

Potent Pharmaceuticals in Ventilated Weighing Cabinets



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Ventilated Weighing Cabinets

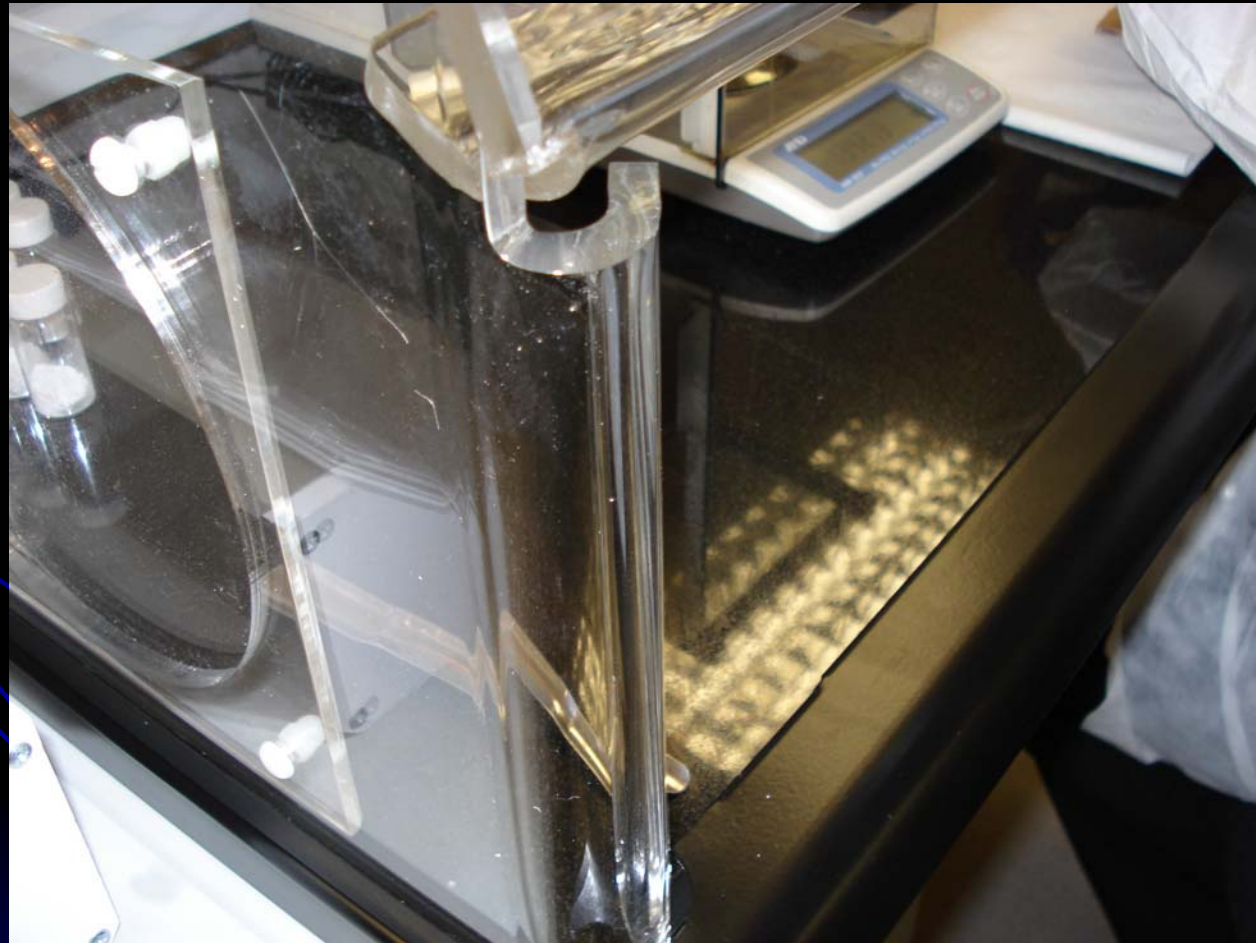
- Active pharmaceutical ingredients (APIs) have steadily increased in potency
- OELs 40 ng/m³ TWA or lower now common
- Greater protection required
- Development of specialist control options
- A convenient and economical solution for handling small quantities (mg)
- QC laboratories
- **Prevention of exposure highly dependant on procedural and human factors**

