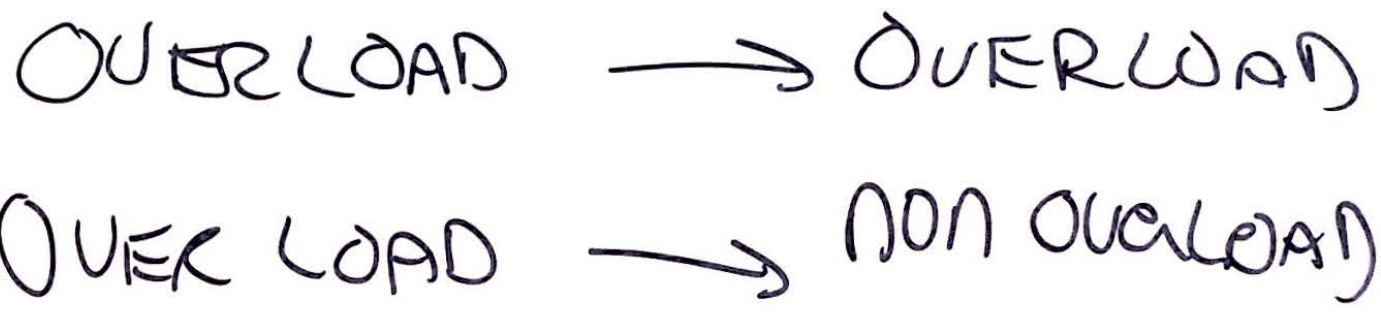


Implications of lung overload

- Check TRAN DATA on lung burden
- Correct units — Volumentec

Human Health HAZARD

Gleason's Study - human
lung clearance rate



Overload (1)

- 1) Include PSP in overload definition?
(PSP-PSLT=?)
- 2) instillation studies ARE problematic not to be used for this purpose.
- 3) ~~Elaborate or~~ remove "certain circumstances"
- 4) Add/specify processes after translocation
"endocytosis"
non-macrophage Add ~~no~~ tissue-resident macrophages

① PSP VS PSLT

- Discussion ON WORD
Toxicity - Remove it (V ^{bullet} #3)
- Is there a way to simplify PSP definition. What does "flipped over mean"?
- 6 Remove "MMAD"

2)

PSLT/PSF - LT PART

- Inflammation - why only at overload
- Bullets change order bullet # 1 + 2
- Installation exposure will be problematic for company + setting information requirements. Installation procedure itself elicits inflammation in the fat dose-rate effects

3) PSLT/PSP - LT Component

- Use lung burden vs "overload"
Lung burden causing overload
- neutrophilic to define (Rats)
human lymphocytes
- Decision tree PSP → LT → PSLT
- Benchmarking is useful for
evaluation; inflammatory potential.
- Benchmarking Relative to exposure
Response assessment
- Benchmarks - Need to get very
specific on what they are
and characteristics

Position to be added:

- HQ not enough information on humans to take position on sensitivity
- UH number 2
- FM in number 1, since exp in humans can never be done (Bradford-Hill criteria).

Epidemiology evidence. (Br. Hill)

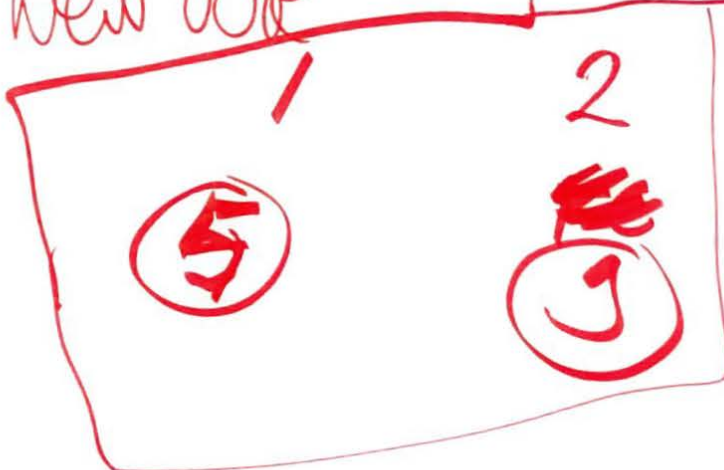
Consistency

Causality

Biological plausibility.

Different opinion among experts about oral cancer risk.

New vote



Lang missing^D

~~5~~
~~UH~~ HQ

3 is removed

EPA

AOP accepted for risk assessment - needs to be made quantitative.

AOP (Silica and lung hazard supports AOP similarity is being discuss
- Supports adequacy of rat as a test species ~~for this~~.

bullet on balance of evidence epidemiology vs toxicology
1 expert believed ~~see new coal~~ studies ~~see~~ affect opinion of coal as class III carcinogen

Consensus (19) on non-rat Rat
for human non-overload

missing
Wafeng
Lang

Human lung overload?

- lung burden studies (coal miners) show interstitial & lymph node cumulation.

- PSLT \neq inflammation at overload; accepting overload in species \rightarrow accepted day 1.

- Define kinetic differences qualitative vs quantitative
Consider dynamics. (AOE)

- OLD \neq (< 1974) vs
RECENT (> ~~1975~~) coal
miner studies

- (MD benchmarked as PSLT?)

- Humans have lung overload?

- What data analysis needed to ~~come~~ inform interpretation?

- How important is the difference in localisation of PSLT in human vs rodent in ~~the~~ interpret

- Is overload a prerequisite for PSLT lung cancer?

- Define data gaps to create meeting of minds? and improve extrapolation

NOT RE-discuss
RAC Classification

1) Will include other relevant lung endpoints to assess ~~lung cancer!~~

Exposure to be included
- internal dose

Overload in humans?

1 Accept CMD data
for PSP

2 Accept CMD data for
elaborating overload in

✓ humans

- metric

- animal data.

3 What is the next best
species (to the rat) to
evaluate PSLT induced
effects?

Define the gaps

I will then find
the money

Link to Product
Stewardship.