Supplementary Table 1. Individual values comprising the exposure dose range listed in Figures 3 and 4

Exposure dose range[a]	Virus	Exposure dose[a]	Critical values[b]		MOI[c]	
			Lower	Upper	Calu-3	Alveolar
2,224 - 4,448	Thai/16	2,608	2,509	2,708	4x10^{3}	2x10^{3}
	Anhui/1	2,224	2,132	2,316	3x10^{3}	2x10^{3}
	Panama/99	4,448	4,318	4,578	7x10^{3}	4x10^{3}
283 – 1,152	Thai/16	384	346	423	6x10^{4}	3x10^{4}
	Anhui/1	283	251	316	4x10^{4}	2x10^{4}
	Panama/99	1,152	1,086	1,219	2x10^{3}	1x10^{3}
9.7 - 16	Thai/16	9.7	4	16	1x10^{5}	8x10^{6}
	Anhui/1	16	9	24	2x10^{5}	1x10^{5}
	Panama/99	13	6	20	2x10^{5}	1x10^{5}
1.2 - 4.3	Thai/16	2.0	0	5	3x10^{6}	2x10^{6}
	Anhui/1	1.2	0	4	2x10^{6}	1x10^{6}
	Panama/99	4.3	1	9	7x10^{6}	4x10^{6}

[a]Expressed as PFU/well
[b]Values for a 95% confidence level assuming that presented dose follows a binomial distribution with $N = N_{cham}$ and $p = SA/XA$. The true presented dose for any given well has a 95% chance of falling between these two values.
[c]Multiplicity of infection (MOI) calculated for alveolar or Calu-3 cells exposed

Supplementary Table 2. Individual values comprising the exposure dose range listed in Figure 5

Exposure dose range[a]	Virus	Exposure dose[a]	Critical values[b]		MOI[c]	
			Lower	Upper	LLI	ALI
116 - 260	Thai/16	126	105	149	2x10^{4}	6x10^{5}
	Anhui/1	281	249	315	5x10^{4}	1x10^{4}
	Panama/99	138	115	161	2x10^{4}	7x10^{5}
7.2 - 17	Thai/16	16	9	25	3x10^{5}	8x10^{6}
	Anhui/1	18	11	27	3x10^{5}	9x10^{6}
	Panama/99	8	3	14	1x10^{5}	4x10^{6}
1.3 - 1.6	Thai/16	1	0	4	2x10^{6}	7x10^{7}
	Anhui/1	2	0	5	3x10^{6}	9x10^{7}
	Panama/99	1	0	4	2x10^{6}	7x10^{7}

[a]Expressed as PFU/well
[b]Values for a 95% confidence level assuming that presented dose follows a binomial distribution with $N = N_{cham}$ and $p = SA/XA$. The true presented dose for any given well has a 95% chance of falling between these two values.
[c]Multiplicity of infection (MOI) calculated for alveolar or Calu-3 cells exposed to virus, expressed as PFU/cell

Supplementary Experimental Procedures

Derivation of exposure dose formula

The concentration of infectious virus in an aerosol (C_{aer}) can be calculated using the media volume (V_{samp}), concentration (C_{samp}), and flow rate (Q_{samp}) of the sampler as well as the exposure time (t) (equation 1). When the system is used for animal inoculation, presented dose—the dose inhaled by the animal—is estimated by multiplying C_{aer} by the animal's minute volume (MV) and the exposure time (equation 2) (Gustin et al., 2011). Combining equations 1 and 2, and representing the total number of infectious virus particles in the sampler as N_{samp}, allows for the calculation of presented dose based on measured parameters (equation 3). Because the ratio of viral particles in the sampler (N_{samp}) to the total number of aerosolized infectious particles passed through the chamber (N_{cham}) is equal to the ratio between the flow rate of the sampler and the flow rate of the chamber (equation 4), equation 3 can be rewritten in terms of the flow rate and number of infectious viral particles to pass through the entire chamber (equation 5). Multiplying the right side of this equation by time/time shows that the presented dose is equal to the total number of aerosolized particles passing through the chamber multiplied by the ratio of the total volume of air inhaled by the ferret (V_{fer}) to the total volume of air that passed through the chamber during the exposure period (V_{cham}) (equation 6).

In order to account for the fact that we were exposing a two-dimensional, rather than three-dimensional surface to the aerosol, we modified this equation so as to determine the dose of virus contacting the surface of each well by multiplying the total number of aerosolized particles passing through the chamber (N_{cham}) by the ratio of the surface area of the well (SA) to the cross-sectional area (XA) of the chamber. Substituting measured parameters for the N_{cham} term (equation 4) yields equation 7. Exposure dose was substituted for presented dose as the deposition efficiency was found to be approximately 100%. The concentration in the nebulizer needed to achieve a particular exposure dose can be calculated using equation 8, where SF represents the spray factor, the ratio of the concentration of virus in the aerosol to its concentration in the nebulizer, for a given virus stock (Hartings and Roy, 2004).

Equations

1) $C_{aer} = \frac{(C_{samp})(V_{samp})}{(Q_{samp})(t)}$

2) $PD_{fer} = (C_{aer})(MV)(t)$

3) $PD_{fer} = \frac{(N_{samp})(MV)}{Q_{samp}}$

4) $\frac{N_{samp}}{N_{cham}} = \frac{Q_{samp}}{Q_{cham}}$ $\quad N_{samp} = \frac{(Q_{samp})(N_{cham})}{Q_{cham}}$ $\quad N_{cham} = \frac{(N_{samp})(Q_{cham})}{Q_{samp}}$

5) $PD_{fer} = \frac{(\not{Q}_{samp})(N_{cham})(MV)}{(\not{Q}_{samp})(Q_{cham})}$

6) $PD_{fer} = \frac{(N_{cham})(V_{fer})}{(V_{cham})}$

7) $ED_{cells} = PD_{cells} = \frac{(SA_{well})(N_{samp})(Q_{cham})}{(XA_{cham})(Q_{samp})}$

8) $C_{neb} = \frac{(XA)(ED)}{(SA)(Q_{cham})(SF)(t)}$