Design Basics

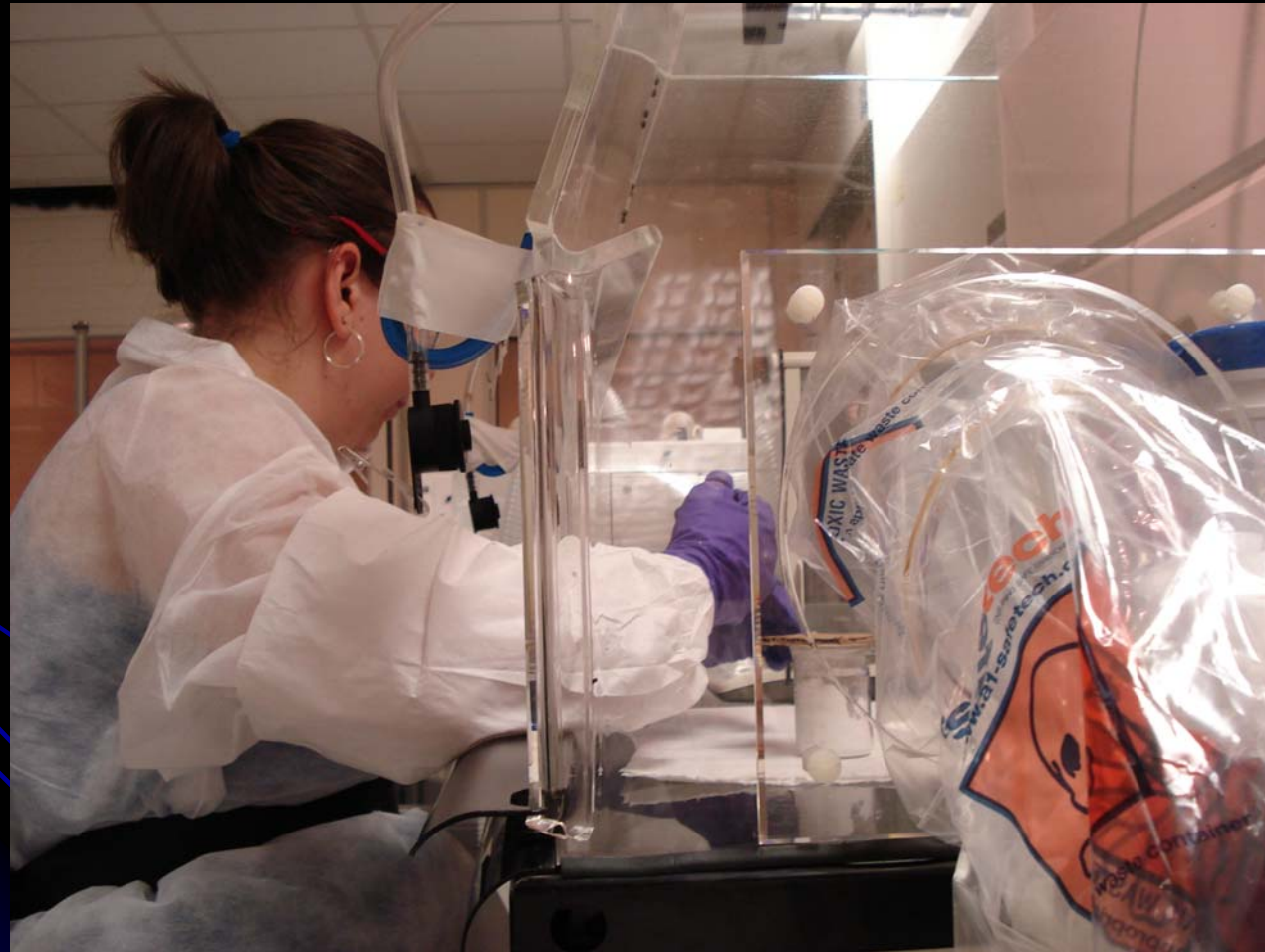
- Clear perspex
- Ergonomic
- Laminar airflow
- 0.4 m/s FV
- Balance stability
- Minimal 'dead' spots
- Hinged front panel
- Bag-out facility for waste, samples



