Maximum Possible Risk Modeling

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Abstract

Counterfactual assumptions enable a maximum possible risk analysis of the possibility of an aerosol release of pathogens such as anthrax spores from a biological research laboratory. Eight counter-factual assumptions ensure that any actual laboratory accident would pose a risk of exposure that is smaller than the hypothetical exposure risk generated by the model. The final counter-factual assumption sets an unrealistically low threshold of risk. The inflated risk is still less than the deflated risk threshold, so it is possible to conclude the laboratory is safe without attempting to measure its actual risk or specify an actual threshold of acceptable risk.

Keywords: Possibility, Risk, Counterfactual Conditionals, Counterfactual Assumptions, Biosafety

1. Introduction

This paper illustrates the use of counterfactual assumptions [5] [7] in a maximum possible risk analysis of the possibility of a release of pathogens via aerosol from a biological research laboratory. A companion paper [1] discusses the possibility of a contagious disease being spread to the community as a result of a laboratory worker becoming infected.

Within the scope of human error and mechanical failure, prior work in the United States for high containment biological facilities demonstrates that the worst-case event is the release of anthrax spores to the environment [6] because, unlike most viruses and bacteria, they can withstand the conditions of release and survive for long periods outside a laboratory or animal host.

A conceivable event is that viable anthrax spores would escape the laboratory as an aerosol release via the normal exhaust stack as a result of research materials being accidentally mishandled inside the laboratory.

2. Definition of risk

For a potentially harmful event, the classical definition of risk incorporates the probability than an event occurs and how great the impact (loss or cost) of that event would be if it occurred. Mathematically, the risk of a potentially harmful event is determined by the possible adverse impacts and the probability of each one. [8]

The standard model of the total risk of an action (or inaction) is the sum of the risk of the different potentially harmful events that might follow the action.

If one or more potentially harmful events that might or might not arise from an action or inaction have probability that is well measurably greater than zero and significant impact, the action has some risk and it becomes necessary to weigh the level of risk against the benefits expected and the risks and benefits of alternative actions or inaction.

On the other hand, if the action (in this

Proceedings of the 11th Joint Conference on Information Sciences (2008)
Published by Atlantis Press

case, operation of a high containment biological laboratory) includes sufficient countermeasures to reduce the probability and/or the impact of each potentially harmful event to zero, or a number too small to be meaningfully measured, there is no need to attempt the extremely questionable exercise of establishing an “acceptable" level of risk -- in effect, the acceptable level of risk that a member of the community will get sick as a result of a laboratory accident can be considered to be zero.

3. Maximum Possible Risk (MPR) Model

A commonly used risk assessment model developed by the U.S. military is based on a concept of "maximum credible event" or MCE. [4] Since the deadly airplane hijackings and anthrax attacks of 2001 in the U.S., the more extreme description of “barely conceivable” or “inconceivable” is a more appropriate planning basis. Accordingly, the approach of "maximum possible risk" (MPR) was used instead. This approach bypasses the issue of what is credible and what is not. The release scenarios modeled here are *not* credible; they are barely conceivable, but evaluation of even these seemingly-impossible scenarios is the crux of MPR modeling. Mathematically, they have a probability indistinguishable from zero but a small nonzero value of possibility. [7]

The logic of MPR modeling is that if it is possible to prove that the model risk is greater than the actual risk without precisely quantifying the actual risk, and it is possible to prove that the model risk is less than the acceptable risk without precisely quantifying the acceptable risk, then we can be certain that the actual risk is less than the acceptable risk without precisely quantifying either.

$$\begin{bmatrix} \text{Actual} \\ \text{Risk} \end{bmatrix} < \begin{bmatrix} \text{Model} \\ \text{Risk} \end{bmatrix} < \begin{bmatrix} \text{Acceptable} \\ \text{Risk} \end{bmatrix}$$

3.1 Real risks are even lower than risks reported here

In keeping with the MPR philosophy, simplifying assumptions were made which are worse, i.e. higher risk, than analogous "credible" assumptions. This approach makes the calculations easier to understand by eliminating the complexity of assessing statistical probability rather than mere possibility. It gives extra confidence that the actual risks are less than the risks that are calculated and presented in the analysis.

