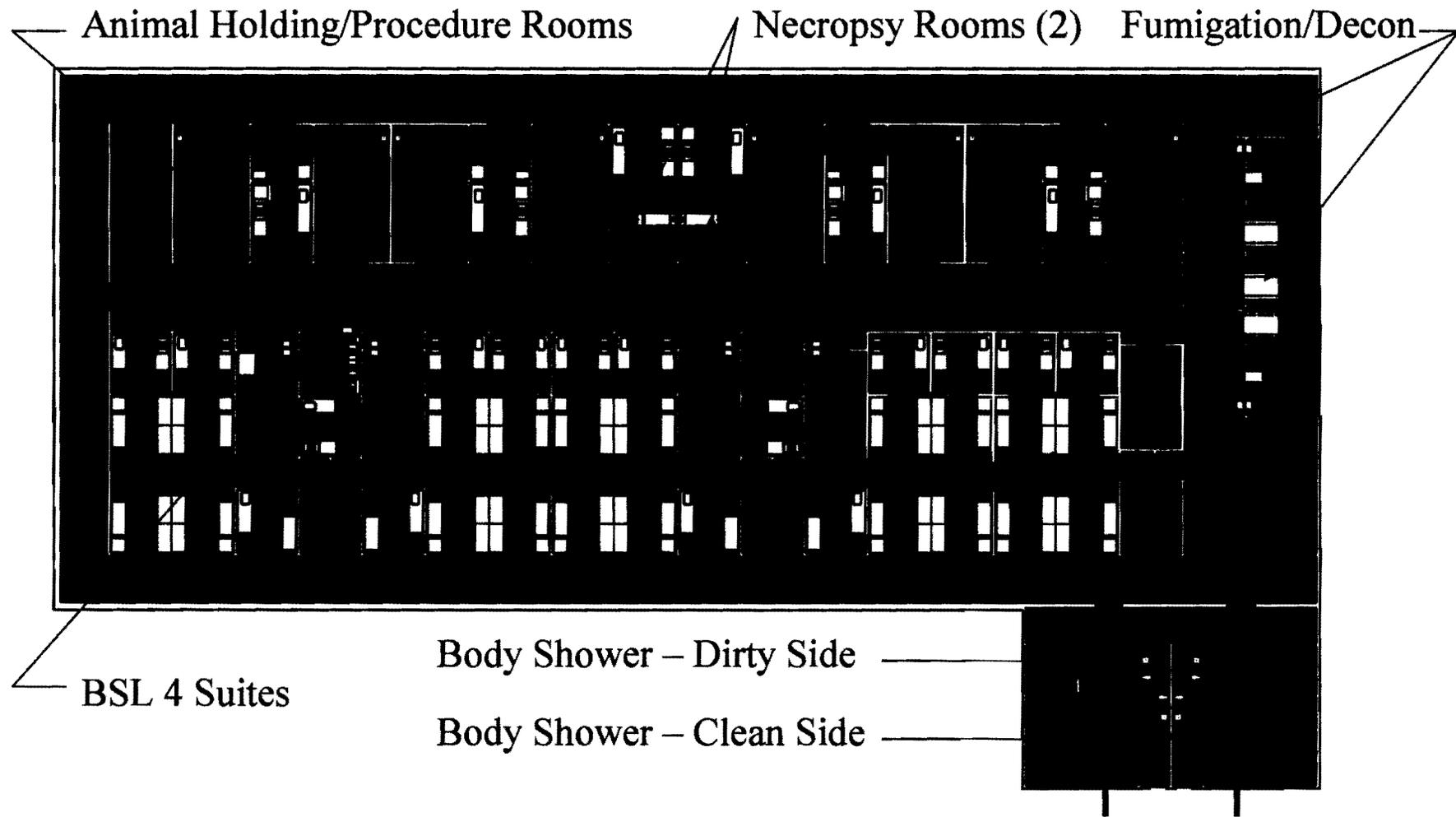


Fictional Pharma BSL4



The previous slide shows 5 separate suites which you can easily identify by the 5 chemical decon showers. Your pharmaceutical BSL4 facility may use a couple of the suites for R&D using live virus and 2-3 suites for the high throughput demands of drug trials.

