

Pharma&Biotech

Why OEL is an OEL and what is its limit

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The number
that represents
the best estimate
of biological processes

How accurate is mathematical representation of biological processes?



Wrist based heart rate accuracy: The wrist band provides accurate estimation of the users heart rate at any given point in time.

How is OEL assigned

A number of adjustments need to be made

- Related to biology:
 - Differences between species
 - Differences within response of different people
 - Difference in exposure duration
 - Difference in how severe effects are expected
 - Do we know the dose that caused no effects
 - How well is the substance inhaled
 - How quickly does it leave the body

- Related to the available data:
 - Quantity of available data
 - Quality of available data
 - Completeness of available data
 - Reliability of data

- Related to the expertise:
 - Knowing how to find the reliable data
 - Knowing how to interpret the data

PoD¹:	Dog, oral 52-week study; NOAEL: 1 mg/kg	
Critical effects:	Target Organs: Liver Remarks: No significant adverse effects were reported	
Adjustment factors (AF)	Value	Rationale for value selection
Interspecies variability (F1)	2	POD from a dog study
Intraspecies variability (F2)	5	Default for worker population
Exposure duration (F3)	1	POD is a 52 week study in non-rodent species
Severity of effect (F4)	1	No adjustment required
LOAEL ² to NOAEL ³ (F5)	1	POD is a NOAEL
Database completeness	1	Database complete
Bioaccumulation	13	The elimination half-life ranges between 9.3 to 16.2 days, average of 13 days is taken for calculation
Absorption (α)	1	Well absorbed orally
CAF ⁴	130	Multiplication of all assigned AFs
OEL	55	$\mu\text{g}/\text{m}^3$ for 70 kg worker

How is OEL assigned

OEL (µg/m3)		POD (mg/kg/day) * BW (kg)
	=	-----
		Composite Adjustment Factor * Volume of air

OEL (µg/m3)		1 (mg/kg/day) * 70 (kg)	
	=	-----	55
		130* 10	

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How is OEL assigned

OEL (µg/m ³)		POD (mg/kg/day) * BW (kg)
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OEL (µg/m ³)		1 (mg/kg/day) * 70 (kg)	
	=	-----	55
		130* 10 m ³	

OEL (µg/m ³)		1 (mg/kg/day) * 70 (kg)	
	=	-----	9
		780 * 10 m ³	

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Critical effects:	Target Organs: Liver Remarks: No significant adverse effects were reported	
Adjustment factors (AF)	Value	Rationale for value selection
Interspecies variability (F1)	2	POD from a dog study
Intraspecies variability (F2)	10	Default for worker population
Exposure duration (F3)	1	POD is a 52 week study in non-rodent species
Severity of effect (F4)	1	No adjustment required
LOAEL ² to NOAEL ³ (F5)	1	POD is a NOAEL
Database completeness	3	Database incomplete- no human clinical data available
Bioaccumulation	13	The elimination half-life ranges between 9.3 to 16.2 days, average of 13 days is taken for calculation
Absorption (α)	1	Well absorbed orally
CAF	780	Multiplication of all assigned AFs
OEL	9	µg/m³ for 70 kg worker

O E L

- Consistency

Of the approach

- Measurability

Of the outcome

External consistency

A cross-industry workshop was held in 2015 to advance science and practice for

deriving HBELs: <https://www.ncbi.nlm.nih.gov/pubmed/27531049>

Harmonization efforts for deriving health-based exposure limits in the pharmaceutical industry - Advancing the current science and practice

Topics covered

- Regulatory guidance and application
- Operational and process management
- **HBEL derivation methodology**

HBEL = Health Based Exposure Limit, such as Permitted Daily Exposure (PDE) and OEL

Internal consistency

Must have

- **Procedure** followed by all internal and external toxicologists working for the company
- **Peer review** and not a one person's opinion

