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An Expanded Evidence-based Risk Model to Help Prevent a Facility-Associated Release of Poliovirus: The Mitigation Power of Environmental Controls

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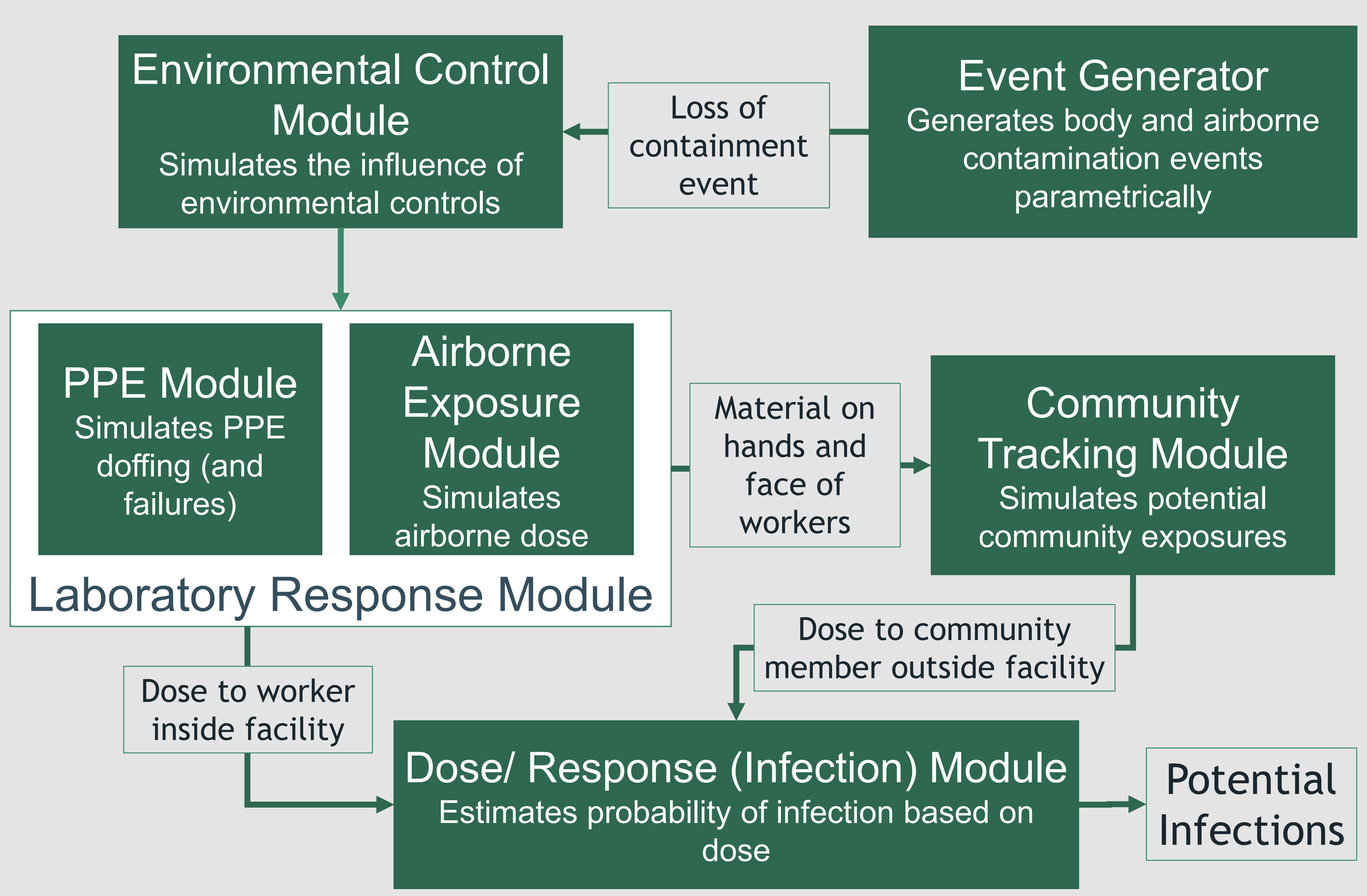
Abstract

