Supporting Appendix

This appendix describes the mathematical model that generated the results reported in the main text. The supply chain is introduced in Section 1, the dissemination of the biological agent is analyzed in Section 2, the pasteurization inactivation of toxin is computed in Section 3, the number poisoned is calculated in Section 4, and secondary contamination, product tracing and the amount of product recalled are discussed in Section 5. Graphs from the sensitivity analysis described in the main text appear in Fig. 5.

1 The Supply Chain

We consider the nine-stage supply chain associated with a single milk-processing plant, as pictured in Fig. 1. Table 4 provides a description of the nine stages and their associated parameter values; values of the other model parameters are given in Table 5. The parameter values in Table 4 are representative of the California dairy industry (www.dairyforum.org/cdf.html, accessed on May 18, 2004), which produces $> 20\%$ of the nation's milk. Although we do not use all of the parameter values in Table 4, they help to articulate the scale of the system. Let $X_i(t)$ be the number of gallons of milk at stage i at time t for $i = 1, \ldots, 8$, and let N_i denote the total number of entities at stage i for $i = 0, \ldots, 7$. We assume a symmetric supply chain, in that all entities within a stage are identical. If we define X_{ij} to be the number of gallons at entity $j = 1, \ldots, N_i$ of stage $i = 1, \ldots, 7$, then our symmetry assumption implies that

$$X_{ij}(t) = \frac{X_i(t)}{N_i} \quad \text{for } \; i = 1, \ldots, 7, \;\; j = 1, \ldots, N_i, \tag{1}$$

which is used in Section 5.

We assume that each cow is milked twice per day and produces λ gallons of milk daily. We model the flow of milk through these stages as a system of linear first-order differential equations, where μ_i^{-1} is the mean delay at stage i of the supply chain. Milk is stored in tanks and picked up

daily by 5,500-gallon trucks. Each truck makes two round trips daily. The trucks' contents are drained into a raw milk silo upon arrival at the processing facility, where the milk is processed and packaged. Packaged milk makes its way through the distribution channel and is eventually purchased and consumed. The parameters μ_1 and μ_2 are based on two daily trips within a 200-mile radius of the processing plant, μ_3 is based on Little's formula (1) (i.e., $H_3 = \frac{\Lambda_3}{\mu_3}$, where Λ_3 is defined in Eq. 10 and H_3 is the silo capacity), and μ_6 and μ_7 are chosen so that 80% of milk is purchased within 48 hr of leaving the processing facility. In the sensitivity analysis in the main text, $\mu_6^{-1} = \mu_7^{-1} = 6.17$ hr leads to 90% of the milk purchased within 24 hr. We assume perfect yield throughout the supply chain, thereby ignoring the 2-3% yield loss at typical processing facilities. The model dynamics are

$$\underbrace{\dot{X}_1(t)}_{\text{farms}} = \underbrace{\lambda N_0}_{\text{production}} - \underbrace{\mu_1 X_1(t)}_{\text{pickup}}, \tag{2}$$

$$\underbrace{\dot{X}_2(t)}_{\text{trucks}} = \underbrace{\mu_1 X_1(t)}_{\text{pickup}} - \underbrace{\mu_2 X_2(t)}_{\text{delivery}}, \tag{3}$$

$$\underbrace{\dot{X}_3(t)}_{\text{silos}} = \underbrace{\mu_2 X_2(t)}_{\text{delivery}} - \underbrace{\mu_3 X_3(t)}_{\text{process initiation}}, \tag{4}$$

$$\underbrace{\dot{X}_4(t)}_{\text{processing lines}} = \underbrace{\mu_3 X_3(t)}_{\text{process initiation}} - \underbrace{\mu_4 X_4(t)}_{\text{process completion}}, \tag{5}$$

$$\underbrace{\dot{X}_5(t)}_{\text{finished goods}} = \underbrace{\mu_4 X_4(t)}_{\text{process completion}} - \underbrace{\mu_5 X_5(t)}_{\text{distribution}}, \tag{6}$$

$$\underbrace{\dot{X}_6(t)}_{\text{distributors}} = \underbrace{\mu_5 X_5(t)}_{\text{distribution}} - \underbrace{\mu_6 X_6(t)}_{\text{transportation and storage}}, \tag{7}$$

$$\underbrace{\dot{X}_7(t)}_{\text{retailers}} = \underbrace{\mu_6 X_6(t)}_{\text{delivery}} - \underbrace{\mu_7 X_7(t)}_{\text{purchases}}. \tag{8}$$

$$\underbrace{\dot{X}_8(t)}_{\text{consumers}} = \underbrace{\mu_7 X_7(t)}_{\text{purchases}} - \underbrace{\mu_8 X_8(t)}_{\text{consumption}}. \tag{9}$$