4. Nine Counterfactual Assumptions

The following nine assumptions used in the model are all "counterfactual" assumptions; each one is not utterly impossible under any circumstances, but each one has a probability exceedingly close to or actually indistinguishable from zero. [7]

4.1 Counterfactual Assumption 1: Magnitude of Release

The standard form of anthrax "technical powder" comes from laboratory-supply companies in a one-gram vial which is labeled to contain $7\text{x}10^{11}$ spores. A series of laboratory experiments was performed using *B. subtilis*, a standard laboratory surrogate for *B. anthracis*, in technical powder form. For each replication, the total number of respirable spores that were aerosolized was calculated as (respirable particles > 0.3 microns minus respirable particles > 10 microns). The mean was 371,522 aerosolized respirable particles, with standard deviation of 178,251 particles.

In order to ensure an estimate for the number of respirable particles which was essentially certain to be well above anything that might actually occur, six times the standard deviation ("six sigma") was added to the mean, leading to a worst-case release of 1,441,025 respirable particles from one gram of technical powder. The actual number of respirable spores will be less than 1,441,025 of the 700 billion total spores, 99.9999999 % of the time.

(Research studies in which the consequences of error are less severe traditionally use a factor of roughly two times sigma to generate a 95% confidence level. In the present example, this would correspond to a more realistic upper bound on the number of spores roughly half of the six sigma level, but the objective of a Maximum Possible Risk analysis is safety rather than theoretical realism.)

4.2 Counterfactual Assumption 2 No pre-dilution

The lab itself has volume, as does the stack. If a spill occurred, the spores would fill up the lab first, then begin to escape through the event-related release point. This pre-dilution is ignored for the computation, relying on the assumption that all the spores get out and into the dispersed half-cone or cone, essentially instantaneously. This assumption clearly overstates the true risk.

4.3 Counterfactual Assumption 3: Missing HEPA Filter

According to international guidelines and the national biosafety regulations, exhaust air from high-containment laboratories has to pass through one or more stages of HEPA filters. [9] Multiple provisions are mandated both to make any lapses in this principle virtually impossible, and if such a lapse were to occur, to provide automatic interlocks and alarms to make sure that laboratory operations immediately cease until the problem is fixed and measures are taken to ensure it does not recur.

Contrary to these facts, the model assumes that all HEPA filters between the spilled material and the outside are completely missing.

4.4 Counterfactual Assumption 4: Half Cone

The half cone dispersion pattern is a simple model of the dispersion of pathogens into the surrounding environment following a laboratory accident. The shape assumes the release is close to the ground and the flat side of the half-cone *is* the ground. In reality the ground would absorb most of the spores striking it, but the counterfactual model assumes spores are reflected from the ground to fill the half cone with no attrition.

In addition, a release would not be at ground level, but from the exhaust stack of the laboratory; aerosolized spores would disperse both upwards and downwards from this elevated point, resembling a larger and thus more dilute full cone rather than the assumed half cone.

Thus, the half cone gives a dispersion pattern which is certain to deliver a higher proportion of the pathogens released in a laboratory accident to a given location than would actually occur in the real world.

In the half cone model there is a wind that confines the pathogens to the "forward" direction. If the release point is high above the ground and there is no turbulence, the pathogens disperse in a conical pattern. At a distance from the release point depending on its height and the cone's opening angle, the pathogens encounter the ground. In a real incident, many of them would remain on the ground and pose no further inhalation threat; however, to be sure of overstating risk, we assume all pathogens are "reflected" from the ground back into the cone, leading to a concentration of pathogens per cubic meter twice that of the simple cone.

