ISO 18562 Series

Biocompatibility evaluation of breathing gas pathways in healthcare applications

BRANDWOOD BIOMEDICAL

SOT | Society of Toxicology

Creating a Safer and Healthier World by Advancing the Science and Increasing the Impact of Toxicology

James Morrison

LIVE WEBINAR

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James (Morrison) has 30 years experience in product development. The last 13 years in medical devices, particularly for Respiratory Medicine.

Expertise materials for respiratory devices and device validation, including biocompatibility. Materials Science and Toxicology background.

A member of ISO/TC 194 (Biocompatibility, ISO 10993) for some years and current Head of the Australian delegation.

Was very active in the development of the ISO 18562 series through ISO/TC 194 Task Force in liaison with ISO/TC 121 (Lung Ventilation)

Currently heavily engaged in ISO 10993 Part 17 & Part 18 revisions.

Brandwood Biomedical is a Sydney, Australia based consultancy to the global medical device industry.

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ISO 18562:2017

Biocompatibility evaluation of breathing gas pathways in healthcare applications –

- Part 1: Evaluation and testing within a risk management process
- Part 2: Tests for emissions for particulate matter
- Part 3: Tests or emissions of volatile organic compounds [VOCs]
- Part 4: Tests for leachables in condensate

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Context

- Gas pathway medical devices are ubiquitous
- Limited standardisation: equipment or air
- Contact durations: Transient, Limited – Long term
- Single use – Multiple uses/multiple users (years)
- Device derived substances (not environmentals)
- Particles, vapours & leachables
- CO_2, CO, O_3 possible future parts

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Part 1 “Evaluation & Testing”

- Covering document
- ISO 10993 doesn’t really cover gas pathways
- Type tests
- Duration of use
- Flowchart to determine testing required
- Toxicological considerations introduced
- Body weights
- Breathing volumes

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Part 1 (cont.)

Allowable limits

Deriving tolerable intakes

Threshholds of Toxicological Concern (in the absence of tox data)

- ≤ 24 h → 360 µg/d
- > 24 h, < 30 d → 120 µg/d
- > 30 d → 40 µg/d (VOCs)
- 1.5 µg/d (Leachables in condensate)*

* Note the ICH M7 correlation

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Part 2 Particulates

Particle diameters 0.2 – 10 µm

$PM_{2.5} < 12\ \mu g/m^3$

$PM_{10} < 150\ \mu g/m^3$

Independent of particle chemistry/material

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Part 2 Tests

- Largely based on historical environmental air quality monitoring methods (filter mass balance, etc)
- These may be difficult to apply to medical devices
- Particle counters are acceptable (with calibration!)
- Use worst case conditions
- Understand particle source/origin & causes
- Consider “time varying emissions”

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Part 3 Volatile Organic Substances

$50^{o}C < T_b < 250^{o}C$

Toxicological Risk Assessment

- Dose to patient
- Tox data available
- Dose < TI

No tox data → TTC

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Part 3 (cont.)