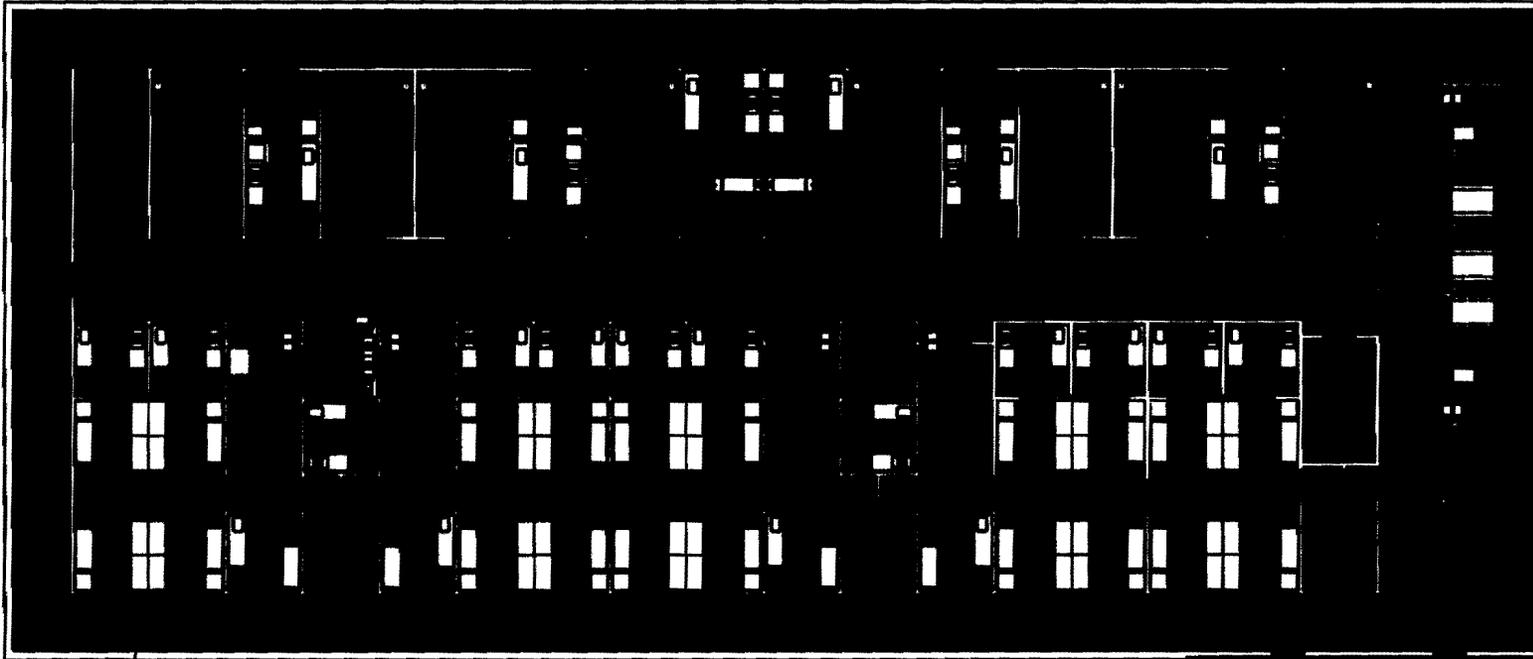
By high throughput I mean – each trial may need 4 groups of 10 animals. One group would be a control group (no vaccination), one would receive only the media, and the other two groups may be receiving different dosages of the drug. They would then all be exposed to the pathogen (via aerosol). Consequently, you can see the huge need for lots of animal holding rooms.

If a pharmaceutical company did not have this much space they would have a huge “bottleneck” in the trials stage – this is where the drug would really prove itself.

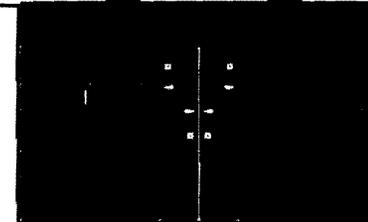
Presently there are no labs like this because (a) there really isn't much money in vaccine research for the masses (the unfortunate west Africans usually affected don't hold many shares at Novartis...) and (b) the military doesn't spend this kind of money on biology – cruise missiles cost too much.....

Recently the US NIH is releasing funding for this kind of lab – our legislature is granting the money due to 9/11 and the Anthrax mailings.

