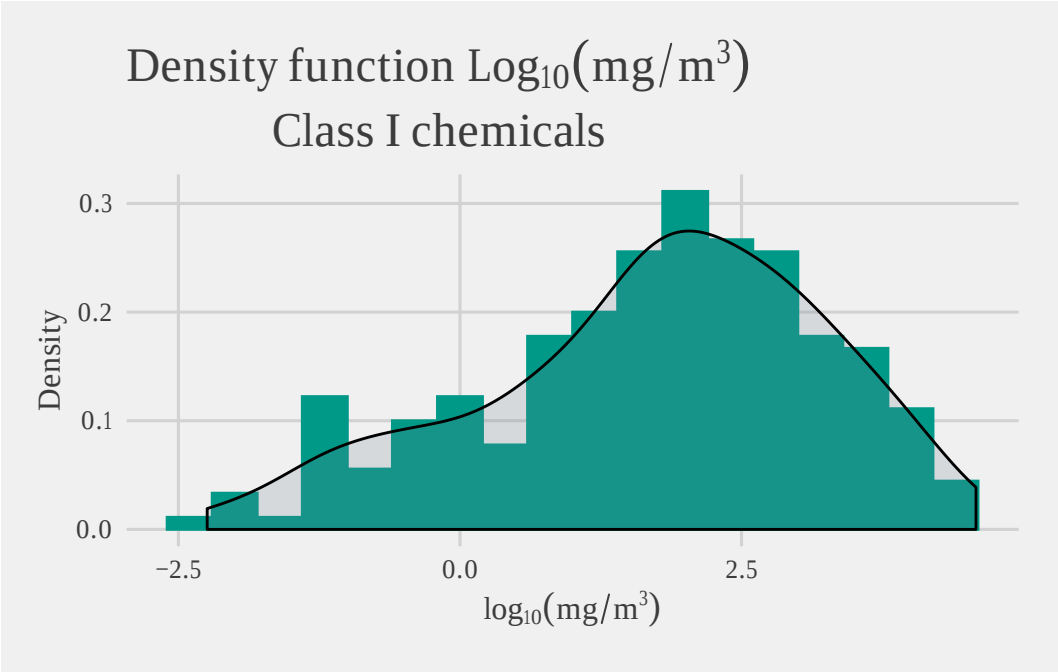


Figure 2: Density plot of toxicity values for Cramer class I chemicals

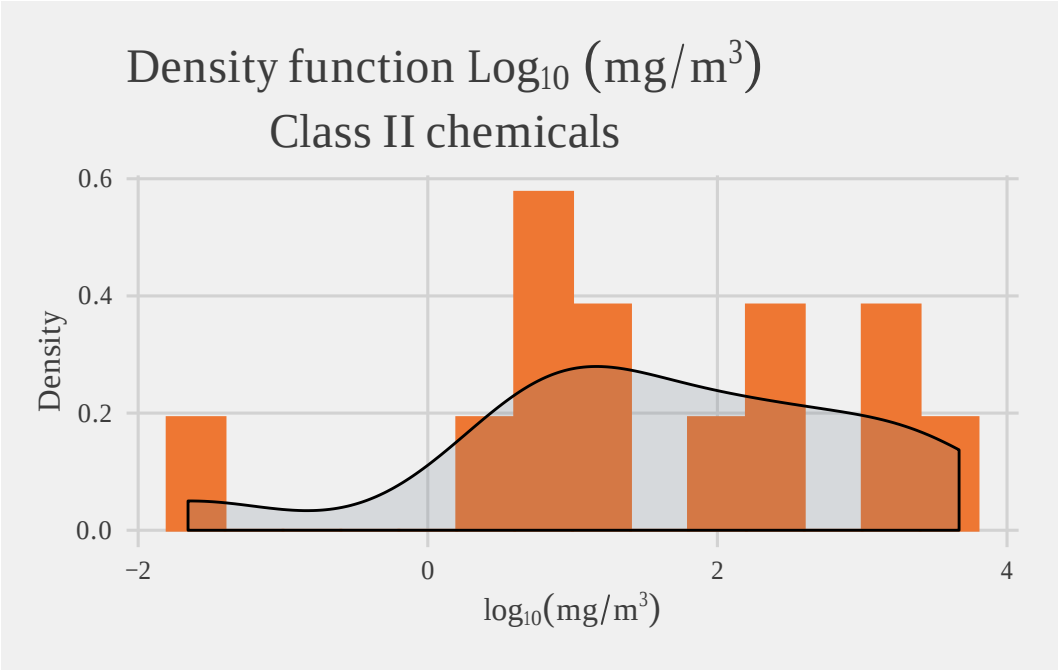


Figure 3: Density plot of toxicity values for Cramer class II chemicals

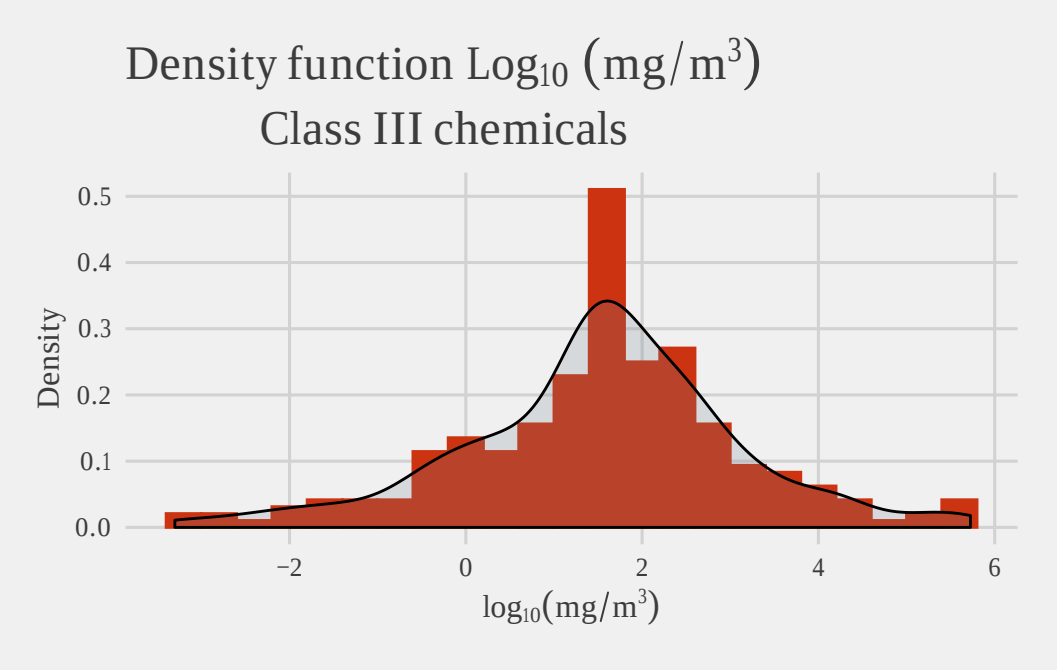


Figure 4: Density plot of toxicity values for Cramer class III chemicals

As you can see from the density lines (in black) the $\log_{10}$mg/m³ values are approximately lognormal for Cramer classes I and III. There aren't enough data points for Cramer class II to be able to get a good feel for the density function.

1.4 5th Percentiles using the Cramer classes

As we had the TTC decision tree results I decided to see what we would get if we used the Cramer classes to calculate the 5th percentile values (in mg/m³).

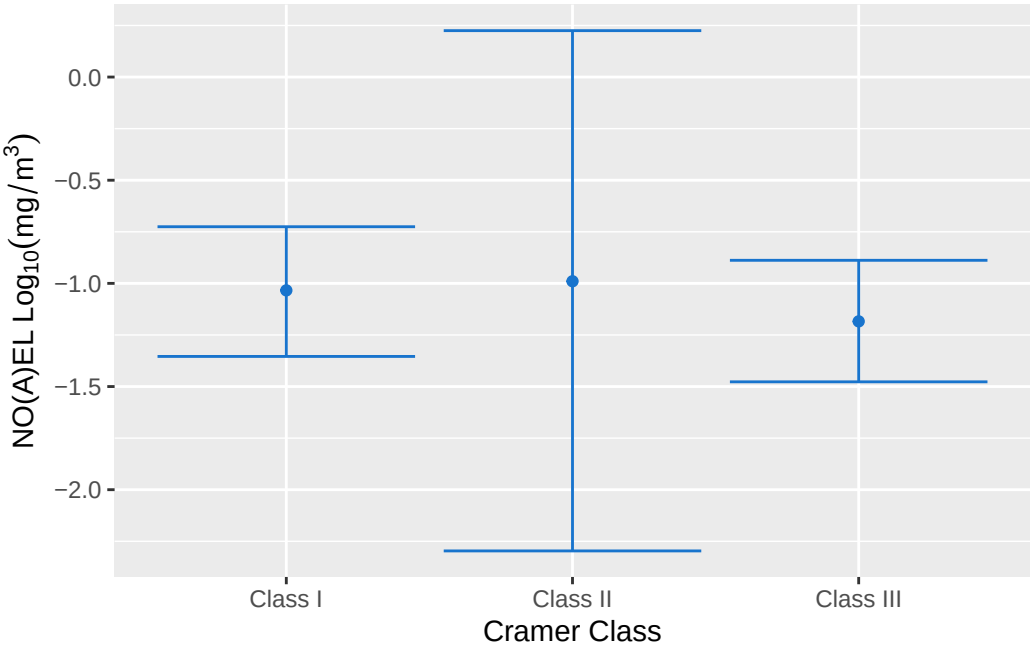
Overall: 0.122mg/m³ (478 chemicals)

Cramer class I: 0.173mg/m³ (225 chemicals)

Cramer class II: 0.212mg/m³ (13 chemicals)

Cramer class III: 0.088mg/m³ (240 chemicals)