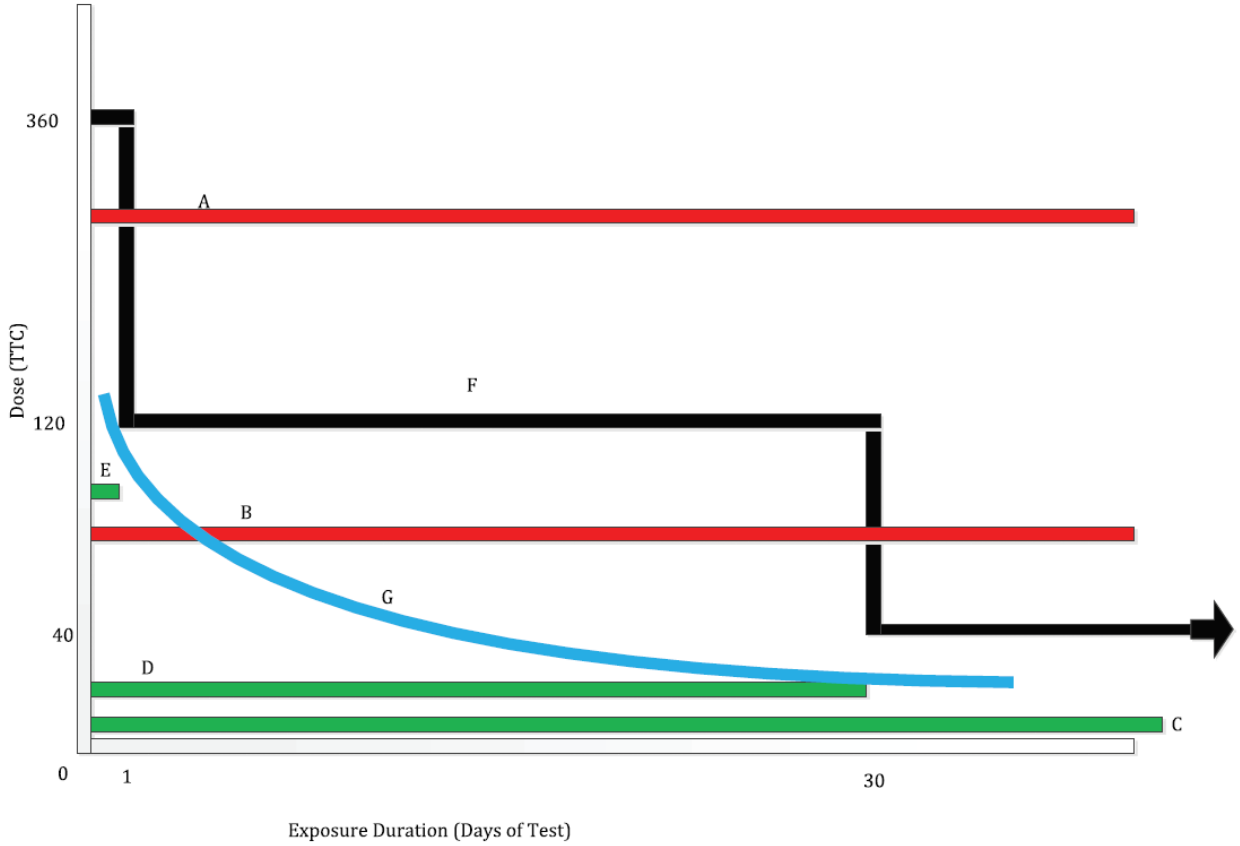
TTCs by exposure duration

Table AND Graph

Table 1 — TTC limits by exposure

Exposure category	Length of PATIENT exposure	TTC ug/d		
Limited exposure	≤24 h	360	—	—
Prolonged exposure	>24 h and <30 d	360, for first 24 h	120, for the subsequent 29 d	—
Permanent contact[a]	≥30 d	360, for first 24 h	120, for the subsequent 29 d	40, beyond 30 d

[a] Figure 1, green bar E or blue curve G.



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Part 3 Tests

- Largely based on historical environmental air quality monitoring methods (steel chamber/traps, etc)
- These may be difficult to apply to medical devices
- Absorption tubes acceptable (e.g. Tennax, activated charcoal & specifics)
- Use worst case conditions
- Understand particle source/origin & causes
- Consider “time varying emissions”