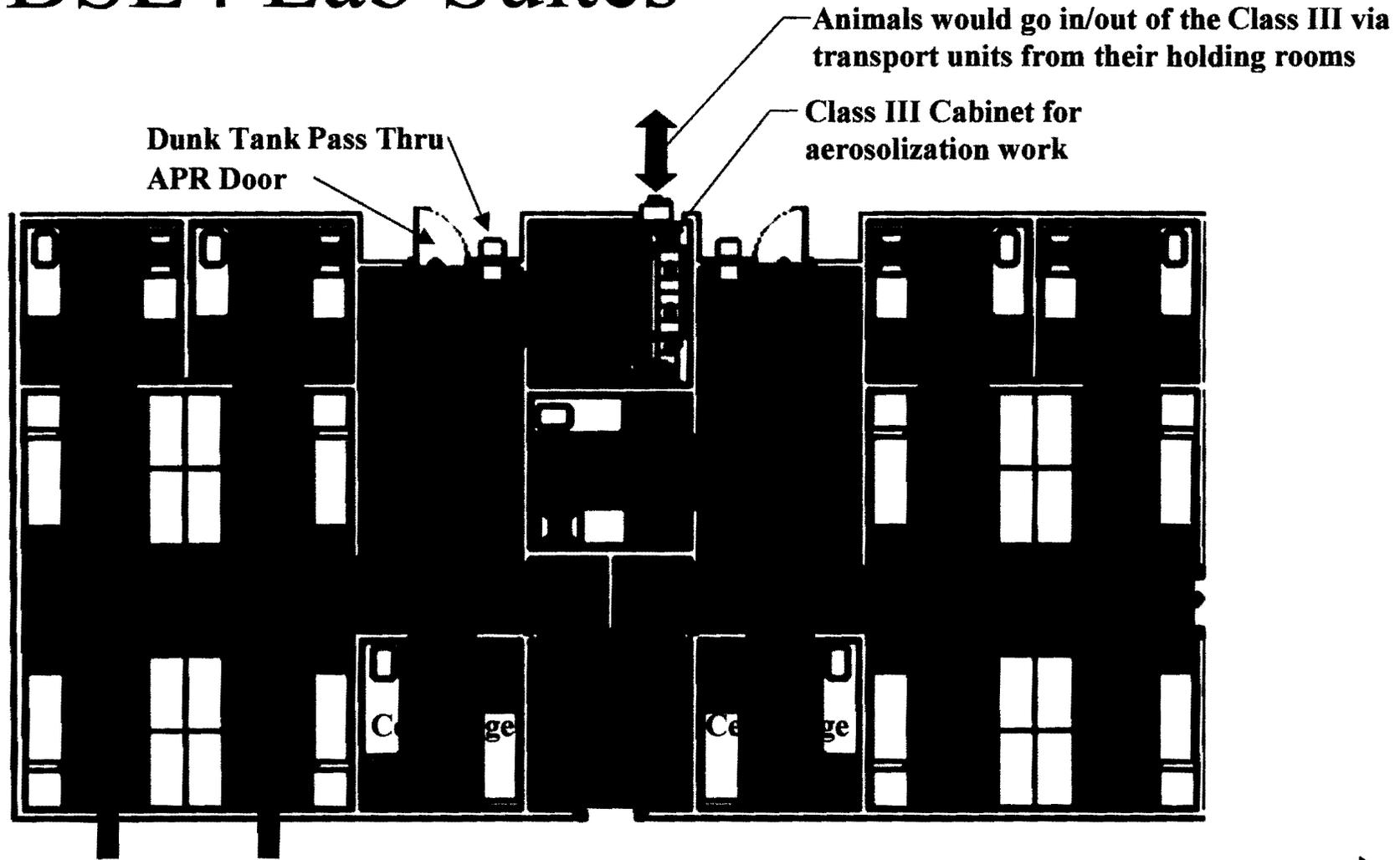
BSL4/3-AG Lab Suites



Next slide is plan enlargement of dashed area.
Orange spaces versus red spaces is simply indicating flexibility of rooms that may be “hot” versus “deconned” or simply not working on live virus. The entire space (except perimeter corridor) could ultimately be all RED.