As the globe nears total eradication of wild poliovirus, there is a reintroduction risk due to facility-associated release of poliovirus, necessitating biosafety enhancements to prevent this potential outcome. At the request of the US National Authority for Containment of Poliovirus (US NAC), within the Centers for Disease Control and Prevention (CDC), Gryphon Scientific developed a quantitative risk model to understand the specific risks of various loss of containment (LOC) pathways in poliovirus facilities to better inform choices of risk mitigation measures. In this model, we defined consequential LOCs as events that result in poliovirus (a) laboratory acquired infections (LAIs), (b) infectious material (IM) leaving the laboratory on a person and/or (c) IM leaving the laboratory in the wastewater stream. We expressed the outcome of LOCs in terms of their route, likelihood of occurrence, amount escaping the laboratory boundary and probability that any laboratory worker or community member is infected by the IM or by human transmission caused by a facility associated release . To conduct this analysis, we built a quantitative, stochastic, event tree-based model that was parameterized using available primary data. In an earlier stage of the model, we investigated the relative risk mitigation potential of enhanced PPE vs exit showers (as required by the World Health Organization's poliovirus biosafety standard known as GAPIII) and demonstrated that enhanced PPE provides better risk mitigation in nearly every LOC we simulated.[1] In this earlier model, scenarios began with contamination already on the body of the worker. In recent updates, we now initiate the model earlier, as the release first occurs, and incorporate environmental controls (principally, the biosafety cabinet including both class II and class III cabinets) as potential risk mitigators that can reduce the severity of LOCs or prevent them entirely. Here, we present results from this latest version of the model and compare the relative risks of facility associated release with and without environmental controls in use. Overall, these updates to the model expand the "toolkit" available for biosafety assessments. They also provide additional insights into how environmental controls and PPE can best mitigate the risk of facility-associated reintroduction of poliovirus, helping secure the global public health achievement that is polio eradication.

Model Architecture

- We built a modularized model that simulates the fate of infectious material from a loss of containment event through potential infections in the community