1.4.1 Comparison of inhalation 5th percentiles between Cramer classes




```
## List of 67
##  $ line                      :List of 6
##   ..$ colour       : chr "black"
##   ..$ size         : num 0.545
##   ..$ linetype     : num 1
##   ..$ lineend      : chr "butt"
##   ..$ arrow        : logi FALSE
##   ..$ inherit.blank: logi FALSE
##   ..- attr(*, "class")= chr [1:2] "element_line" "element"
##  $ rect                      :List of 5
##   ..$ fill         : Named chr "#F0F0F0"
##   .. ..- attr(*, "names")= chr "Light Gray"
##   ..$ colour       : logi NA
##   ..$ size         : num 0.545
##   ..$ linetype     : num 0
##   ..$ inherit.blank: logi FALSE
##   ..- attr(*, "class")= chr [1:2] "element_rect" "element"
##  $ text                      :List of 11
##   ..$ family       : chr "Alegreya"
##   ..$ face         : chr "plain"
##   ..$ colour       : Named chr "#3C3C3C"
##   .. ..- attr(*, "names")= chr "Dark Gray"
##   ..$ size         : num 12
##   ..$ hjust        : num 0.5
##   ..$ vjust        : num 0.5
##   ..$ angle        : num 0
##   ..$ lineheight   : num 0.9
##   ..$ margin       : 'margin' num [1:4] 0pt 0pt 0pt 0pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : logi FALSE
##   ..$ inherit.blank: logi FALSE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ axis.title.x              :List of 11
```

```
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : NULL
##   ..$ vjust        : num 1
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 3pt 0pt 0pt 0pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ axis.title.x.top          :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : NULL
##   ..$ vjust        : num 0
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 0pt 0pt 3pt 0pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ axis.title.y              :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : NULL
##   ..$ vjust        : num 1
##   ..$ angle        : num 90
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 0pt 3pt 0pt 0pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ axis.title.y.right        :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : NULL
##   ..$ vjust        : num 0
##   ..$ angle        : num -90
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 0pt 0pt 0pt 3pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : NULL
```

```
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ axis.text                 :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : 'rel' num 0.8
##   ..$ hjust        : NULL
##   ..$ vjust        : NULL
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : NULL
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi FALSE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ axis.text.x               :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : NULL
##   ..$ vjust        : num 1
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 2.4pt 0pt 0pt 0pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ axis.text.x.top           :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : NULL
##   ..$ vjust        : num 0
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 0pt 0pt 2.4pt 0pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ axis.text.y               :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : num 1
##   ..$ vjust        : NULL
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 0pt 2.4pt 0pt 0pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
```

```
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ axis.text.y.right         :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : num 0
##   ..$ vjust        : NULL
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 0pt 0pt 0pt 2.4pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ axis.ticks                : list()
##   ..- attr(*, "class")= chr [1:2] "element_blank" "element"
##  $ axis.ticks.length         : 'unit' num 3pt
##   ..- attr(*, "valid.unit")= int 8
##   ..- attr(*, "unit")= chr "pt"
##  $ axis.ticks.length.x       : NULL
##  $ axis.ticks.length.x.top   : NULL
##  $ axis.ticks.length.x.bottom: NULL
##  $ axis.ticks.length.y       : NULL
##  $ axis.ticks.length.y.left  : NULL
##  $ axis.ticks.length.y.right : NULL
##  $ axis.line                 : list()
##   ..- attr(*, "class")= chr [1:2] "element_blank" "element"
##  $ axis.line.x               : NULL
##  $ axis.line.y               : NULL
##  $ legend.background         :List of 5
##   ..$ fill         : NULL
##   ..$ colour       : logi NA
##   ..$ size         : NULL
##   ..$ linetype     : NULL
##   ..$ inherit.blank: logi FALSE
##   ..- attr(*, "class")= chr [1:2] "element_rect" "element"
##  $ legend.margin             : 'margin' num [1:4] 6pt 6pt 6pt 6pt
##   ..- attr(*, "valid.unit")= int 8
##   ..- attr(*, "unit")= chr "pt"
##  $ legend.spacing            : 'unit' num 12pt
##   ..- attr(*, "valid.unit")= int 8
##   ..- attr(*, "unit")= chr "pt"
##  $ legend.spacing.x          : NULL
##  $ legend.spacing.y          : NULL
##  $ legend.key                :List of 5
##   ..$ fill         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ linetype     : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_rect" "element"
##  $ legend.key.size           : 'unit' num 1.2lines
##   ..- attr(*, "valid.unit")= int 3
```

```
##   ..- attr(*, "unit")= chr "lines"
##  $ legend.key.height         : NULL
##  $ legend.key.width          : NULL
##  $ legend.text               : list()
##   ..- attr(*, "class")= chr [1:2] "element_blank" "element"
##  $ legend.text.align         : NULL
##  $ legend.title              :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : num 0
##   ..$ vjust        : NULL
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : NULL