2 Agent Dissemination

Just as agent dissemination in airborne and contagious attacks needs to be analyzed via atmospheric dispersion and epidemic models, so too do we need a mathematical model to understand the dissemination of a foodborne attack. This section calculates the amount and concentration of contaminated milk resulting from a release of Q kg of botulinum toxin. Although the agent can be released at any point throughout the supply chain, any introduction of botulinum toxin after packaging (i.e., stages 5-8) would be tedious and would lead to a small number of poisoned individuals. A release at stage 4 is possible, although the processing facility is likely to have reasonably good security. An introduction at stage 0 would be ineffective, because cows would die before producing tainted milk. The silo (stage 3) is difficult to access, making an introduction here improbable. The most likely scenarios are stage 1 (the agent is deposited in the storage tank at a farm) or stage 2 (the agent is deposited directly into the truck tanks, some of which are left unattended and unlocked during rest stops along the truck route), and we assume that the release occurs at one of these two stages. However, whether the milk is deposited in a tank, a truck, or a silo, the contaminated milk eventually makes its way into a silo, where the agent is well mixed by the mechanical agitators in the silo (the milk is also well mixed while in the truck, due to the driving motion). Milk is piped from the silos into the processing plant, undergoes a sequence of continuous-flow processes (separation, pasteurization, homogenization, and vitamin fortification), and then is placed in post-pasteurization holding tanks, awaiting packaging. Hence, our dissemination analysis consists of two steps: the dynamics of the raw milk silos and the postpasteurization holding tanks.

In steady-state conditions (i.e., setting the left sides of Eqs. 2-9 equal to zero), the throughput rate of the supply chain is λN_0. In particular, this is the average rate at which milk is flowing through the silos. We assume all N_3 silos are functioning simultaneously. Although processing facilities maintain spare silos to buffer against uncertainties in arrivals and production, as well as to allow for silo cleaning, these spare silos are not included among the N_3 silos. Hence, the

throughput rate for a given silo, denoted by Λ_3, is

$$\Lambda_3 = \frac{\lambda N_0}{N_3}. \qquad 10$$

Fig. 4 depicts the dynamics of a silo over one operation cycle. We assume the entire facility is operating three shifts per day, even though some facilities may process milk for fewer hours per week than they receive milk. The silo is empty and clean at time 0 and is filled up at rate Λ_3 from time 0 until it reaches its capacity of H_3 gallons at time $\frac{H_3}{\Lambda_3}$. From time $\frac{H_3}{\Lambda_3}$ to $\tau_c - \frac{H_3}{\Lambda_3}$, milk is simultaneously inserted at rate Λ_3 from arriving trucks and depleted at rate Λ_3 for processing. From time $\tau_c - \frac{H_3}{\Lambda_3}$ to τ_c, the silo receives no input and is drained at rate Λ_3 until it is empty. At time τ_c, the empty silo is cleaned in preparation for the next cycle. Hence, we view the silo operation cycle $[0, \tau_c]$ as being composed of three intervals: the filling interval $\left[0, \frac{H_3}{\Lambda_3}\right)$, the replenishment interval $\left[\frac{H_3}{\Lambda_3}, \tau_c - \frac{H_3}{\Lambda_3}\right)$ and the draining interval $\left[\tau_c - \frac{H_3}{\Lambda_3}, \tau_c\right]$.

We assume that the contaminated truck, which may have received the Q kg of botulinum toxin directly or from a farm tank, arrives at a silo at a random time during the filling and replenishment intervals, i.e., the arrival time τ_a is uniformly distributed between 0 and $\tau_c - \frac{H_3}{\Lambda_3}$. For simplicity, we assume that the Q kg are simultaneously deposited into the silo at time τ_a. Our analysis in this section and in Section 4 are in terms of the random time τ_a, and at the end of Section 4, we integrate over the uniform distribution of τ_a to find the mean number poisoned from an attack.