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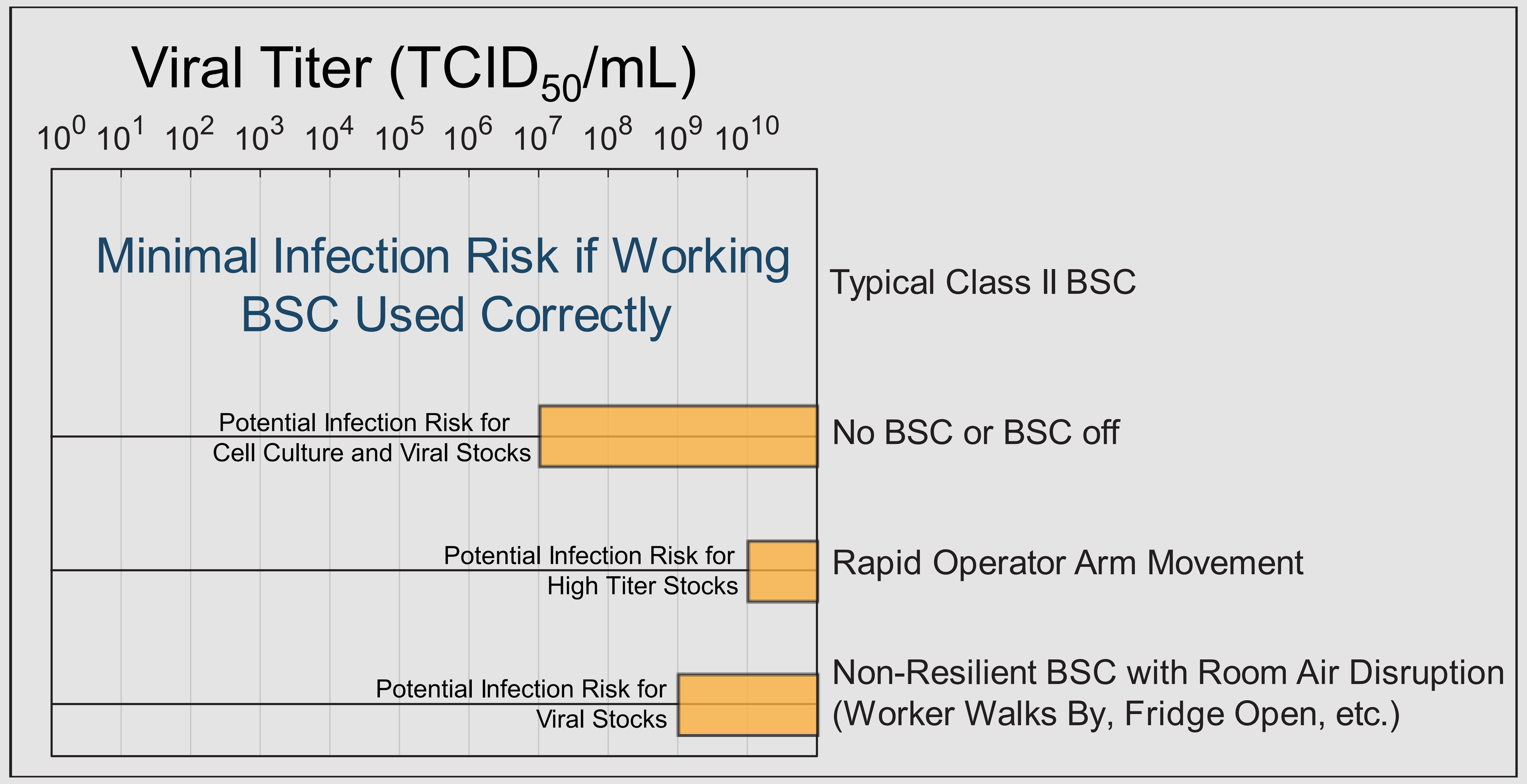
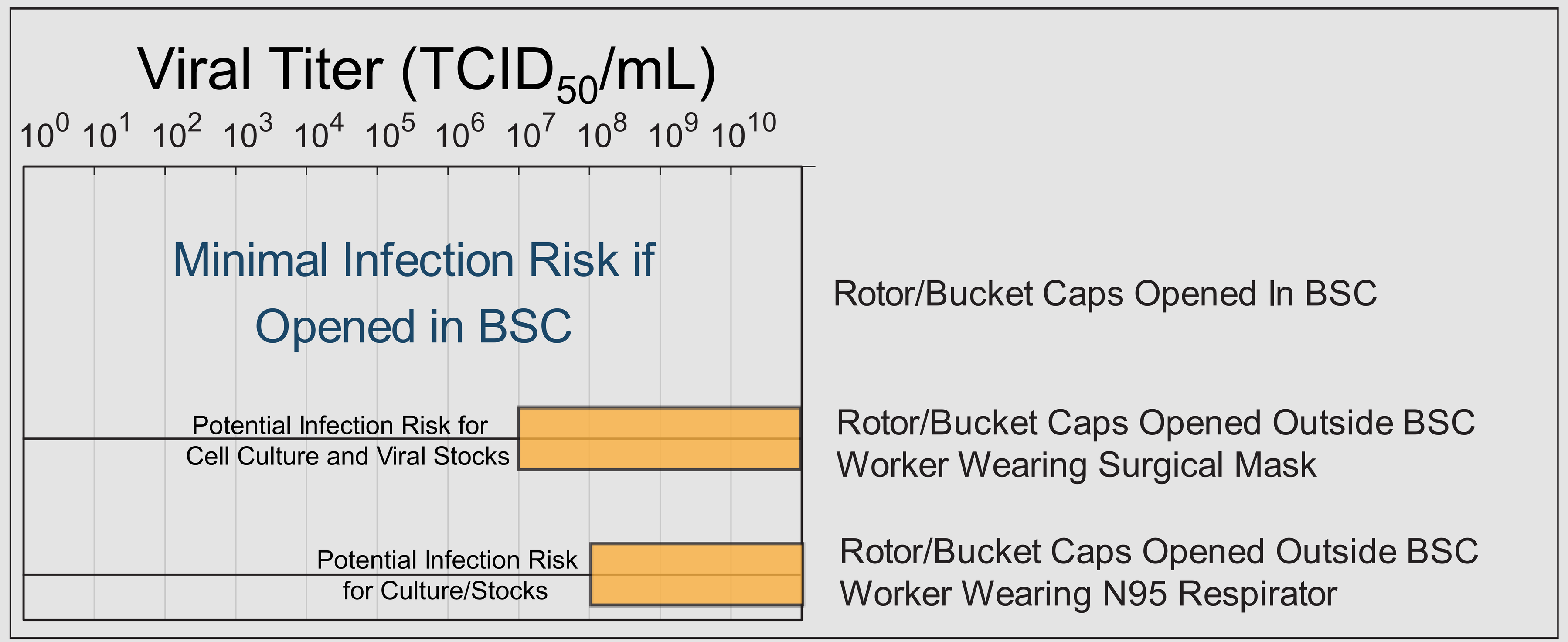
BSCs May Not Mitigate Airborne Hazards If Mistakes or Faults Occur During Their Use