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ legend.title.align        : NULL
##  $ legend.position           : chr "bottom"
##  $ legend.direction          : chr "horizontal"
##  $ legend.justification      : chr "center"
##  $ legend.box                : chr "vertical"
##  $ legend.box.margin         : 'margin' num [1:4] 0cm 0cm 0cm 0cm
##   ..- attr(*, "valid.unit")= int 1
##   ..- attr(*, "unit")= chr "cm"
##  $ legend.box.background     : list()
##   ..- attr(*, "class")= chr [1:2] "element_blank" "element"
##  $ legend.box.spacing        : 'unit' num 12pt
##   ..- attr(*, "valid.unit")= int 8
##   ..- attr(*, "unit")= chr "pt"
##  $ panel.background          :List of 5
##   ..$ fill         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ linetype     : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_rect" "element"
##  $ panel.border              :List of 5
##   ..$ fill         : logi NA
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ linetype     : NULL
##   ..$ inherit.blank: logi FALSE
##   ..- attr(*, "class")= chr [1:2] "element_rect" "element"
##  $ panel.spacing             : 'unit' num 6pt
##   ..- attr(*, "valid.unit")= int 8
##   ..- attr(*, "unit")= chr "pt"
##  $ panel.spacing.x           : NULL
##  $ panel.spacing.y           : NULL
##  $ panel.grid                :List of 6
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ linetype     : NULL
##   ..$ lineend      : NULL
##   ..$ arrow        : logi FALSE
```

```
##   ..$ inherit.blank: logi FALSE
##   ..- attr(*, "class")= chr [1:2] "element_line" "element"
##  $ panel.grid.minor          : list()
##   ..- attr(*, "class")= chr [1:2] "element_blank" "element"
##  $ panel.ontop               : logi FALSE
##  $ plot.background           :List of 5
##   ..$ fill         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ linetype     : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_rect" "element"
##  $ plot.title                :List of 11
##   ..$ family       : NULL
##   ..$ face         : chr "bold"
##   ..$ colour       : NULL
##   ..$ size         : 'rel' num 1.5
##   ..$ hjust        : num 0
##   ..$ vjust        : num 1
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 0pt 0pt 6pt 0pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi FALSE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ plot.subtitle             :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : num 0
##   ..$ vjust        : num 1
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 0pt 0pt 6pt 0pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ plot.caption              :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : 'rel' num 0.8
##   ..$ hjust        : num 1
##   ..$ vjust        : num 1
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 6pt 0pt 0pt 0pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
```

```
##  $ plot.tag                  :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : 'rel' num 1.2
##   ..$ hjust        : num 0.5
##   ..$ vjust        : num 0.5
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : NULL
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ plot.tag.position         : chr "topleft"
##  $ plot.margin               : 'unit' num [1:4] 1lines 1lines 1lines 1lines
##   ..- attr(*, "valid.unit")= int 3
##   ..- attr(*, "unit")= chr "lines"
##  $ strip.background          :List of 5
##   ..$ fill         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ linetype     : NULL
##   ..$ inherit.blank: logi FALSE
##   ..- attr(*, "class")= chr [1:2] "element_rect" "element"
##  $ strip.placement           : chr "inside"
##  $ strip.text                :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : 'rel' num 0.8
##   ..$ hjust        : NULL
##   ..$ vjust        : NULL
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : 'margin' num [1:4] 4.8pt 4.8pt 4.8pt 4.8pt
##   .. ..- attr(*, "valid.unit")= int 8
##   .. ..- attr(*, "unit")= chr "pt"
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ strip.text.x              : NULL
##  $ strip.text.y              :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : NULL
##   ..$ vjust        : NULL
##   ..$ angle        : num -90
##   ..$ lineheight   : NULL
##   ..$ margin       : NULL
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi TRUE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ strip.switch.pad.grid     : 'unit' num 3pt
##   ..- attr(*, "valid.unit")= int 8
##   ..- attr(*, "unit")= chr "pt"
```

```
##  $ strip.switch.pad.wrap     : 'unit' num 3pt
##   ..- attr(*, "valid.unit")= int 8
##   ..- attr(*, "unit")= chr "pt"
##  $ axis.title                :List of 11
##   ..$ family       : NULL
##   ..$ face         : NULL
##   ..$ colour       : NULL
##   ..$ size         : NULL
##   ..$ hjust        : NULL
##   ..$ vjust        : NULL
##   ..$ angle        : NULL
##   ..$ lineheight   : NULL
##   ..$ margin       : NULL
##   ..$ debug        : NULL
##   ..$ inherit.blank: logi FALSE
##   ..- attr(*, "class")= chr [1:2] "element_text" "element"
##  $ panel.grid.major          :List of 6
##   ..$ colour       : Named chr "#D2D2D2"
##   .. ..- attr(*, "names")= chr "Medium Gray"
##   ..$ size         : NULL
##   ..$ linetype     : NULL
##   ..$ lineend      : NULL
##   ..$ arrow        : logi FALSE
##   ..$ inherit.blank: logi FALSE
##   ..- attr(*, "class")= chr [1:2] "element_line" "element"
##  - attr(*, "class")= chr [1:2] "theme" "gg"
##  - attr(*, "complete")= logi TRUE
##  - attr(*, "validate")= logi TRUE
```