Our goal in the first stage of the dissemination analysis is to determine the amount and concentration distribution (i.e., for each value of τ_a, the contaminated milk exiting the silo will have various contamination levels) of contaminated milk that is exiting the silo. The analysis of the concentration distribution relies on the following observations: the concentration in the silo at time τ_a is Q divided by the total amount of milk in the silo at time τ_a, the concentration drops exponentially at rate $\frac{\Lambda_3}{H_3}$ during the replenishment interval, and the concentration remains constant during the draining interval.

Let $c_3(u, \tau_a)$ be the toxin concentration in the silo at time $u \in [0, \tau_c]$. Because the silo is not drained during the filling interval, we need not be concerned with $c_3(u, \tau_a)$ for $u \in \left[0, \frac{H_3}{\Lambda_3}\right)$. If u is in the replenishment interval $\left[\frac{H_3}{\Lambda_3}, \tau_c - \frac{H_3}{\Lambda_3}\right)$, then

$$c_3(u, \tau_a) = \begin{cases} \frac{Q}{H_3} e^{-\frac{\Lambda_3}{H_3}\left(u - \frac{H_3}{\Lambda_3}\right)} & \text{if} \quad \tau_a \leq \frac{H_3}{\Lambda_3}; \\ \frac{Q}{H_3} e^{-\frac{\Lambda_3}{H_3}(u - \tau_a)} & \text{if} \quad \frac{H_3}{\Lambda_3} < \tau_a \leq u; \\ 0 & \text{if} \quad u < \tau_a \leq \tau_c - \frac{H_3}{\Lambda_3}. \end{cases} \tag{11}$$

The three cases in Eq. 11 represent the attack occurring during the filling interval, during the replenishment interval and before u, and after u.

For u in the draining interval $[\tau_c - \frac{H_3}{\Lambda_3}, \tau_c]$, we have

$$c_3(u, \tau_a) = \begin{cases} \frac{Q}{H_3} e^{-\frac{\Lambda_3}{H_3}\left(\tau_c - \frac{2H_3}{\Lambda_3}\right)} & \text{if} \quad \tau_a \leq \frac{H_3}{\Lambda_3}; \\ \frac{Q}{H_3} e^{-\frac{\Lambda_3}{H_3}\left(\tau_c - \frac{H_3}{\Lambda_3} - \tau_a\right)} & \text{if} \quad \frac{H_3}{\Lambda_3} < \tau_a \leq \tau_c - \frac{H_3}{\Lambda_3}, \end{cases} \tag{12}$$

where the two cases refer to the attack occurring during the filling and replenishment intervals.

Now we turn to the second stage of the dissemination analysis. We assume that milk from the N_3 silos are piped into the N_4 processing lines such that the milk from $\frac{N_3}{N_4}$ silos (for simplicity, we assume this ratio is an integer) is piped into each of the N_4 processing lines. After pasteurization, milk is stored in tanks that can hold H_4 gallons. We multiply all concentrations in the postpasteurization holding tanks by the factor f_p, which is the fraction of toxin that survives pasteurization; this quantity is computed in Section 3. For mathematical convenience, we assume that the quantities

$$k_4 = \frac{N_3 H_3}{N_4 H_4} \quad \text{and} \quad n_4 = \frac{N_3 \Lambda_3 \left(\tau_c - \frac{H_3}{\Lambda_3}\right)}{N_4 H_4} \tag{13}$$

are integer (see Table 5). Suppose that the first milk out of a silo within an operation cycle enters an empty holding tank. Then Eq. 13 implies that the contaminated milk fills exactly n_4 holding tanks, with the first $n_4 - k_4$ tanks containing milk drained during the replenishment interval, and the last k_4 tanks containing milk drained during the draining interval. Our integrality assumption in Eq. 13 ignores the possibility that the first and last holding tanks contain a mixture of contaminated

and previously uncontaminated milk; however, this omission is insignificant, because typically $n_4 \gg 1$.