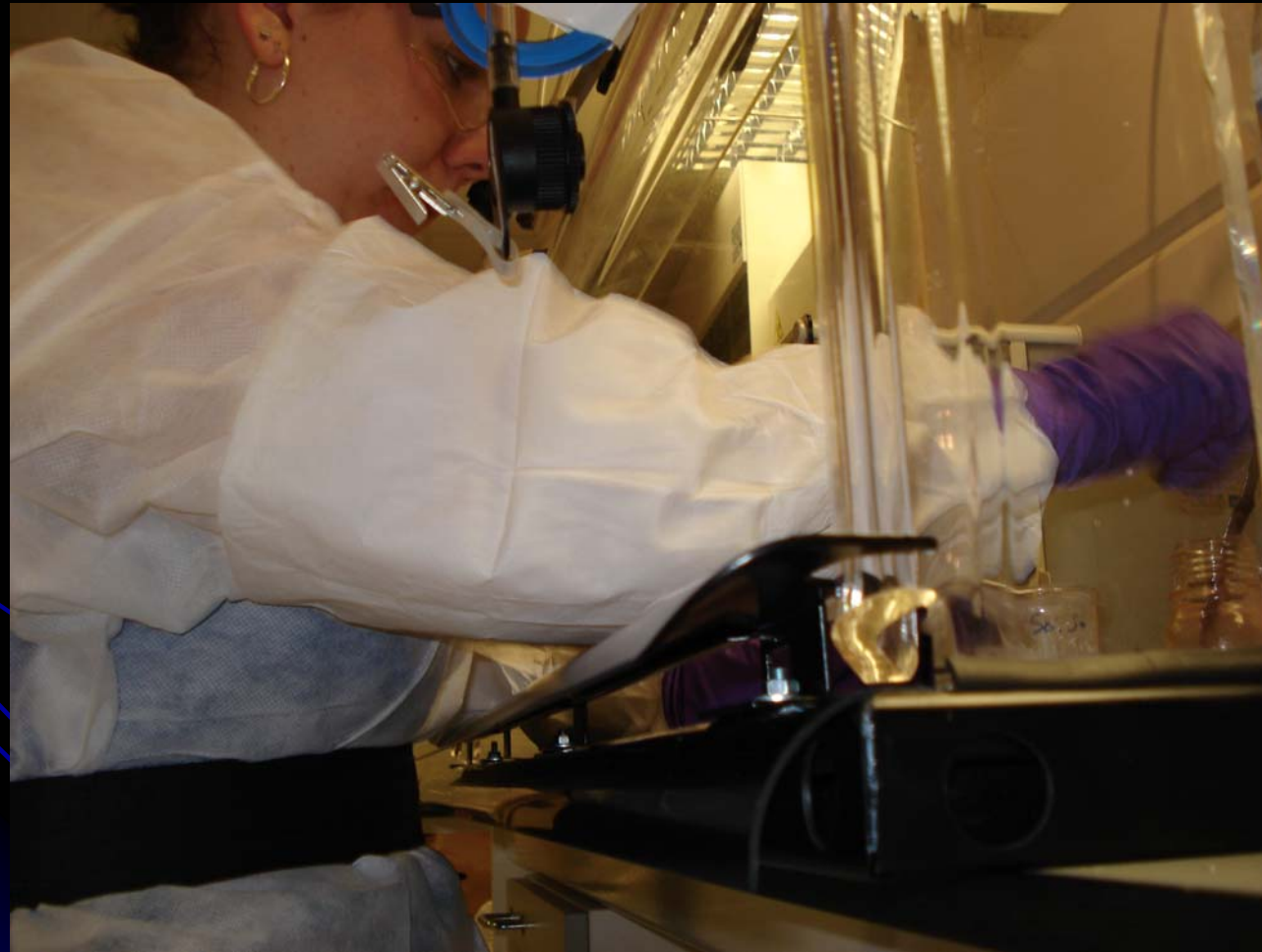
Smooth airflow, to side

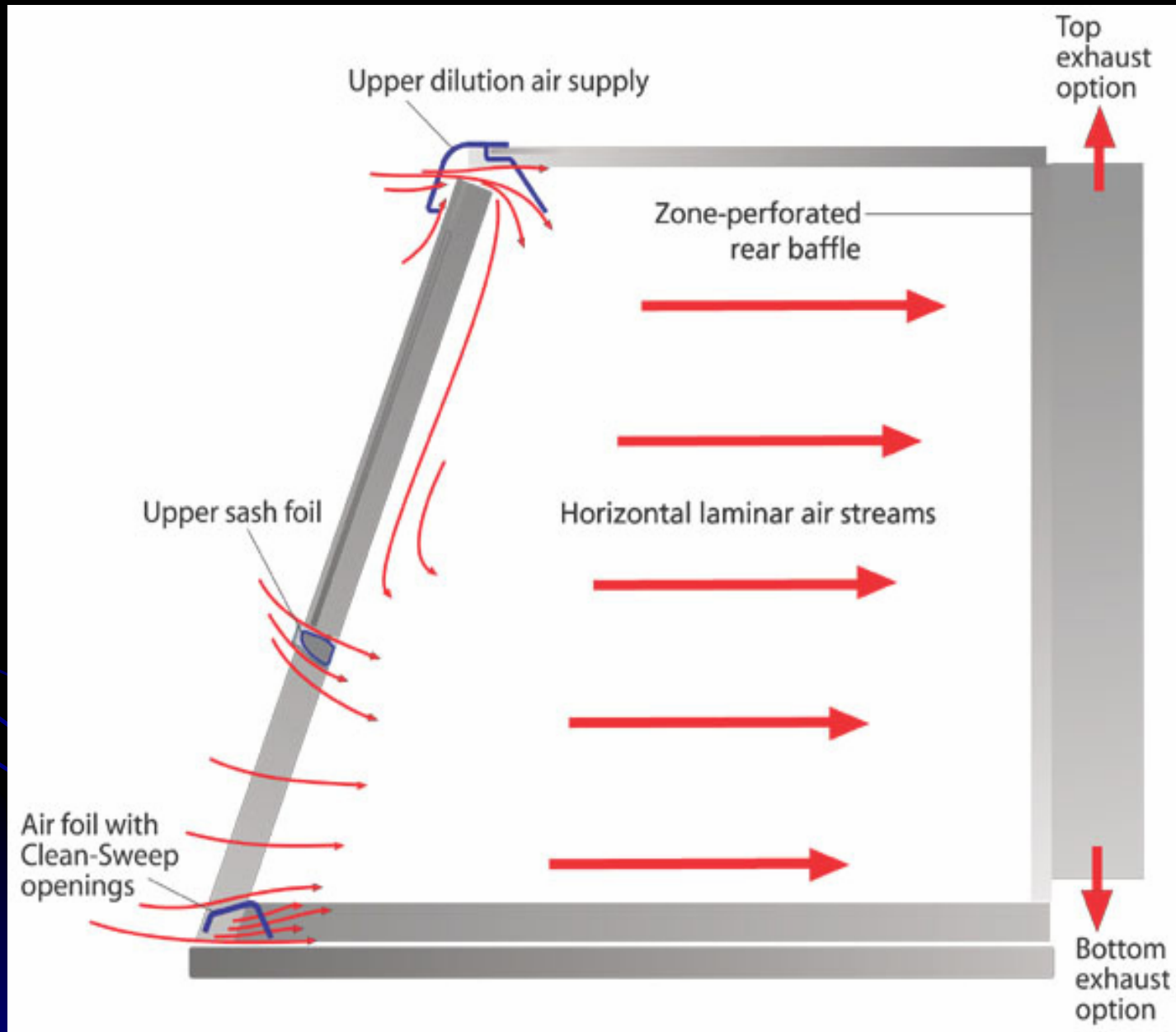


Smooth airflow, top edge

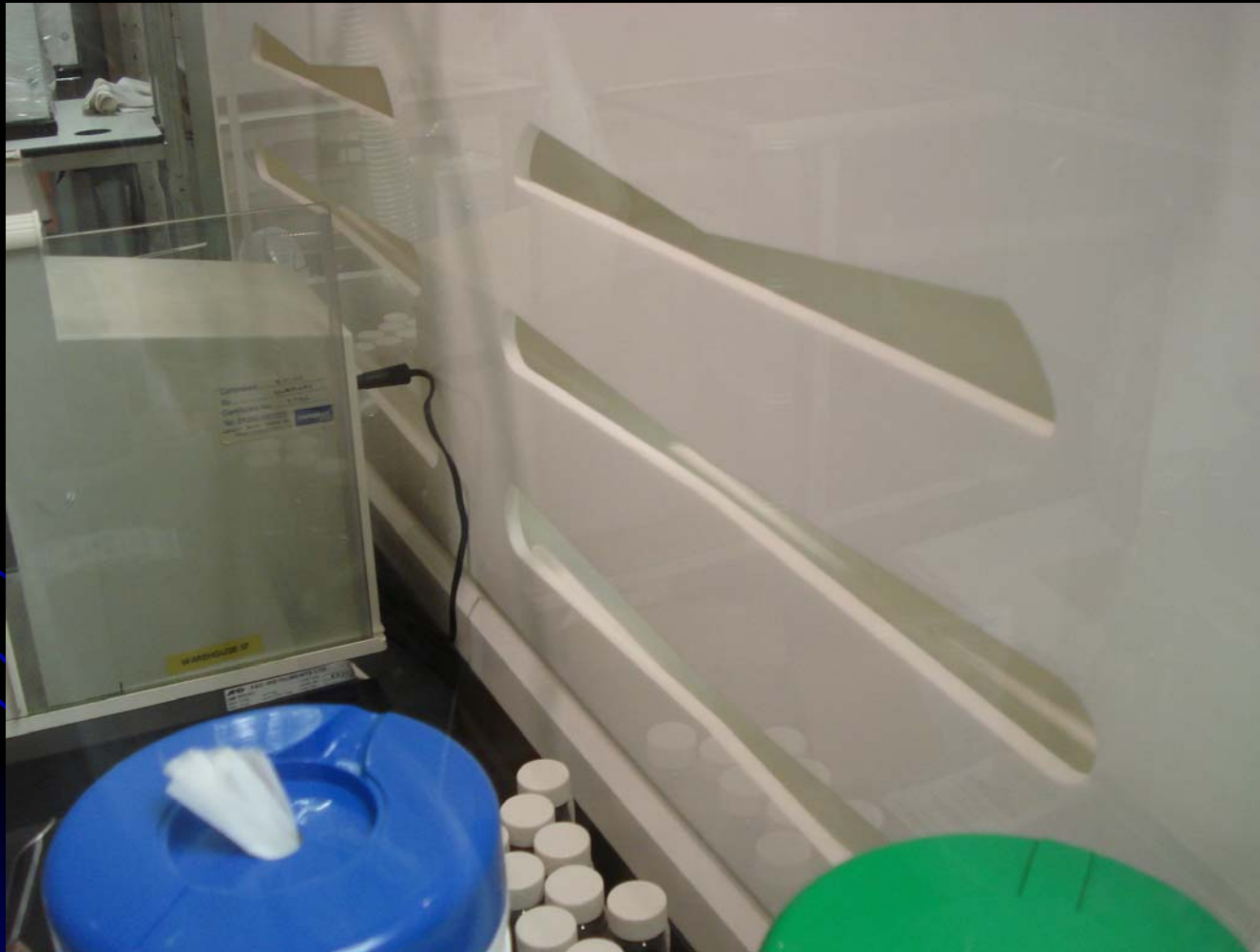


Aerofoil below wrist support





Rear plenum



Typical Personal Protective Equipment

- Tyvek suit
- Oversleeves
- Double nitrile gloves
- Safety glasses
- Disposable mask



Factors Affecting Control

- Positioning in room – traffic, disturbing air currents
- Quantity, dustiness of material, frequency of use
- Equipment – spatulas, weigh boats, flasks