BSL4 Lab Suites



A view into this lab (if I had drawn a window) would be a lot like looking in the lab at Winnipeg

Body shower down the corridor is shared between all the BSL4 suites

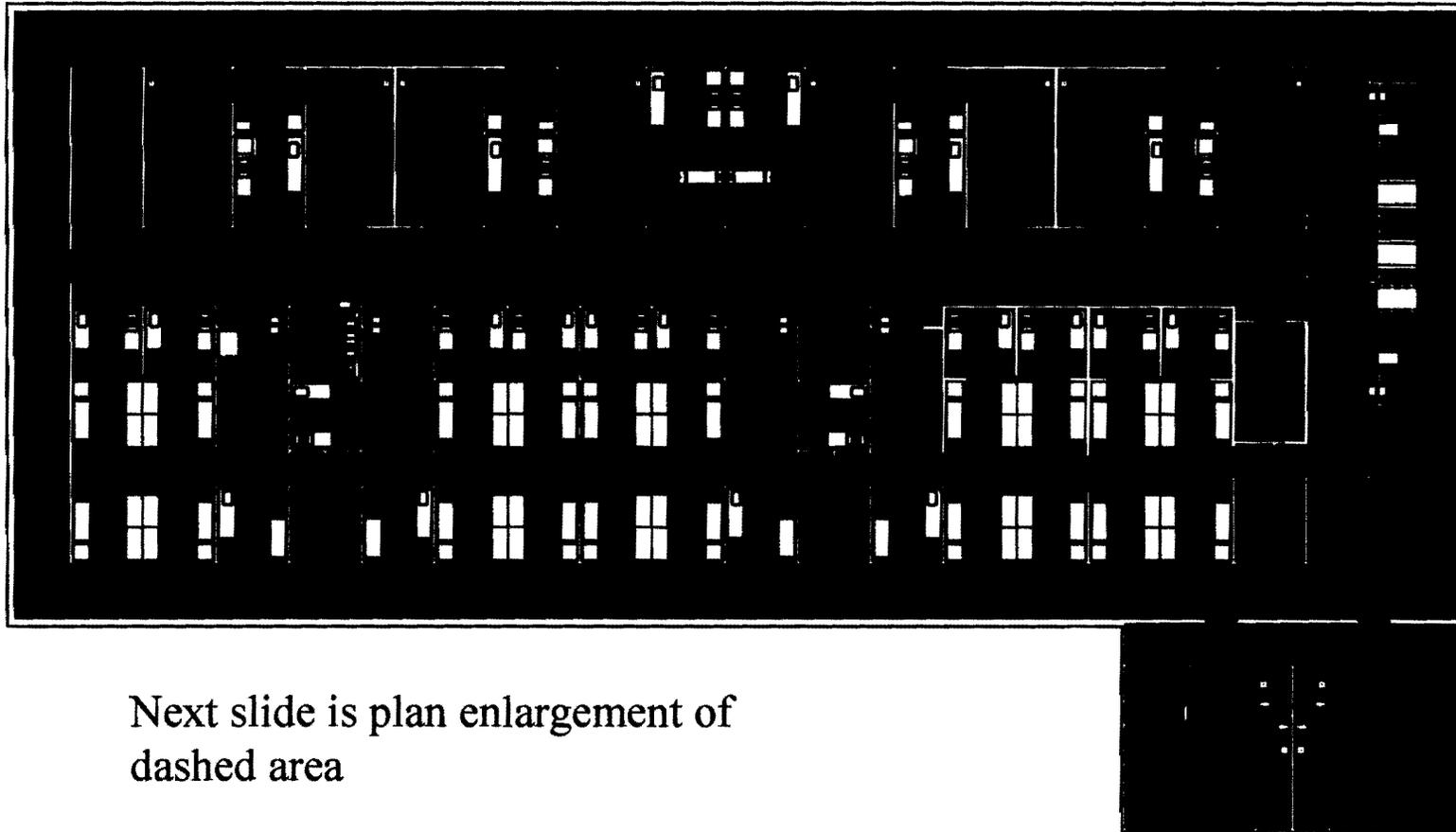




These are some images of the Winnipeg Lab. It's a little hard to grasp the openness, but notice the windows between the rows of workbenches. The image above is looking through two windows – one onto an outer corridor and the next window is to the exterior.