These n_4 tanks will have distinct concentration levels, and we let $c_{4i}(\tau_a)$ be the toxin concentration in tank $i = 1, \ldots, n_4$. Define $\Lambda_4 = \frac{N_3\Lambda_3}{N_4}$ as the filling rate for a tank. Because tank i contains milk that is drained during the time interval $\left[\frac{H_3}{\Lambda_3} + (i-1)\frac{H_4}{\Lambda_4}, \frac{H_3}{\Lambda_3} + i\frac{H_4}{\Lambda_4}\right)$, we have

$$c_{4i}(\tau_a) = \frac{f_p\Lambda_3}{H_4} \int_{\frac{H_3}{\Lambda_3}+(i-1)\frac{H_4}{\Lambda_4}}^{\frac{H_3}{\Lambda_3}+i\frac{H_4}{\Lambda_4}} c_3(u, \tau_a)\, du. \tag{14}$$

Substituting Eq. 11 into Eq. 14 and integrating shows that for $i = 1, \ldots, n_4 - k_4$, the concentrations of tanks containing milk drained during the replenishment interval are

$$c_{4i}(\tau_a) = \begin{cases} \frac{f_pQ}{H_4}(e^{-\frac{i-1}{k_4}} - e^{-\frac{i}{k_4}}) & \text{if} \quad \tau_a \le \frac{H_3}{\Lambda_3}; \\ \frac{f_pQ}{H_4}(e^{\frac{\tau_a\Lambda_3}{H_3}-1-\frac{i-1}{k_4}} - e^{\frac{\tau_a\Lambda_3}{H_3}-1-\frac{i}{k_4}}) & \text{if} \quad \frac{H_3}{\Lambda_3} < \tau_a \le \frac{H_3}{\Lambda_3} + (i-1)\frac{H_4}{\Lambda_4}; \\ \frac{f_pQ}{H_4}(1 - e^{\frac{\tau_a\Lambda_3}{H_3}-1-\frac{i}{k_4}}) & \text{if} \quad \frac{H_3}{\Lambda_3} + (i-1)\frac{H_4}{\Lambda_4} < \tau_a \le \frac{H_3}{\Lambda_3} + i\frac{H_4}{\Lambda_4}; \\ 0 & \text{if} \quad \frac{H_3}{\Lambda_3} + i\frac{H_4}{\Lambda_4} < \tau_a \le \tau_c - \frac{H_3}{\Lambda_3}. \end{cases} \tag{15}$$

The four cases in Eq. 15 represent that the attack occurs in the silo-filling interval, in the replenishment interval and before the milk that ends up in tank i is drained, while the milk that ends up in tank i is drained, and after the milk that ends up in tank i is drained.

Similarly, Eqs. 12 and 14 imply that the concentrations of tanks containing milk drained during the draining interval (i.e., $i = n_4 - k_4 + 1, \ldots, n_4$) are

$$c_{4i}(\tau_a) = \begin{cases} \frac{f_pN_4Q}{N_3H_3}e^{-\frac{\Lambda_3}{H_3}(\tau_c - \frac{2H_3}{\Lambda_3})} & \text{if} \quad \tau_a \le \frac{H_3}{\Lambda_3}; \\ \frac{f_pN_4Q}{N_3H_3}e^{-\frac{\Lambda_3}{H_3}(\tau_c - \frac{H_3}{\Lambda_3} - \tau_a)} & \text{if} \quad \frac{H_3}{\Lambda_3} < \tau_a \le \tau_c - \frac{H_3}{\Lambda_3}; \\ \frac{f_pN_4Q}{N_3\Lambda_3(\tau_c - \tau_a)} & \text{if} \quad \tau_c - \frac{H_3}{\Lambda_3} < \tau_a \le \frac{H_3}{\Lambda_3} + (i-1)\frac{H_4}{\Lambda_4}; \\ \frac{f_pQ}{H_4(\tau_c - \tau_a)}(\frac{H_3}{\Lambda_3} + i\frac{H_4}{\Lambda_4} - \tau_a) & \text{if} \quad \frac{H_3}{\Lambda_3} + (i-1)\frac{H_4}{\Lambda_4} < \tau_a \le \frac{H_3}{\Lambda_3} + i\frac{H_4}{\Lambda_4}; \\ 0 & \text{if} \quad \frac{H_3}{\Lambda_3} + i\frac{H_4}{\Lambda_4} < \tau_a \le \tau_c - \frac{H_3}{\Lambda_3}, \end{cases} \tag{16}$$

where the five cases correspond to the attack occurring in the filling interval, in the replenishment interval, in the draining interval and before the milk that ends up in tank i is drained, while the milk that ends up in tank i is drained, and after the milk that ends up in tank i is drained. Eqs. 15 and 16 specify the amount and concentration of contaminated milk that is distributed to the downstream portion of the supply chain (i.e., stages 5 - 8).