- Ergonomics – height, leg room, size of balance
- Operator awareness, training, habits
- Physical attributes
- Distractions – people, telephones
- Handling methods, mass transfers
- Management of cleaning – contaminated units stay on
- Waste disposal
- Method of recording weighing

Background to testing

- SafeBridge requested to evaluate potential capability of seven safety weighing cabinets/powder handling enclosure systems (a1-safetech)
- Surrogate API, naproxen sodium
- Standardised weighing procedure
- Controlled conditions
- Training for inexperienced operators
- Control performance target (CPT) 10 ng/m^3



OH Sampling Strategy

- Naproxen sodium – ideal surrogate
- High analytical sensitivity, 0.25 ng per filter
- Area and personal samples
- Three evaluations per cabinet
- 25% of CPT required (EN 689)
- 10 x 1g weighings per evaluation, cleaning
- Challenge samples inside cabinet
- IOM heads, 2 l/min, PTFE 1um pore

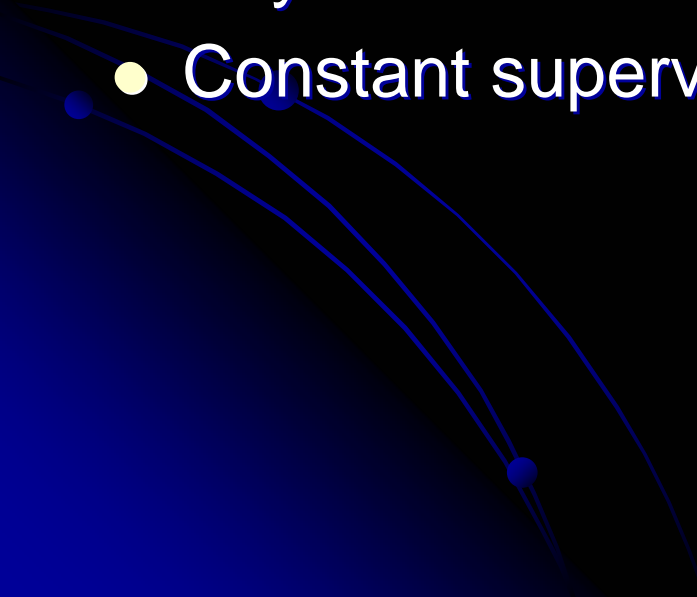
Area samples – face of SWC



Area samples – inside unit



Operators

- Seven operators, inexperienced
 - Five males, two females
 - Provided with basic training
 - Different operator for each evaluation
 - Physical attributes varied
 - Constant supervision of hygienist
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Training

- Correct donning of PPE
- Principles of potent compound handling
- Recognition of 'clean' and 'dirty' sides
- Weighing techniques
- Cleaning
- Removal of contaminated PPE
- Disposal of waste
- Safe removal of items