BSL4/3-AG Animal



Next slide is plan enlargement of
dashed area

BSL4 Animal Holding

Rooms can be isolated from one another with air-pressure resistant doors, decontaminated (with paraformaldehyde gas), then “clean” animals can be brought into rooms through airlock for next trial.

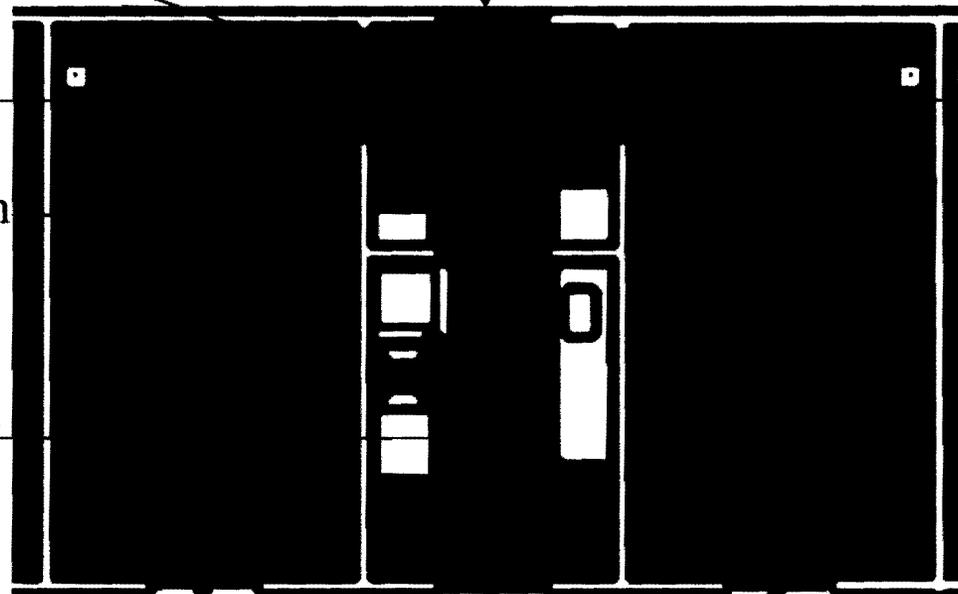
.....high throughput

APR Door

BSL Ante Room

BSL4 Holding Room

Procedure Room—~~for~~
vaccinations, etc.



BSL4 Holding Room

- 24 Group 3 NHP
- >240 Rodent Boxes @
3 -4 per Box= 960

P31

Chapter Three: 8am (pps31-41)

Toni & Stanley watch the robbery on video

KF: First off, Stanley does something thoughtful for Toni, maybe just asks her if she's okay; making her think he cares for her. Asks if she's slept? Maybe she recalls more of the earlier phone call.

KF: Bring in Susan Mackintosh here, so that we care when she's coshed later. Also Toni's secretary, so that we know someone admires her and likes her.

AZ: This is all good information, but it feels a bit flat because there's little personal going on between Toni and Stanley

- With her starting to like him, could she be hopeful that this episode might bring them closer together?
- Does his physical closeness alongside her at the computer affect her?
- Is she eager for a word of praise that she's made this discovery?
- Does she admire him in the clothes that she hasn't seen before?
- In terms of dramatic action, it would be good for her to have a goal vis-à-vis Stanley that she does or does not attain.

EF: We miss Stanley's PoV. How does he feel about Toni?

LG: Toni didn't grab me, she wasn't that dynamic and I didn't feel a real connection with her. I would have liked to know her better, even where her feelings for Stanley were concerned.

KF: Odette phones. She has an interest in Madoba-2. Is Toni sure Michael was working alone? There is a terrorist group that has been trying to buy an Ebola-type virus.

IT: 1.8 Mark Ross here, and several times on forthcoming pages. I haven't noted them all

SE: Rabbits, particularly the type used in containment laboratories, don't usually bite.