Good to have

- Input by IH is beneficial
- Not needing to band the values

Measurability

DOSE NO(A)EL
DOSE LO(A)EL
from animal
or human
study

DOSE Adjust for
worker
biology and
exposure to
get an OEL

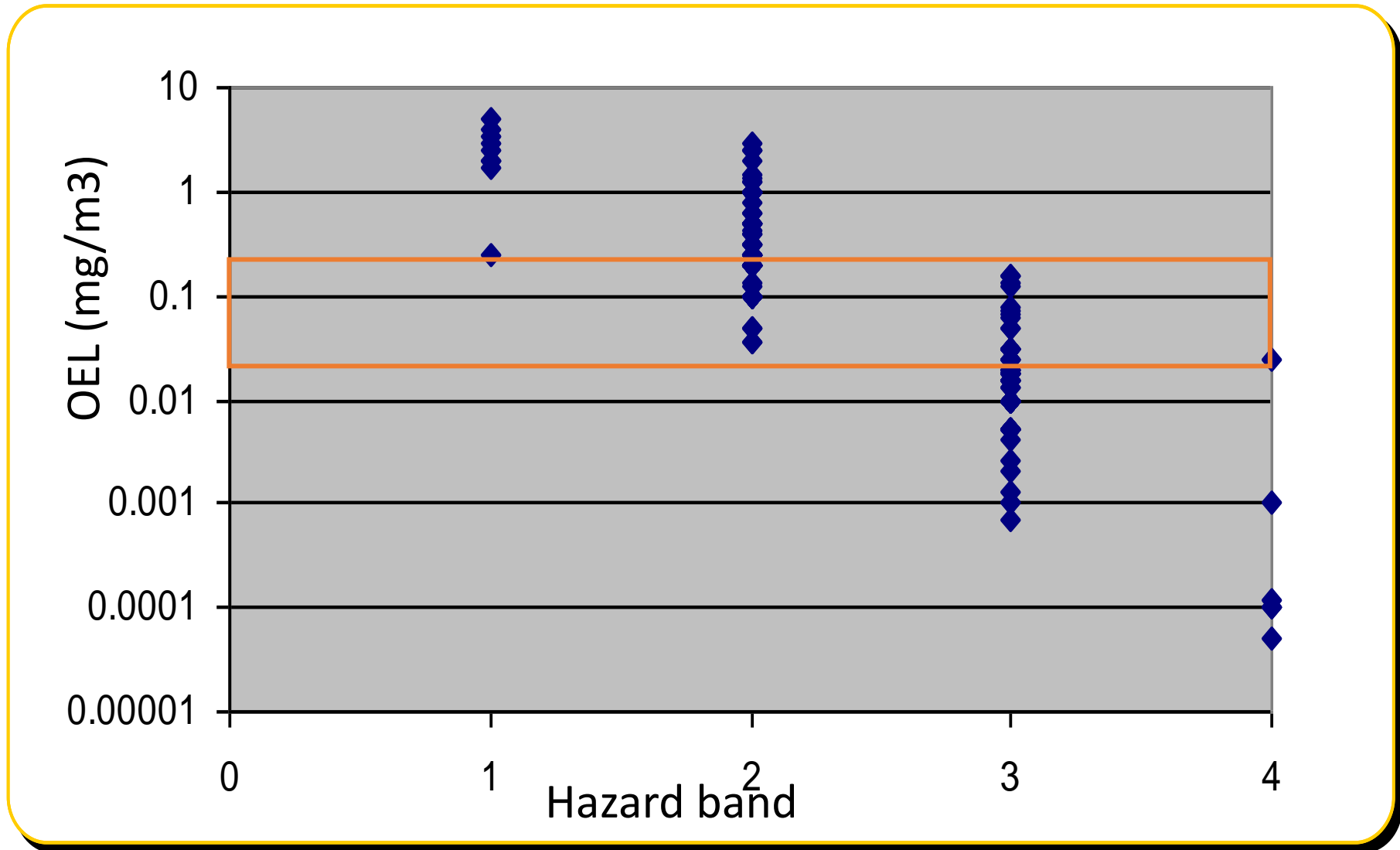
DOSE Assess actual
worker
exposure with
IH
measurement

BANDING

How is hazard banding assigned

1	2	3	4
<p>H304 – May be fatal if swallowed and enters airways H315 – Causes skin irritation H319 – Causes serious eye irritation H335 – May cause respiratory irritation H336 – May cause drowsiness or dizziness</p>	<p>H302 – Harmful if swallowed H312 – Harmful in contact with skin H314 – Causes severe skin burns and eye damage. H332 – Harmful if inhaled H371 – May cause damage to organs H373 – May cause damage to organs through prolonged or repeated exposure</p>	<p>H301 – Toxic if swallowed H331 – Toxic if inhaled H311 – Toxic in contact with skin H317 – May cause an allergic skin reaction H334 – May cause allergy or asthma symptoms or breathing difficulties if inhaled H318 – Causes serious eye damage H336 – May cause drowsiness or dizziness. H370 – Causes damage to organs H372 – Causes damage to organs through prolonged or repeated exposure</p>	<p>H300 – Fatal if swallowed H310 – Fatal in contact with skin H330 – Fatal if inhaled</p>
		<p>H341 – Suspected of causing genetic defects H351 – Suspected of causing cancer</p>	<p>H340 – May cause genetic defects H350 – May cause cancer</p>
	<p>H361 – Suspected of damaging fertility or the unborn child</p>	<p>H360 – May damage fertility or the unborn child</p>	
<p>Dust >1 mg/m³ Vapour >50 to 500 ppm</p>	<p>Dust 1- 0.1 mg/m³ Vapour >5 to 50 ppm</p>	<p>Dust 0.1- 0.001 mg/m³ Vapour >0.5 to 5 ppm</p>	<p>Dust <0.001 mg/m³ Vapour <0.5 ppm</p>
<p>Standard laboratory work practices and engineering controls</p>	<p>Standard work practices and engineering controls</p>	<p>No open handling without stringent procedural controls and protective equipment</p>	<p>Barrier or specialized exhaust ventilation coupled with stringent work practices</p>

Hazard band and OELs



Qualitative
hazard from
animal or
human study

Assign
predefined
exposure
control values

Assume
containment
capabilities

What should be your questions?

- What kind of hazards does the chemical have?

Carcinogen	Carcinogen
Hepatotoxic	Hepatotoxic
Intrauterine growth restriction, premature delivery, and pregnancy loss	Miscarriage, stillbirth, premature birth, small birth weight, and Foetal A. Spectrum Disorder (FASD)

How accurate is containment based on a hazard band

HAZARD is about:

What substances do to the body

While OEL also tells you:

What body does to the substance
and at what dose



Summary

Do

- Ask your toxicologist to calculate an OEL
- Verify containment with IH measurements

Don't

- Ask your toxicologist to band
- Assume your containment based on hazard bands



#alwaysOEL