Standardised Weighing Procedure

- 40g supply of naproxen sodium
- Approximately 10 x 1g weighings - 20 ml scintillation vials
- Tolerance +/- 10%
- Actual weights not recorded
- Filled vials placed to 'clean' left hand side



Removal of Gloves, Waste Disposal



Safe Removal of Items

- Item held through plastic bag
- Avoids touching surfaces
- Bag turned inside out on removal



Concentrations Inside Unit

Model	Evaluation	Sample period (mins)	Concentration (ng/m ³)
SWC T-900	1 st	46	769
SWC T-900	2 nd	47	6,126
SWC T-900	3 rd	47	226
ST1-1500	1 st	46	1903
ST1-1500	2 nd	37	3662
ST1-1500	3 rd	47	20,319

Results – Area Samples Outside

Model	Number of samples	Sample period range (mins)	Concentration range (ng/m ³)
SWC 1200	n = 15	47 - 59	<2.3 - <2.9
SWC 900	n = 14	43 - 63	<2.1 - 5.3
SWC T-1200	n = 15	43 - 61	<2.2 - <3.2
SWC T-900	n = 15	49 - 49	<2.8 - <2.8
ST1 – 1200	n = 15	49 - 59	<2.3 – 7.2
ST1 – 900	n = 15	41 - 60	<2.2 – <3.3
ST1 – 1500	n = 15	48 - 56	<2.4 – <2.8

Results – Personal Samples

Model	Number of samples	Sample period range (mins)	Concentration range (ng/m ³)
SWC 1200	n = 3	47 - 59	<2.3 - <2.9
SWC 900	n = 3	43 - 63	<2.2 - <3.2
SWC T-1200	n = 3	43 - 61	<2.2 - <3.2
SWC T-900	n = 2	49 - 49	<2.8 - <2.8
ST1 – 1200	n = 3	49 - 58	<2.2 - <2.7
ST1 – 900	n = 3	41 - 60	<2.2 - <3.2
ST1 – 1500	n = 3	48 - 56	<2.4 - <2.8

Indicative Control Performance Concentrations (EN 689)

SWC 1200	12 ng/m ³
SWC 900	32 ng/m ³
SWC T1200	12 ng/m ³
SWC T900	12 ng/m ³
ST1-1200	11 ng/m ³
ST1-900	14 ng/m ³
ST1-1500	12 ng/m ³

Study Conclusions

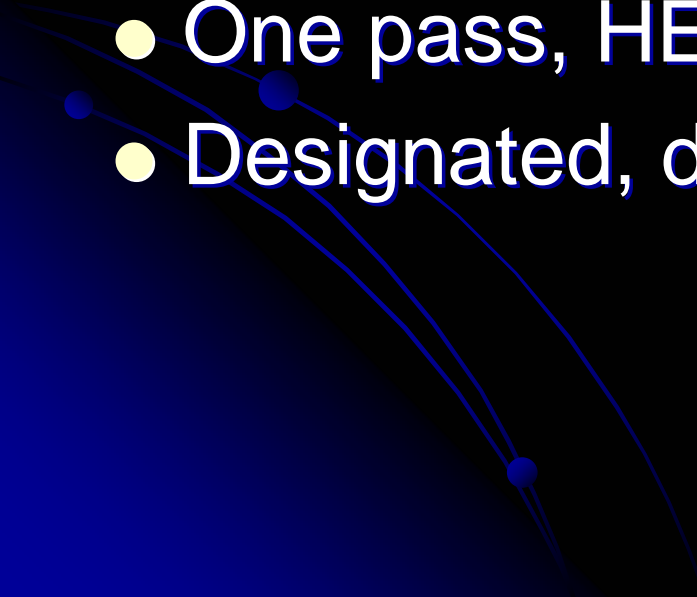
Under the test conditions:

- Indicative control performance concentration of 32 ng/m³ or better
- High level of control possible, with correct training and supervision
- OELs as low as 30 ng/m³ possible