The half cone model is an alternative to far more complex models that use computational fluid dynamics to attempt to create a realistic model of the dispersion of a particulate aerosol. Fluid dynamics is a notoriously difficult field even when modeling engineered surfaces. The difficulties multiply when it is used to model meter-scale flows in the presence of localized wind currents, topographic features, moving vehicles, and trees and other vegetation that changes from season to season, The half cone model, while not realistic, gives more confidence that the actual pattern will pose less risk than the model risk.

4.5 Counterfactual Assumption 5: Uniform Distribution

When the leading edge of the plume reaches a specified distance d from the release point, the concentration of particles is below what it would be under a uniform distribution. Somewhere closer to the "origin" of the plume the concentration is at a maximum that is higher than what it would be under a uniform distribution. Because the plume is moving, the initial exposure to a human at the edge of the cone would be lower than that associated with a uniform distribution. As the cloud moved over the individual, offsetting effects would occur:

(a) the concentration would reduce due to further dispersion,
(b) more spores would arrive from the relatively more concentrated portion of the cone, and
(c) spores would continue to settle, reducing the overall number of spores in the immediate atmosphere.

The uniform distribution provides an upper limit on the true and complex distribution which varies with time.

Reality: Particles may be systematically concentrated nearer the release point, leading to lower transient peak concentration away from the stack. Turbulent eddies will produce small parcels of concentration higher or lower than the model but (especially in wind) the time it takes to inhale means that each breath takes an average over multiple parcels.

4.5 Counterfactual Assumption 5: Wind Speed and Dispersion Angle

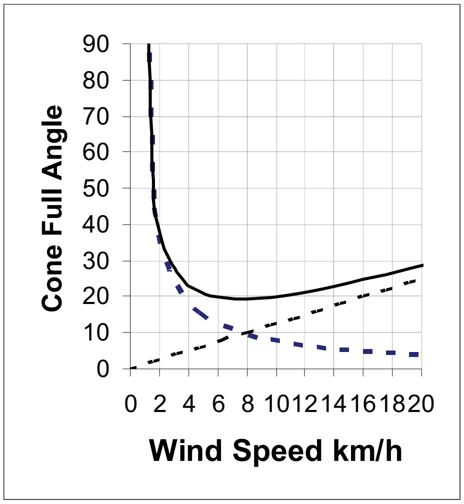
In a very light wind, pathogens would disperse broadly before they were carried far from the release point, leading to a wide opening angle and thus a low concentration of pathogens per cubic meter at a given downwind location. The pathogens would be well confined to this wide cone due to low turbulence.

In a stronger wind, the basic cone would open at a narrower angle. In the absence of turbulence, this would lead to a higher concentration of pathogens per cubic meter at a given downwind location. However, higher winds speed produces greater turbulence, which would blow pathogens outside the basic cone, leading to a wider equivalent opening angle and lower concentrations.

Based on laboratory experiments, a conservative estimate of the rate that respirable particles disperse in still air is about 11 cm/sec (0.4 km/hr). In a world without turbulence, a wind of W km/hr would result in a plume of particles that disperse in a half cone with a "half angle" (the angle formed by the edge of the half cone and its centerline) with a tangent of 0.4/W. Thus, the turbulence-free half angle would be $\cot^{-1}(W/0.4)$ radius.

The model assumes that turbulence widens the half angle at a rate of 0.6 degree (0.01 radians) per kilometer per hour of wind speed. In reality the effect would be greater, especially near ground level. Using these numbers with the formulas in the Appendix yields a worst case wind speed of 7.9 km/hr, a cone half angle of 0.166 radians and a whole angle of 0.332 radians or 19 degrees.

The graph shows cone opening angle as a function of wind speed. The lower curve is the turbulence-free cone angle. The effect of turbulence is conservatively estimated as a linear increase in the half angle of the cone of 0.6 degrees per kilometer per hour. The "extra" degrees of cone angle are shown by the straight line, and the upper curve is the effective cone opening angle as a function of wind speed taking turbulence into account.