3 Inactivation by Heat Pasteurization

Little published work exists on the effect of heat pasteurization on botulinum toxin in milk. Typical milk pasteurization, which occurs at $\approx 170°$-174°F (77°C - 79°C) for 15 sec [the legal minimum requirement is 161°F (72°C) for 15 sec], allows survival of some *Clostridium botulinum* spores (2), and studies have shown that 257°F (125°C) for 5 sec is necessary to completely destroy botulinum toxin in milk (3). Ultra-high temperature (UHT) pasteurization [i.e., at least 280°F (138°C) for at least 2 sec] appears to completely inactivate botulinum toxin. There have been studies of heat inactivation in other foods with similar pH (milk has pH 6.4), which is one of the key drivers of heat sensitivity (4). More specifically, $\approx$ 90% of botulinum toxin A is inactivated by heating canned corn (with pH 6.2) to 174°F for 30 sec (Fig. 2 of ref. 3). We estimate that the fraction of toxin surviving 174°F for 15 sec is $e^{-0.5 \ln 10} = 0.316$. This is a rough estimate, because there are other factors besides pH that affect the heat sensitivity of toxin.

4 The Number Poisoned

As mentioned earlier, the number poisoned depends on the random time τ_a within the silo operation cycle that the attack takes place. In this section, we first find the number poisoned for a fixed τ_a and then determine the mean number poisoned by integrating over all possible values of τ_a. We assume the attack occurs at time 0 in real time; to avoid confusion, we use the dummy variables s and t to represent real time, in contrast to the dummy variable u used to represent an arbitrary time within the silo cycle in Eqs. 11-12 and 14-16.

Suppose in the silo cycle $[0, \tau_c]$, the attack happens at τ_a, which is set to be $t = 0$ in real time. Then the silo starts draining at $t_0 = \frac{H_3}{\Lambda_3} - \tau_a$ in real time, which might be negative if the attack happens in the draining interval. Hence, tank i is filled at $t_i = t_0 + i\frac{H_4}{\Lambda_4}$ in real time. To compute the downstream impact of the contaminated milk, we need to solve for each tank $i = 1, \ldots, n_4$,

$$\dot{X}_4^i(t) = -\mu_4 X_4^i(t), \;\; t \geq t_i, \tag{17}$$

together with

$$\dot{X}_j^i(t) = \mu_{j-1} X_{j-1}^i(t) - \mu_j X_j^i(t), \;\; t \geq t_i, \;\; j = 5, \ldots, 7, \tag{18}$$

and the initial conditions

$$\begin{cases} X_4^i(t_i) = H_4; \\ X_j^i(t_i) = 0, \;\; j = 5, \ldots, 7. \end{cases} \tag{19}$$

We denote the solution to Eqs. 17-19 by $X_j^i(t; \tau_a)$ for $t \geq t_i$ and $j = 4, \ldots, 7$, where the superscript i refers to milk from tank i, and the dependence of the solution on the random time τ_a within the silo operation cycle is explicitly incorporated.

Nearly two-thirds of fluid milk sold in the retail market is packaged in gallon containers (5), and we let n_8 denote the average number of people consuming a single gallon of milk, so that $n_8 \mu_7 X_7^i(t; \tau_a)$ people begin consuming contaminated milk at time t that was stored in tank i. Children aged 2-11 represent $\approx$ 25% of all milk consumers and consume $\approx$ 40% of all milk in the U.S. (5). Hence, we define $f_c = 0.25$ and $\tilde{f}_c = 0.4$ to represent the fraction of child consumers and milk consumed by children, respectively, and let $f_a = 1 - f_c$ and $\tilde{f}_a = 1 - \tilde{f}_c$ be the corresponding fractions for adults (due to lack of data, teenagers are treated as adults in our model). According to Eq. 9, it follows that each of $f_c n_8$ children and $f_a n_8$ adults consume 1 gallon of milk at the respective rates of $\frac{\tilde{f}_c \mu_8}{f_c n_8}$ and $\frac{\tilde{f}_a \mu_8}{f_a n_8}$, so that the gallon of milk is consumed in $\mu_8^{-1} = 84$ hr, which is consistent with the per capita consumption rate of $\approx$ 25 gallons per person (5).