As you can see there's quite a large amount of overlap between the 95% confidence intervals between all of the 5th percentile values. It seems like the Cramer class is probably not the best way to descriminate between the chemicals.

This is backed up by using the qcomhd function. The p-value of 0.752 shows that the 5th percentiles are not significantly different between Cramer class I and III.

1.5 Comparison of inhalation distributions using Cramer classes

Comparison of CDFs

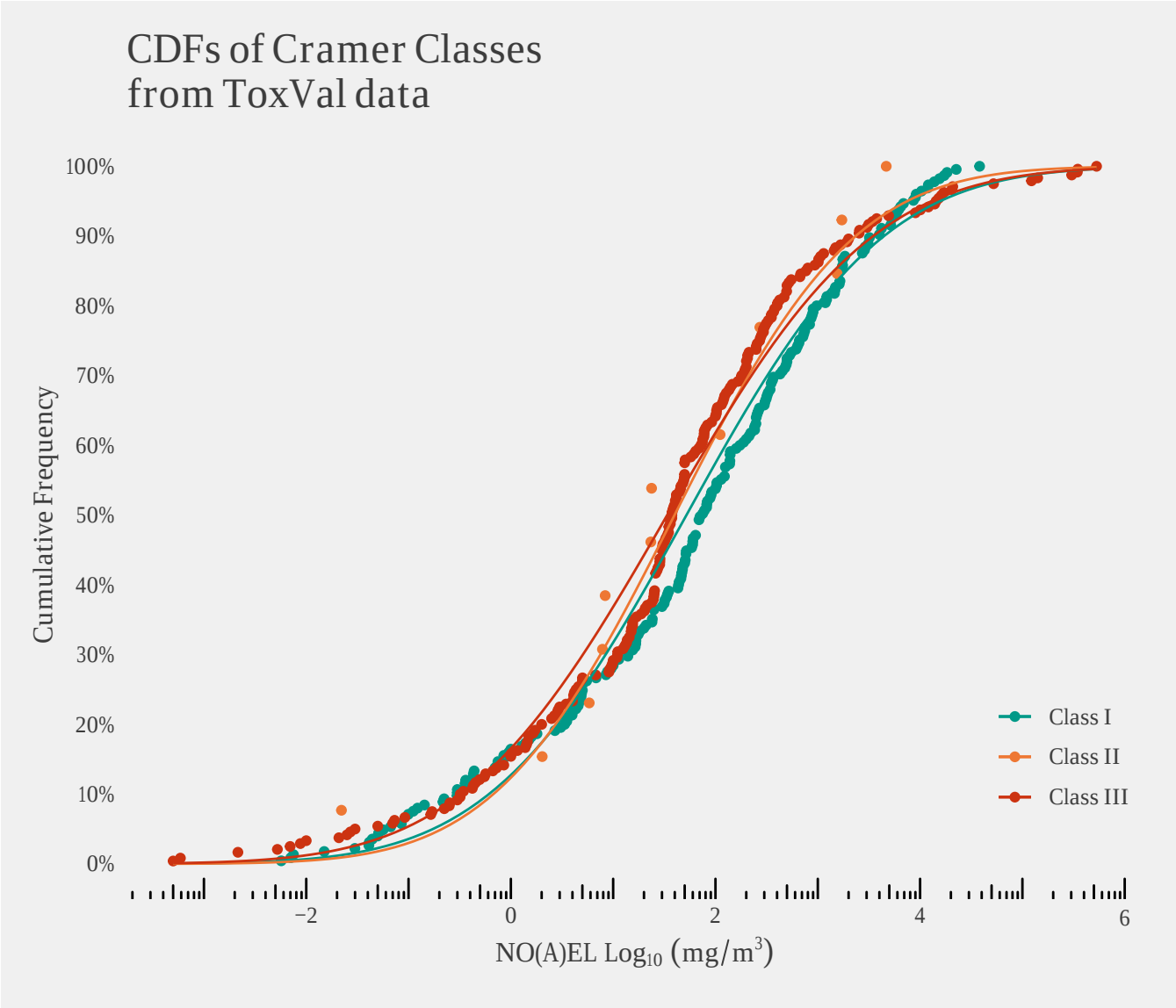


Figure 5: Cumulative distributions of each Cramer class

Using K-S test

Class I vs Class II:
D = 0.196
p-value = 0.731

Class I vs Class III:
D = 0.148
p-value = 0.012

Class II vs Class III:
D = 0.168
p-value = 0.879

According to the K-S test, only the class I and class III distributions are significantly different. However, looking at the figure above this is hard to see how this is the case.