I don't quite follow the logic of Michael exchanging rabbits including the effort to infect the replacement, but it is also obvious that Michael is not all together. Anyhow.... It would be difficult to impossible to get a rabbit out of the lab because of the Chemical shower routine. He would have to put it into some sort of container so the rabbit would not die from the Chemical exposure. Since Michael is as illogical as he sounds – I suppose he could unzip his suit, put the rabbit in a "papoose" and carry it out. Opening your suit in a BSL4 lab is not a dangerous as it sounds, because most live agents are either containerized, opened in a BSC or deconned immediately (spray solution, etc.) as part of basic safety protocol. If Michael (mistakenly) thought the rabbit was "clean" because it was not yet part of an exposure study, then he would only have to be mildly insane to put it into his suit. If the rabbit had been exposed (when Michael didn't know about it), then Michael would be exposed to Madoba in his suit. Michael would also not have to expose the poor replacement bunny. This scenario would account for the exposure through breathing (in the suit) in lieu of the "Monty Python Killer Rabbit". There is the issue of exposing the shower, locker room etc., so maybe you need a little UV exposure? Blind bunny?

...sorry, I am an architect- not a writer, I feel like it would be easier to draw a picture!

GK:

- Under procedures that would have been in place in our biocontainment facility, if something like this had happened, we would have notified the boss immediately. Why would Toni not be instantly on the phone with the owner, if she had no qualms about calling all other types of employees during the early morning hours ?"
- "Someone would have also brought the rabbit back to the lab as well. If the rabbit was dead, one would assume that it too had experienced a hemorrhagic episode and would be easily identified as having been infected.

8 a.m.

feeling how?

Toni Gallo waited in the Great Hall. It was like the nave of a church, with tall windows and an open hammer-beam roof, except that there was a modern oval reception desk with high counters stuck in the middle of the floor. A uniformed security guard sat inside the oval.

She had phoned Stanley Oxenford, the chairman and majority owner of Oxenford Medical, at home a few minutes before six o'clock this morning to tell him that a lab assistant had died of a hemorrhagic fever, probably caused by Madoba-2.

"Who?"

"~~Mark~~ Ross."

Does she feel in any way responsible? Does she imagine she might in some way have prevented this?

"I know him. Nice kid. He's been with us for years. Damn." He spoke with the trace of an Edinburgh accent. *- Is this an accent one can describe?*

"And an experienced technician, not likely to make a careless mistake."

Stanley let his anger show. "So how the hell did it happen?"

"I found a white rabbit in his garden shed, dead. I think he brought home a laboratory animal and it bit him."

"I doubt it," Stanley said crisply. Early though it was, his brain ~~seemed~~ fired up like the V8 engine in his sports car. "More likely he cut himself with a contaminated knife. Even experienced people get careless. The rabbit could be a normal pet that died of starvation

I assume we're in her POV.

P32

GK: Good response from the owner - these would have been accurate.

while he was ill.”

Toni hated it when Stanley assumed he knew better than the person on the scene. Trying to keep the irritation out of her voice, she said: “The rabbit was in an improvised biosafety cabinet.”

“I still doubt it,” he said calmly. “There’s a two-person rule in BSL4: Mark can’t have been working alone. Even if his buddy wasn’t looking, there are television cameras in every room—he couldn’t have stolen an animal without being seen on the monitors. Then he had to pass several security guards on his way out—they would have noticed if he were carrying a rabbit. Finally, the scientists working in the lab the following morning would have realised immediately that an animal was missing. They might not be able to tell the difference between one rabbit and another, but they certainly know how many there are in the experiment.”

“I know what security is in place, I’m in charge of it. And I’m telling you that no security system is perfect.”

“You’re right.”

~~She hated how quickly he backed down, too. It gave her no chance to gloat.~~

He went on. “Have you checked the video footage of the last time Mark was in BSL4?”

“I was about to do that.”

“I’ll be there at eight. Have some answers for me then, please.”

“No problem.”

Before Stanley got there, Toni’s assistant arrived. Chris Carter was a pretty girl of twenty-five, with a boyish haircut and a pierced eyebrow. “I’m so sorry about Mark,” she

said. "I saw it on the news."

"Thanks for coming in early," Toni said. "We've got a lot to do. On your desk you'll find faxed pages from Mark's address book. Call every number and find out whether anyone has seen him since he left here on Sunday the eighth of December."

"Eighth of December, right."

"Mark belonged to a group called Animals Are Free. Track them down and tell them that any of their members who saw Mark in that period may be in danger. They won't give us their membership list, but they should contact them all urgently, by phone today, to warn them."

"Got it."

"One more thing. Chris...was Mark gay?"