4.7 Counterfactual Assumption 7: Wind Direction

Computation of spore concentration at specified "targets" within an investigated area assumes that spores travel directly, in a straight line from the point of release to the target, spreading only in accordance with distance from the nearest point of the footprint of the laboratory and the wind-velocity discussion elsewhere in this report. A more realistic event is that spores would exit from a stack above the laboratory roof with an upward velocity, thereby extending the dispersion pattern beyond the half-cone used for computations, and that the wind would not point quite so precisely at any nearby target. The actual event would be fewer spores at the target of interest.

4.8 Counterfactual Assumption 8: Persistence of Plume at Target

The time to accumulate a certain amount (a potential infectious dose) of spores at breathing rate of 12 liters/minute is calculated on the assumption that the plume of spores will spread out from the release point according to the above counterfactual assumptions to the distance of the indicated "target" point, but then stop expanding and behave as if confined to the half cone geometry. The transient peak concentration of the plume is treated as if it remained constant for an extended period. In fact, further expansion and turbulence would dilute the spores, and more and more would settle to the ground and cease to be available for inhalation.

4.9 Counterfactual Assumption 9: 500 Spores Potentially Pathogenic

The most harmful event considered in this report is a pathogenic concentration of *Bacillus anthracis* spores reaching the surrounding community. In the absence of such a harmful spore release, there is no public-health impact. Published evidence suggests that the pathogenic level is greater than 600 spores over an 8-hour period [2] [3]. The present counterfactual conditional analysis, in contrast, treats a total cumulative exposure of 500 spores (in any time frame) as if it were potentially pathogenic.

5. Results

The table below considers four specific distances away from the release point.

The table gives the number of spores per cubic meter of air in the 19° half cone, and the time a person would have to linger in a persistent (non dispersing, non settling) counterfactual plume in order to inhale the 500 spore dose which the model treats as if it were potentially pathogenic.

Distance (m)	Spores per m3	Time to Inhale 500 spores
25	6,290	6.6 Minutes
50	786	53 Minutes
100	98.3	7 Hours
200	12.3	2.4 Days

6. Discussion

Counter-factual assumptions 1-8 ensure that any actual laboratory accident with a release of pathogenic agents through the exhaust air would pose a risk of exposure that is smaller, by an unknown but substantial amount, than the hypothetical exposure risk generated by the model.

Setting the acceptable risk of laboratory-induced disease in the surrounding community to zero does not mean that the acceptable exposure to spores must be zero. [2] [3]. Counter-factual assumption 9, if it were true, would imply that an acceptable (i.e. effectively zero) risk of disease would only apply if nobody in the surrounding community experienced an exposure sufficiently concentrated and persistent that they were to inhale 500 spores. As the release point (exhaust stack of the laboratory) is more than 25 meters from any place anyone would have a reason to linger even for 5 minutes, this will not happen. Since the model risk is below the threshold of acceptable risk implied by counter-factual assumption 9, is also less than the actual risk or spore release that corresponds to the acceptable risk of laboratory induced disease, namely zero.

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Appendix

H = Half angle, radians
S = spreading velocity, km per hour
W - Wind Speed, km per hour
R = turbulence effect on half angle, radians per km per hour
A = turbulence-free half angle, radians
WR= additional angle due to turbulence, radians

$$A = \cot^{-1}\left(\frac{W}{S}\right)$$

$$H = A + WR$$

$$\frac{d}{dh}\cot^{-1}(u) = -\frac{1}{1+u^2}\frac{d}{dx}u$$

$$\frac{w}{dW}H = R - \frac{1}{1+\frac{W^2}{S^2}}\frac{1}{s} = 0$$ at minimum angle

$W = \sqrt{\frac{S}{R} - s^2}$, the wind speed that minimizes the cone half angle

$$A + WR = \cot^{-1}\left(\frac{1}{S}\sqrt{\frac{S}{R} - s^2}\right) + R\sqrt{\frac{S}{R} - s^2}$$

= total half angle of cone at worst case wind speed