1.6 Separating chemicals with a respiratory sensitisation alert

There are a total of 41 chemicals with a respiratory sensitisation alert:

- 29 chemicals from Cramer class I
- 0 chemicals from Cramer class II, and
- 12 chemicals from Cramer class III

The 5th percentile for chemicals with a respiratory sensitisation alert is: 0.006mg/m^3

There are a total of 437 chemicals without an alert After removing the chemcials with a respiratory sensitisation alert the 5th percentile for the remaining chemicals is: 0.188mg/m^3.

1.7 Conclusions of inhalation data

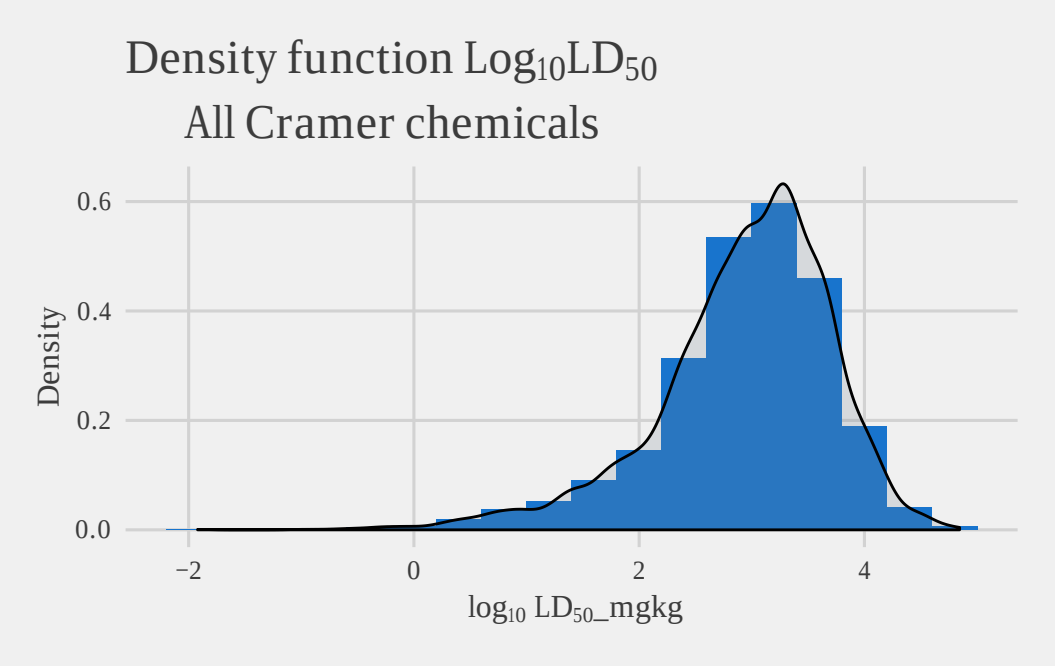
Not worth using the Cramer classes as the 5th percentile NO(A)EL/NO(A)EC values across Cramer classes are not statistically different; therefore, can't use that as a way to separate out the chemicals.
Given the difference in 5th percentile values, I do think we should remove those chemicals with a respiratory sensitisation alert.