For $j = \{a, c\}$, let $P_j(y)$ be the probability that an adult (a) or child (c) who consumes y μg of botulinum toxin gets poisoned. We assume this dose-response curve is governed by the probit model

$$P_j(y) = \Phi\left(\beta \log_{10}\left(\frac{y}{\mathrm{ID}_{50}^j}\right)\right), \quad \text{for} \quad j = \{a, c\}, \tag{20}$$

where $\Phi(\cdot)$ is the standard normal cumulative distribution function, β is the probit slope, and ID_{50}^j is the number of μg of toxin that poisons half of the child or adult population. We consider

two different pairs of values for ID_{50}^{j}, one based on primate data and one based on human data. Intragastric administration of 36 rhesus monkeys (table II of ref. 6) yields a $\mathrm{LD}_{50} = 70$ μg when scaled to a 70-kg human and 30 μg when scaled to a 30-kg child. We performed a least-squares analysis of this data to obtain a probit slope of 4.34. Intramuscular injection of eight monkeys suggests that the ID_{50} is nearly equal to the LD_{50} (the lowest dose that caused toxicity was 0.85 times the LD_{50}) (7), and so we assume that $\mathrm{ID}_{50}^{a} = 70$ μg and $\mathrm{ID}_{50}^{c} = 30$ μg. Human data are meager: the most quantitative study concerns a 104-kg man who died from eating cheese that was estimated (based on testing the uneaten half of a 140-gram block of cheese) to contain 0.1 μg of botulinum type B toxin (8). Morton (9) summarizes 13 additional cases (documented between 1922 and 1958) and concludes that 0.2 μg is a "generous" estimate of the oral LD_{100} for human adults. This scant evidence has been the basis for an estimated LD_{50} of between 0.1 and 1 μg (10), and we assume $\mathrm{ID}_{50}^{a} = 1$ μg, $\mathrm{ID}_{50}^{c} = 0.43$ μg based on the human data, and the same probit slope as in monkeys. Finally, daily sublethal doses summing to 1-10% of the LD_{50} kill guinea pigs, rabbits, and mice (11). If the same is true for humans, then we may be underestimating the ID_{50} by 1-2 logs.

Conditioned on the attack occurring at time τ_a within the silo operation cycle, it follows that the total number of people poisoned up until time t is

$$I(t;\tau_a) = \sum_{i=1}^{n_4} \sum_{j=\{a,c\}} \int_0^t f_j n_8 \mu_7 X_7^i(s;\tau_a) P_j\Big(\frac{c_{4i}(\tau_a)\tilde{f}_j \mu_8 \min\{\mu_8^{-1}, t-s\}}{f_j n_8}\Big)\, ds, \qquad 21$$

where the $\min\{\mu_8^{-1}, t-s\}$ term guarantees that people partake of only 1 gallon of milk. In our model, the attack can be detected either by early symptomatics or by testing within the supply chain. Hence, the total number of people poisoned in the attack is $I(\tau;\tau_a)$, where

$$\tau = \min\{\tau_s + \Delta_s, \tau_d\} \qquad 22$$

is the time of detection, τ_s is the time to detect via symptomatics that an outbreak has occurred, $\Delta_s = 24$ hr is the additional time it takes to identify the attack as being milkborne, and τ_d is the

detection time via testing within the supply chain. Although τ_s, and hence τ, are functions of τ_a, we suppress this dependence in the notation.

To quantify τ_s, let $f_1(t)$ be the probability density function for the incubation period. We assume the incubation period is log-normal with median $e^{\mu_r} = 48$ hr and dispersal factor $e^{\sigma_r} = 1.5$, implying that 95% of the incubation periods fall in the range $[\frac{48}{1.5^2}, 1.5^2(48)] = [21.3, 108]$ hr. These parameter estimates coincide with the incubation period data in Figure 1 in ref. 12, which documents the largest outbreak in the U.S. over the last 100 years. If we assume that detection of an outbreak via symptomatics occurs when the kth person develops symptoms, then τ_s satisfies

$$\int_0^{\tau_s} \frac{dI(t;\tau_a)}{dt} F_1(\tau_s - t)\, dt = k, \tag{23}$$

where, by differentiating Eq. 21, we find that the rate at which people are presenting symptoms at time t is