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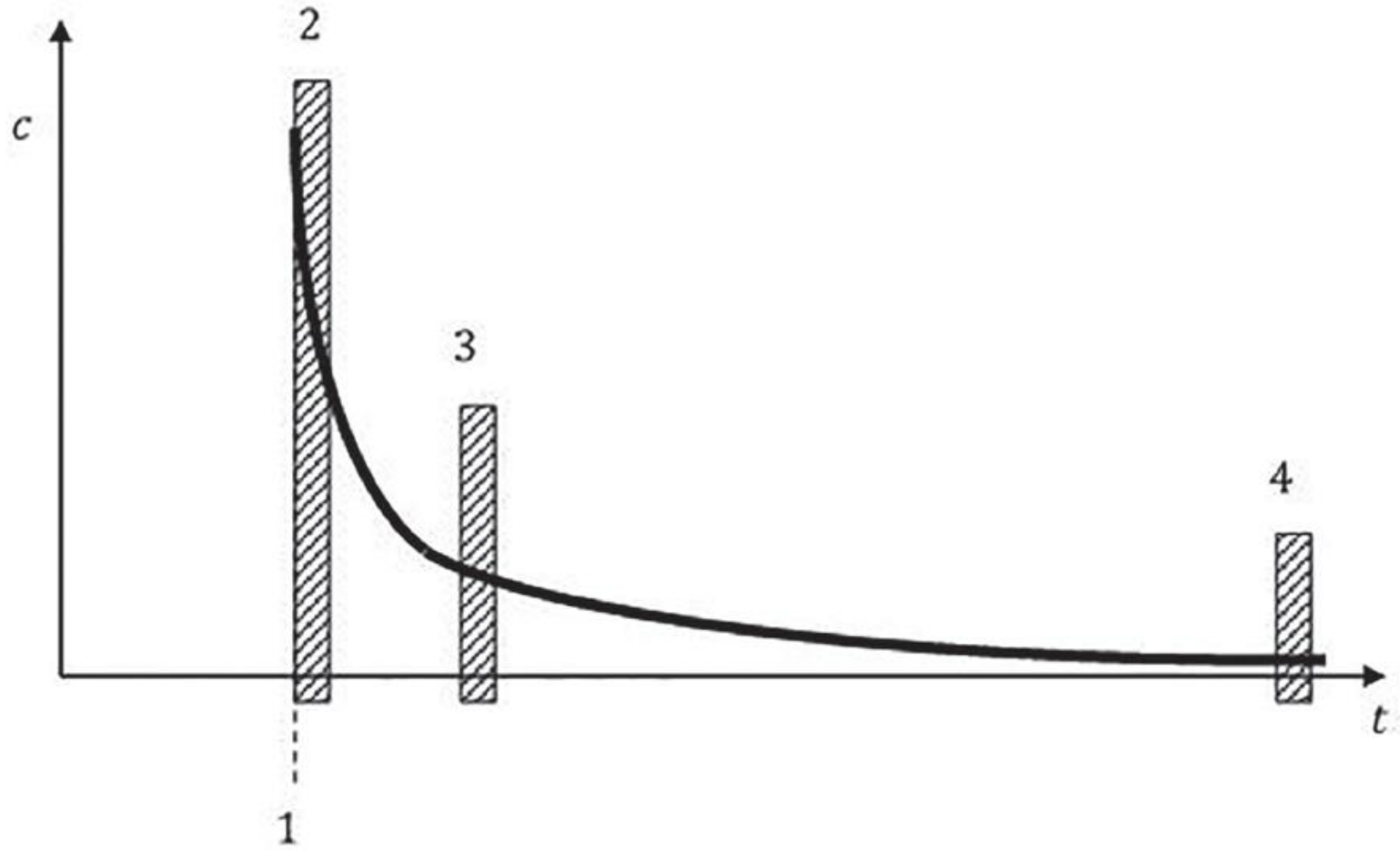
Part 3 Tests (cont.)

Time varying emissions would conform to diffusion models (e.g. Arrhenius)

Exponential power curves – (min 4 points)



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Part 4 Leachables in Condensate

"quantify hazardous water-soluble substances that are leached … by condensate and then conveyed by that liquid to the patient"

Dose determinations may (very likely) be contentious.

Three conditions must be met:

- Gas in the gas pathway can reach 100% saturation with water at some point in the gas pathway
- Condensate can form on the gas pathway surfaces
- Liquid condensate can reach the patient

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Part 4 Tests

- Leachables study, to make an extract
- Instrumented analysis for organics & metals. (e.g. GC/MS & ICP/MS)
- Identify VOCs & SVOCs
- Toxicological Risk Assessment
- Can use exhaustive extraction, but might be unnecessarily expensive
- Environmental contaminants laboratories
- **WILL** need some biological tests

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Part 4 Tox Risk Ass

Types of Analytes	Types of Approaches
Positive ID, with tox data	Calculate TI
Positive ID, with no tox data	QSAR, Read across, etc **OR** TTC
Tentative ID, with tox data	QSAR, Read across **AND** Calc TI
Tentative ID, with no tox data	TTC
Unknown ID, with structural data	QSAR, Read across, etc **AND** TTC
Unknown ID, with no structural data	TTC

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Time for Q&A...

Think of something later? Ask us by email...

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Big THANK YOU to: SOT

& participants and interested parties in this webinar.

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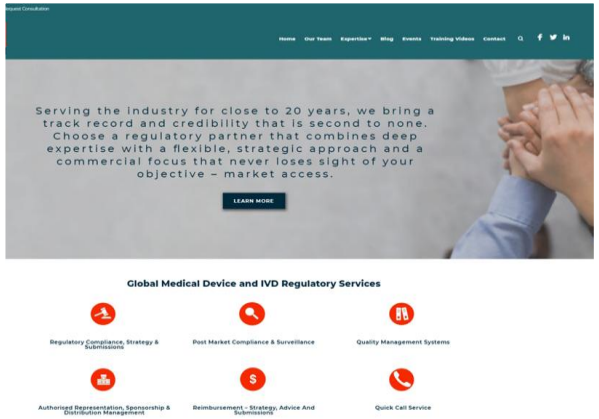

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