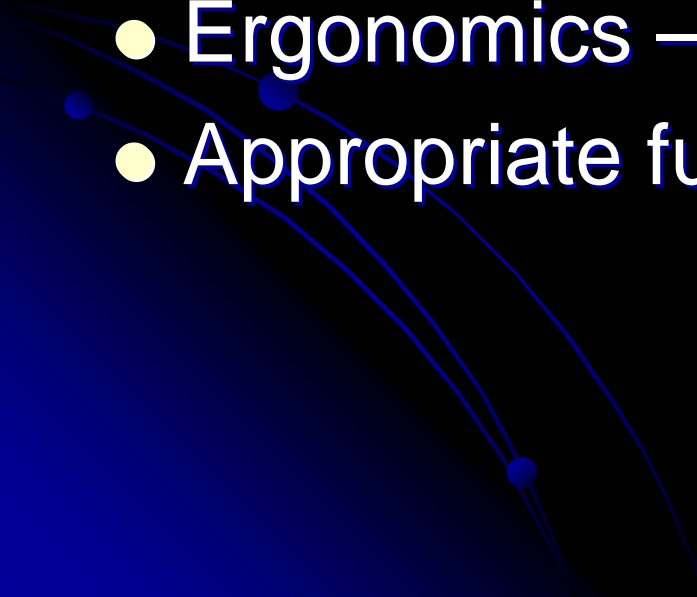
But:

- Very operator dependant
- Control in other situations may differ
- Loss of control – possible over exposure
- An appropriate choice?


Facility Recommendations

- Air locks/anterooms
 - Negative pressure relative to surrounding areas
 - Separate HVAC system, alarms
 - One pass, HEPA filtration
 - Designated, delineated, controlled area
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Set Up

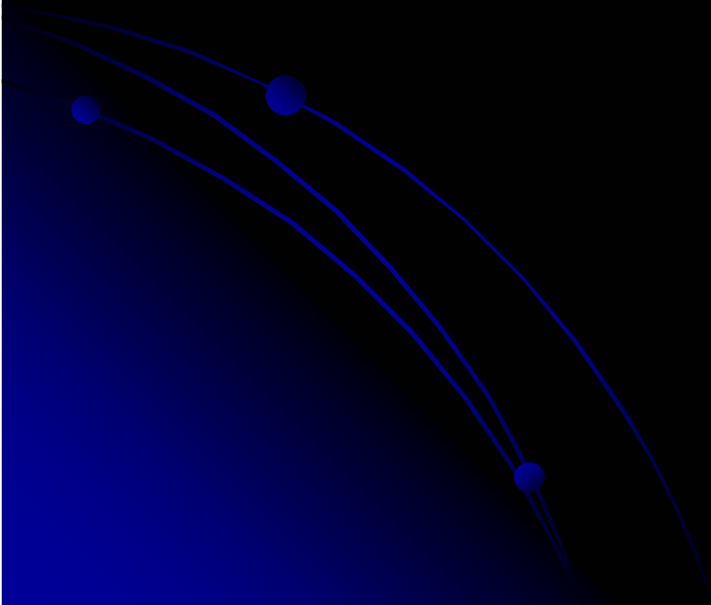
- Appropriate location for unit, and fans
 - Exhaust connected to appropriate LEV system
 - Safe change procedures
 - Ergonomics – height, legroom
 - Appropriate furniture
- 

Administrative Controls

- Training, ongoing
 - Meticulous Procedures
 - Weighing tools and methods
 - Cleaning, validated methods
 - Waste management
 - Exposure monitoring, ongoing
- 

Precautionary RPE

- Why use RPE?
 - Facility does not protect operators
 - Units do not guarantee control of exposure



In Summary

- Units can work well for potent compounds
- Significant facility costs involved
- Significant ongoing costs
 - Testing
 - Maintenance
 - Training
- Control not guaranteed, particularly if placed in a normal laboratory

Acknowledgements

- Martin Axon, Justin Mason, John Farris - SafeBridge
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- a1-safetech operators