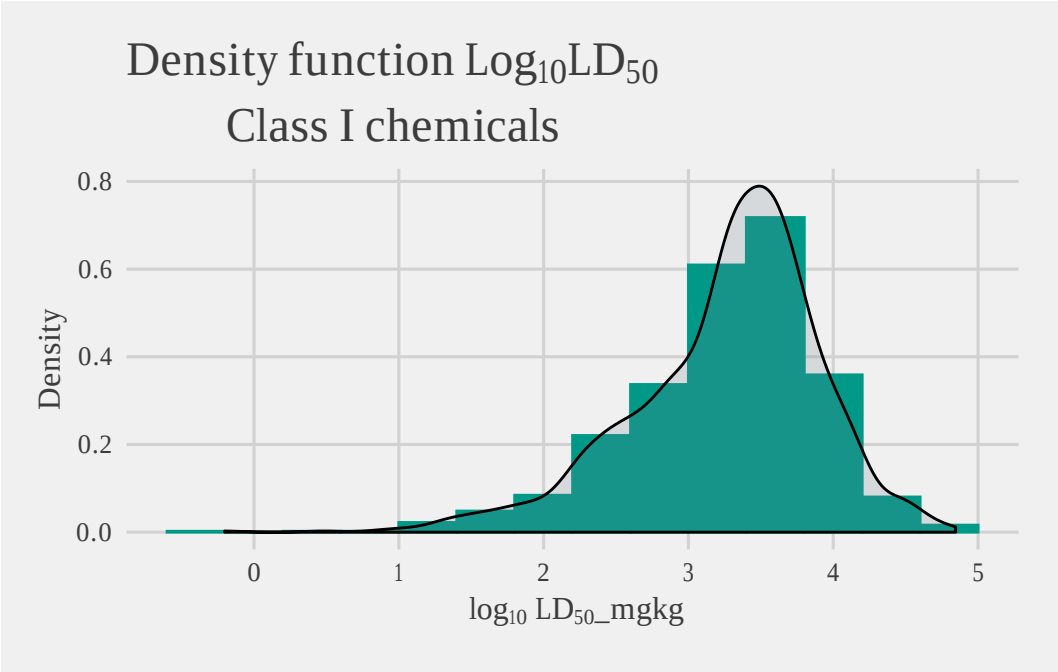
---

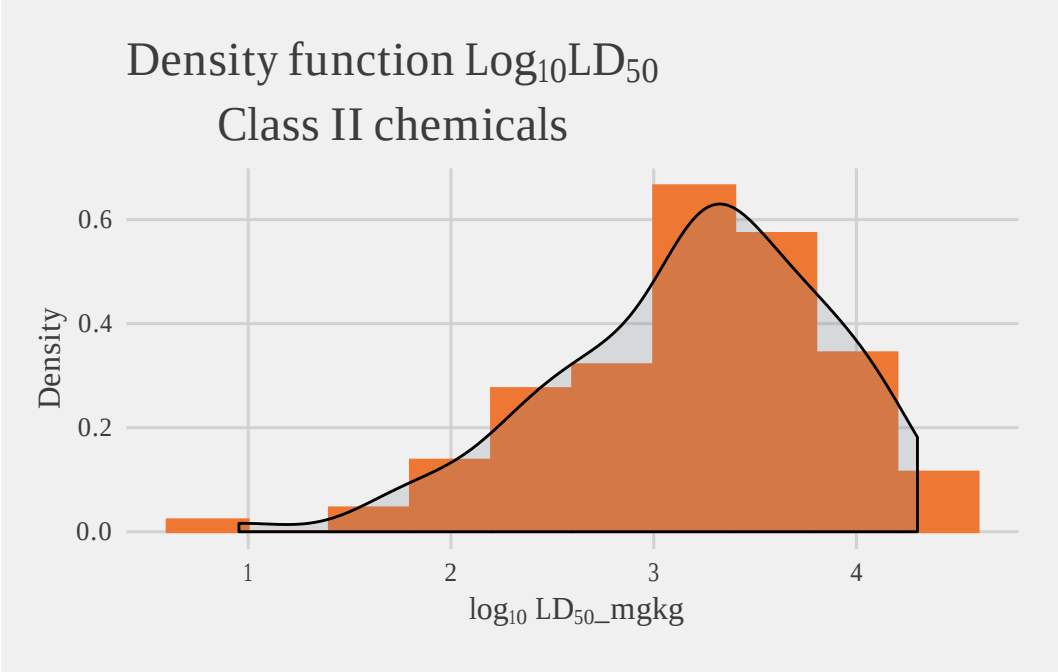
2 Acute Toxicity TTC

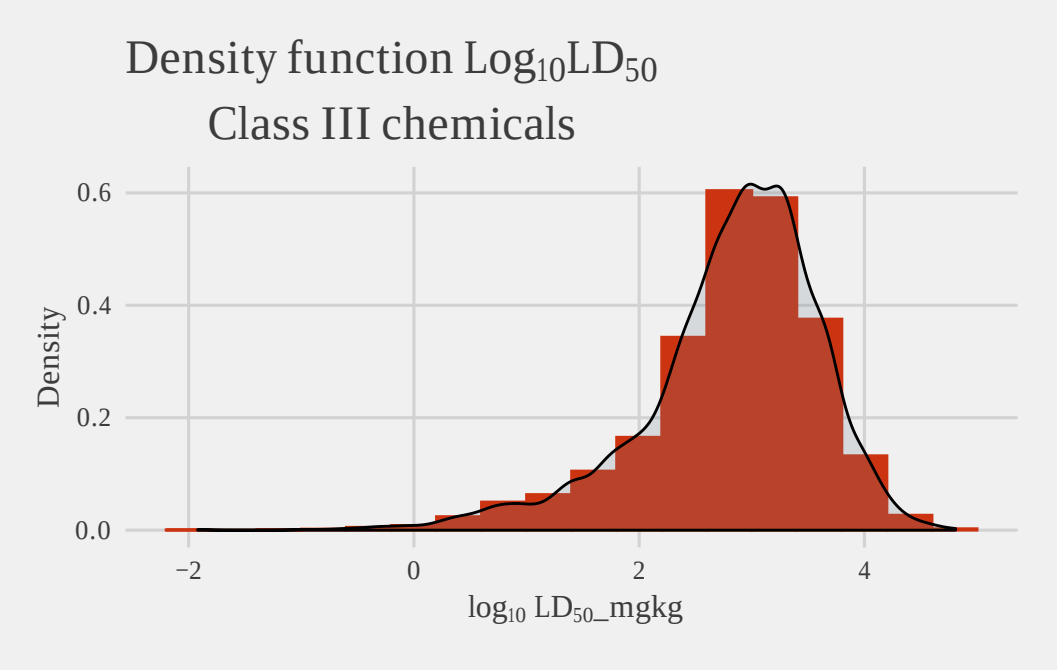
Next I took a look at the Acute toxicity data to see if we could calculate 5th percentile values using this data and how they correlate with the 5th percentile values that we calculated using the ToxVal chronic data.

2.1 Density plots of Acute toxicity $log_{10}LD_{50}$ data




Density function Log10LD50
Class I chemicals
Density
0.8
0.6
0.4
0.2
0.0
0
1
2
3
4
5
log10 LD50_mgkg


Density function Log10LD50
Class II chemicals
Density
0.6
0.4
0.2
0.0
1
2
3
4
log10 LD50_mgkg



As with the inhalation and chronic, oral data the density functions for each Cramer class looks to be lognormal, even if they are right-shifted compared to both those datasets (which isn't surprising).

2.2 Acute 5th percentiles using Cramer classes

Now we've had a look at how the distributions compared let's take a look at the 5th percentile values.

Overall: 45.409mg/m^3 (5,304 chemicals)