$$\frac{dI(t;\tau_a)}{dt} = \sum_{i=1}^{n_4} \sum_{j=\{a,c\}} \int_{\max\{t-\mu_8^{-1},0\}}^{t} f_j n_8 \mu_7 X_7^i(s;\tau_a) \frac{c_{4i}(\tau_a)\tilde{f}_j \mu_8}{f_j n_8} p_j\Big(c_{4i}(\tau_a)\frac{\tilde{f}_j \mu_8}{f_j n_8}(t-s)\Big)\, ds, \tag{24}$$

where

$$p_j(y) = \frac{dP_j(y)}{dy} = \frac{\beta}{y\sqrt{2\pi}\ln 10} \exp(-\frac{1}{2}\beta^2 \log_{10}^2(\frac{y}{ID_{50}^j})). \tag{25}$$

The time to detect via testing depends on the sensitivity, specificity, frequency and location of testing, and the time delay to obtain testing results. We consider two types of tests, the Food and Drug Administration-approved mouse assay and an ELISA test. The mouse assay has a detection limit of 16 pg/ml (60.6 ng/gallon) (13). The time delay to obtain results ranges from 2 to 6 days, although an indication of a positive result is usually exhibited within 12 hr; we assume 48 hr. The ELISA test has a detection limit of 80 pg/ml (303 ng/gallon) (14), and the time delay to obtain results is $\approx$ 3 hr. We consider two testing strategies. The first strategy uses the ELISA test in isolation, thereby assuming that the test is sufficiently specific to act on a positive test result. There are no published data quantifying the false-positive rate of an ELISA test for botulinum toxin in milk. This testing strategy has a detection limit of $l_d = 80$ pg/ml and a testing delay of $t_d = 3$

hr. Front-line testing with the mouse assay appears impractical, given the huge number of mice required, and given that only several laboratories in the U.S. generate results for the mouse assay. Consequently, we consider a sequential strategy that uses a mouse assay as a confirmatory test after a positive ELISA test. This strategy has a detection limit of $l_d = 80$ pg/ml (the maximum of the two tests) and a testing delay of $t_d = 51$ hr (the sum of the two tests).

Among the possible locations to test milk, we focus on testing milk from each truck as the milk is piped into the raw silo, where it is currently tested for antibiotic residue. Although testing milk from the farm tank as it is loaded onto a truck would in theory allow for earlier testing and perhaps higher concentration of toxin, it would also require truck drivers (some of whom are independent contractors) and/or farmers to perform the test. Moreover, depending upon the nature of the test, it may not be practical for the testing process to begin before the truck arrives to the processing facility. Although downstream tests (e.g., as the milk is piped from the silo to the processing plant and at the holding tanks after pasteurization and before packaging) should be performed to detect an introduction at the processing facility, the milk is much more diluted once it enters the silo and hence may be harder to detect.

If each truck is tested as the milk enters the silo, then by our timing convention the test occurs at time 0. If we let H_2 denote the capacity of a truck that delivers milk from the farms to the processing plant, then

$$\tau_d = \begin{cases} t_d & \text{if } \frac{Q}{H_2} \geq l_d; \\ \infty & \text{otherwise.} \end{cases} \tag{26}$$

Although we do not consider it in the main text, if testing could be performed by the truck drivers at the farms, then Eq. 26 would be modified to

$$\tau_d = \begin{cases} t_d - Y_2 & \text{if } \frac{QN_1}{\Lambda_3 N_0} \geq l_d; \\ \infty & \text{otherwise,} \end{cases} \tag{27}$$

where Y_2 is an exponential random variable with mean μ_2^{-1}.

Substituting τ_s from Eq. 23 and τ_d from Eq. 26 into Eq. 22, and substituting the resulting τ into Eq. 21 gives $I(\tau; \tau_a)$, which is the total number of people poisoned for a given value of τ_a.

Finally, because τ_a is uniformly distributed on the interval $[0, \tau_c]$, the mean total number poisoned from the attack is

$$\frac{1}{\tau_c} \int_0^{\tau_c} I(\tau; \tau_a)\, d\tau_a. \tag{28}$$

5 Secondary Casualties, Product Tracing, and Product Recall

This section considers three interrelated issues: the possibility of secondary casualties from cross-contamination while milk is passing through equipment that was not cleaned after being emptied, the ability to trace milk back to various stages in the supply chain, and the amount of milk that needs to be recalled and discarded after the attack is detected.