- Our model predicts workers may be at risk of infection even while using a BSC if mistakes or failures occur
- Some BSCs may not be resilient to airflow disruptions[3], dramatically reducing protection if disruptions occur
- Though we modeled only poliovirus, we expect these risk to be present—or even exacerbated—for other pathogens, especially respiratory pathogens



Aerosol Tight Centrifuge Caps Mitigate Risk Only if Opened in a BSC

- If aerosol-tight centrifuge caps are opened in a BSC, our model predicts they provide significant mitigation against airborne exposure
- If they are opened outside a BSC, workers may be at risk of infection



Acknowledgements

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Combination Hand/Airborne Exposures are Especially Risky

- We predict that moderate exposures entailing both hand contamination and an airborne hazard are as risky as more extreme exposures of either type
- Because workers may contaminate their hands trying to clean up spills that generate aerosols, workers and facilities should be especially mindful of these risks
- Compared to other body parts, contaminated hands more often lead to exposures, further exacerbating risk

Outcomes of 100,000 Simulations

	No Airborne Exposure	Airborne Exposure
No Liquid Exposure	3% of simulations	82% of simulations
Liquid Exposure	1% of simulations	**14% of simulations**

Probability of Infection if Combination Exposure Occurs:

Amount of IM on Body ($TCID_{50}$)	10	100	1000	1e4	1e5	1e6	1e7	1e8	1e9	1e10
10	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	18.8%	41.6%	78.5%
100	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	5.7%	24.8%	57.3%	80.5%
1000	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	9.8%	31.6%	65.8%	89.6%
1e4	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	20.4%	42.2%	72.5%	93.4%
1e5		0.0%	0.0%	0.0%	0.0%	10.1%	28.4%	57.6%	82.0%	95.8%
1e6			0.0%	0.0%	0.0%	17.1%	43.1%	69.5%	88.4%	97.5%
1e7				0.0%	11.8%	20.4%	55.7%	81.5%	95.1%	99.0%
1e8					20.4%	49.5%	63.8%	87.4%	97.2%	99.5%
1e9						64.7%	86.6%	94.1%	98.6%	99.8%
1e10							94.2%	97.4%	99.5%	99.9%

Conclusions

1. Even with a BSC present, facilities should consider respiratory protection or additional containment vessels while working with higher titer viruses (>10^9 $TCID_{50}$/ml), or when performing procedures expected to generate greater than routine airborne hazards
2. Personnel should work in a BSC whenever possible and use aerosol-tight caps for all centrifuge spins.
3. Workers should wear arm PPE and double gloves while using a BSC, because the BSC does not protect these parts of the body.
4. Facilities should factor the enhanced risk of hand/airborne combinations into risk assessments for spills, sprays, and other losses of primary containment where they could happen.

Data Gaps

- Gaps in available biosafety data hinder our ability to model facets of personnel exposure regarding the use of primary containment and the additional mitigation effects provided by PPE

Data Gap	Question	Experiments Needed
Spill/splashes in a BSC	How well do BSCs contain liquid spill/splash?	Simulated spills/splashes in BSC with fluorescent tracer
BSC installation conditions	Does BSC location and air fluctuations interfere with proper operation and effectiveness?	Operator protection measurements of BSCs in the field
BSC model variation	Do BSC manufacturer specifications affect performance?	Operator protection measurements of BSCs in the field