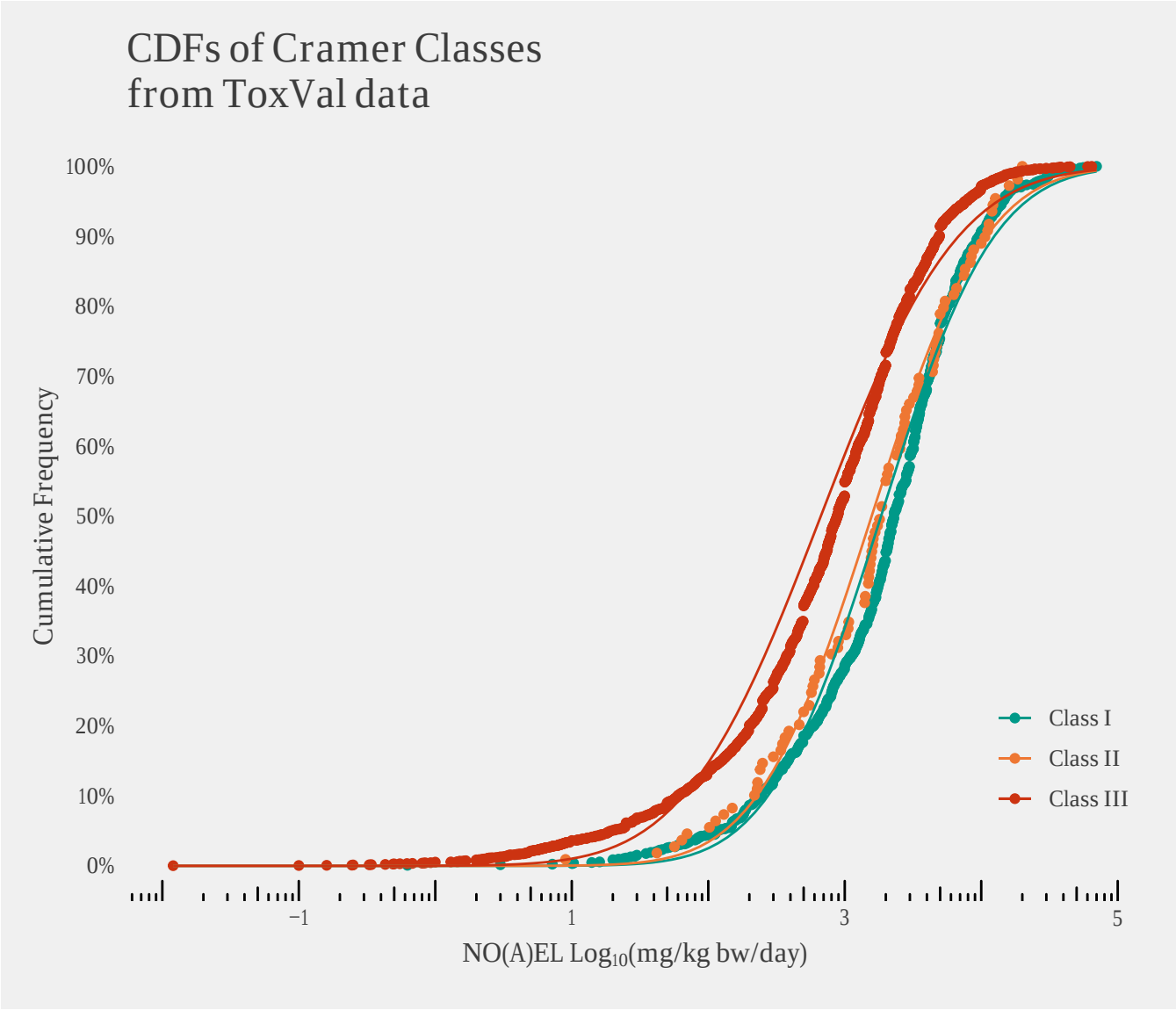
Cramer class I: 159.405mg/m^3 (1,247 chemicals)

Cramer class II: 131.107mg/m^3 (109 chemicals)

Cramer class III: 33.879mg/m^3 (3,948 chemicals)

2.3 Comparison of acute data distributions between Cramer classes

Comparison of CDFs



Using K-S test

Class I vs Class II:
D = 0.103
p-value = 0.235

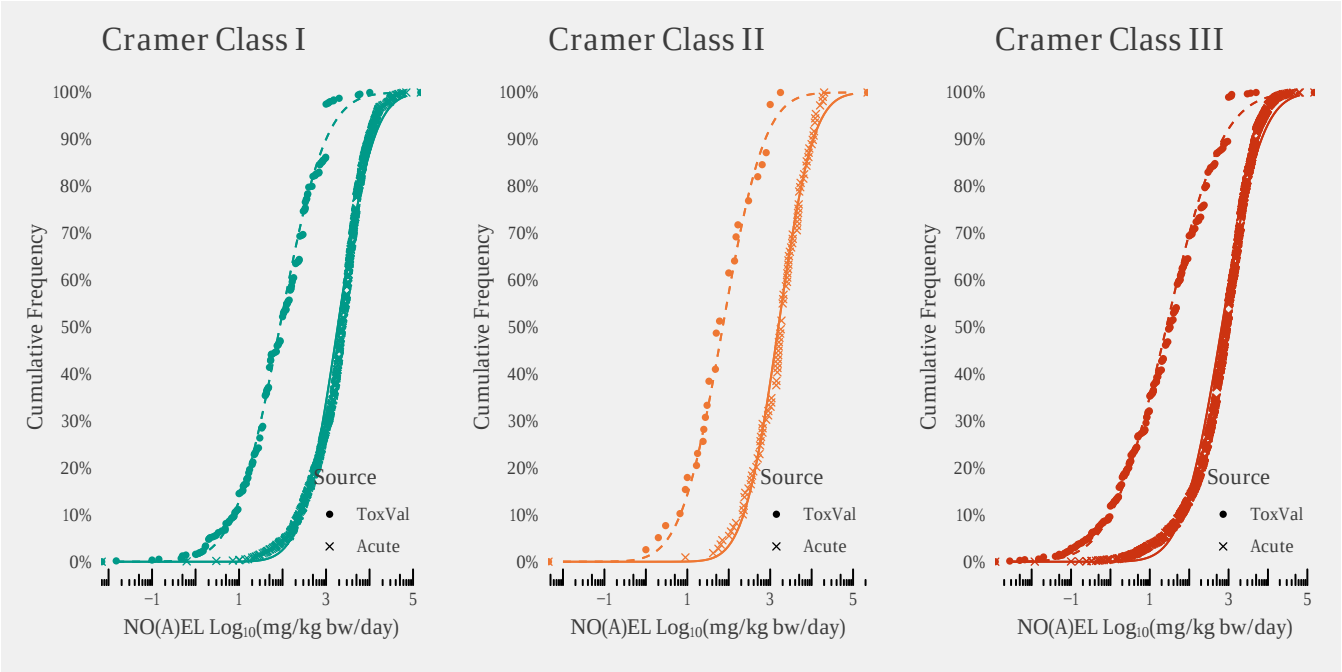
Class I vs Class III:
D = 0.292
p-value = 0

Class II vs Class III:
D = 0.269
p-value = 0

According to the K-S test, the distributions for the Cramer class I and II chemicals are not statistically different. However, the distributions for both Cramer classes I and II are statistically different from Cramer class III.