Starting upstream, farm tanks at stage 1 are cleaned every 24 hr, and so a contaminated farm tank that had been emptied would be toxin-free before the next pickup. Hence, no secondary casualties should occur at stage 1. Trucks are cleaned once per day but make two deliveries per day. Approximately 30 gallons of milk would be left in an emptied 5,500-gallon container. Hence, with probability 0.5, a contaminated truck would make a second delivery of contaminated milk $\approx$ 8 hr after the first delivery, and the contamination level of the second delivery would be 0.5% as much as the first delivery. The probability that the second delivery would be piped into the same silo as the first delivery is approximately $\frac{\frac{\tau_c - 8}{\tau_c}}{N_3}$. Taken together, the mean number of secondary casualties from crosscontamination at stage 2 is equivalent to the mean number of casualties from a release that is 0.5% as large as the primary release, multiplied by $0.5\left(1 - \frac{\frac{\tau_c - 8}{\tau_c}}{N_3}\right)$.

As mentioned earlier, silos are cleaned at the end of each cycle, and so no secondary casualties occur at stage 3. The processing lines are also cleaned every 24 hr. Hence, on average, there will an additional 12 hr worth of milk flowing through the contaminated processing lines. It is difficult to estimate the secondary contamination level as milk is piped through the tainted processing lines.

Because of the potential for crosscontamination of milk while passing through tanks, trucks,

silos, and pipes before being packaged, as a practical matter, all of the milk in the processing facility's supply chain would probably be recalled and discarded at time τ, regardless of the tracing capabilities within the supply chain. Assuming that the system is in equilibrium at the time of the attack, the total amount of milk in the supply chain can be derived by setting the left side of Eqs. 2-9 to zero and computing $\sum_{i=1}^{8} X_i$, which gives

$$\lambda N_0 \sum_{i=1}^{8} \mu_i^{-1} = 4.83 \text{ million gallons}, \tag{29}$$

of which $\lambda N_0 \mu_8^{-1} = 2.24$ million gallons represent partially consumed containers that need to be recalled from consumers. In addition, λN_0 gallons of freshly produced milk need to be discarded for every day it takes to turn the supply chain back on. Better tracing should lead to a more rapid and effective investigation of the attack and to a faster recovery of the supply chain. Moving beyond the specific milk scenario considered here, if the contaminated food could not be traced back to the facility that processed it, then the nation's entire supply of the affected foodtype would conceivably be discarded (15); fortunately, facility tracing is in place in the dairy industry.

In a scenario in which there was no risk of crosscontamination (e.g., if the crosscontamination levels for milk were widely perceived as harmless, or a field of fresh produce was sprayed with a biological agent and the resulting produce was packaged in the field before distribution), then tracing could lead to a significant reduction in product recall. For our dairy supply chain, let us assume the attack is identified to have originated at a particular entity at stage i, for $i = 1, 2, 3$. Furthermore, suppose all milk can be traced back to stage j, i.e., for each container of packaged milk, we have knowledge of which of the N_k entities it passed through for stages $k = j, \ldots, 8$ but have no knowledge of which of the N_k entities it passed through for stages $0, \ldots, j-1$. Because there is no need to discard milk at stages $k < i$ or at the $N_i - 1$ entities at stage i where the introduction did not take place, and because of the mixing of contaminated and uncontaminated milk that occurs in the upstream portion of the supply chain, it follows that the amount of milk that

needs to be discarded is

$$\begin{cases} \lambda N_0 \left(\frac{\mu_i^{-1}}{N_i} + \sum_{k=i+1}^{8} \mu_k^{-1} \right) & \text{if} \quad j > i; \\ \lambda N_0 \left(\frac{\mu_i^{-1}}{N_i} + \sum_{k=i+1}^{8} \frac{\mu_k^{-1}}{N_{\min\{k,3\}}} \right) & \text{if} \quad j \leq i. \end{cases} \tag{30}$$

As an illustration, for the values in Table 4, we use Eq. 30 to compute the amount of milk discarded for various release locations and tracing capabilities (Table 6), hypothetically assuming no crosscontamination.

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