2.4 Comparison of acute data to ToxVal chronic data using Cramer class

Comparison of CDFs



Comparison using K-S test

Class I:
D = 0.688
p-value = 0

Class II:
D = 0.653
p-value = 0

Class III:
D = 0.576
p-value = 0

Looking at the results from the K-S tests, the distribution for each Cramer class is statistically different between the acute toxicity and ToxVal chronic datasets.

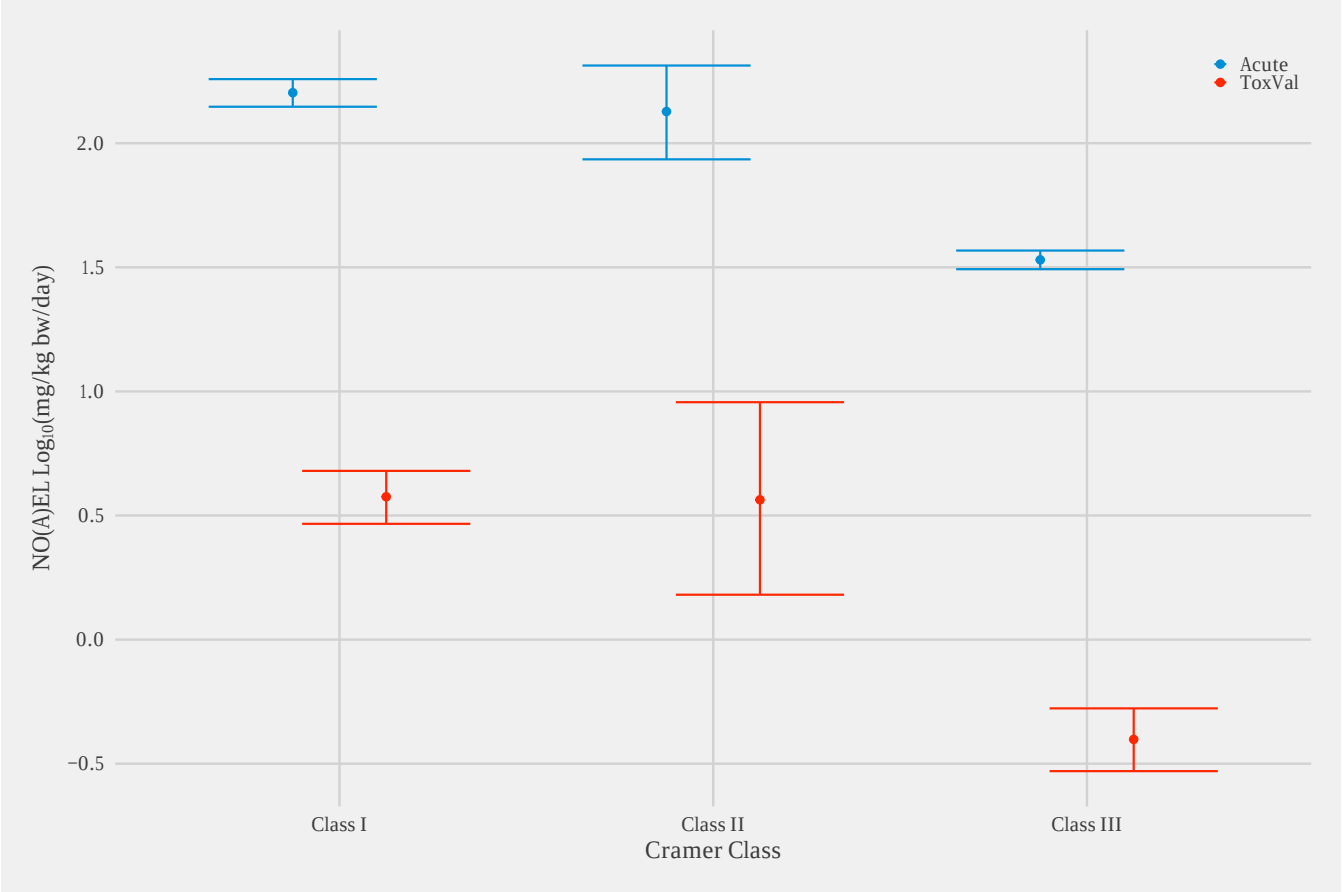
Even though the toxicity values are measuring slightly different outcomes (i.e. dose lethal to 50% of animals and minimum observed (adverse) effect) I'm not wholly surprised that the distributions are so different from one another. However, it's good to see that the data also bears out the fact that higher amounts of chemicals are needed to induce toxicity at acute time points compared to chronic time points.

Comparison of acute 5th percentiles to ToxVal chronic 5th percentiles

Using the qcomhd function I compared the 5th percentiles between the acute and ToxVal chronic dataset. The p-values for Cramer classes I-III are, 0, 0, and 0, respectively.

Unsurprisingly, there is a statistically significant difference between the 5th percentile values for each of the Cramer classes between the acute and ToxVal chronic toxicity data.

2.4.1 Median toxicity value with 95% confidence intervals for each Cramer class, comparing acute and ToxVal chronic data



2.5 Conclusions

The distributions of the LD_{50} data for each Cramer class looks to be lognormal. As such, it seems appropriate to use this as the function when calculating the 5th percentile values.

Additionally, as the distributions are statisitcally different from one another, the use of the Cramer classes seems to be an appropriate way to separate out the chemicals.

Finally, given the separation between both the distributions of the toxicity data and the 5th percentile values I feel like we can use the data we have here to calculate and suggest TTC values that would be of use in instances where someone is only going to be acutely exposed to a chemical.