"Not actively."

"You're sure?"

"Harbourmouth is a small town. There are two gay pubs, one club, a couple of restaurants, a church...I know all those places and I've never seen him in any of them."

~~"Okay. I hope you don't mind my assuming that you would know, just because, you know..."~~

"It's all right." Chris smiled and touched Toni's arm. "You'll have to work a lot ~~harder than that to offend me.~~"

~~"Thanks."~~

As Chris left, Stanley parked his dark-blue Ferrari outside the main entrance. He was a tall man of sixty with thick grey hair and blue eyes. He did not look the part of a scientist—no bald dome, no stoop, no spectacles. Toni thought he was more like ^{CM} ~~the kind of~~ actor who

plays the general in a movie about the Second World War. He wore a grey tweed suit with a waistcoat, a pale blue shirt and—out of respect for the death of Mark Ross, Toni presumed—a black knitted tie.

“Good morning,” he said. “Have you found out how this happened?”

“Yes.”

“And...?”

“I was right. You were wrong. It was the rabbit.”

Despite the tragic circumstances, he looked amused. He liked it when she got feisty.

“How do you know?” he said mildly.

“May I show you the video footage?”

“Of course.”

They walked along a wide corridor with oak linenfold panelling and turned down a side passage to the Central Monitoring Station, normally just called the control room. This was the security centre of the Kremlin. It had once been a billiards room, but the windows had been bricked up for security, and the ceiling had been lowered to create a hiding place for a snake’s nest of cabling. One wall was a bank of television monitors showing key areas of the site, including every room within BSL4. On a long desk were work stations with touch screens for monitoring alarms and intercoms and accessing the central security computer.

When Toni walked in with Stanley, the room was clean and tidy: no dirty coffee cups, old newspapers, half-empty Tupperware lunch boxes, broken biros[?]. A guard in a neat uniform sat at the desk. She glanced into the adjacent equipment room, once the gun room, now full of support devices, including the central processing unit for the phone system. It was brightly lit. Each of a thousand cables was clearly labelled with nonremovable, easy-to-read tags, to

p35

EF: "Stanley was angry". He was amused on P34.

IT: Last para: we, the reader, know about Kit's misdemeanours, so it seems a bit odd to have this background information again so soon.

minimise down time in case of technical failure. She was pleased. Everything was as she liked to see it.

Stanley made no comment. He took it for granted that she ran a tight ship. Which was fine with her.

They sat side by side in front of a monitor, and she tapped at the keyboard to bring up the pictures she wanted him to see. The computer's vast memory stored images for twenty-eight days before erasing them. She was intimately familiar with the program and navigated around it with ease.

Stanley was angry, she could tell, but did not yet know who to be angry with. However, she was the prime candidate. Security was her job and security had been breached.

When Toni first met Stanley, a year ago, she had been at the lowest point of her entire life. She had been fired from a job she loved. She was pretending to be a freelance security consultant, but she had no clients. Her partner of eight years had left her. Her mother had started to become senile and could no longer look after herself. Toni felt like Job after he had been forsaken by God.

*Shouldn't we know what this drug
and what it can do? huh. ✓*

26

Stanley had hired her on a short-term contract. He had invented a drug so valuable that he feared he might be the target of an industrial espionage operation. She had checked the premises for listening devices. Stanley's office had not been bugged—though the office of his head of purchasing had, presumably by a supplier anxious to find out what his rivals were offering.

Next, Toni had looked for signs that key employees were living above their means. To her dismay, she had discovered that Stanley's son, Kit, was stealing from the company. A computer wizard who had devised the security system, Kit had also found a way to siphon off

*Summarise this even more, since we
already know it.*

a percentage from suppliers' invoices.

When she confronted Kit, he had told her that Stanley would never believe her, and would punish her for the allegation by making sure she never got hired by any business in the country. She had taken the warning seriously. It would have been a natural reaction, unjust but human. Kit had proposed a way of covering up his scam, and promised never to do it again if Toni would cooperate. She had been tempted. She could have solved the problem without risking the wrath of the only man in Scotland who had been willing to give her a job. She could even have excused the deception by telling herself she was saving Stanley the pain of knowing his son was a thief. But it would have been dishonest, and in the end she had levelled with Stanley.

It was the right decision. Her integrity had been rewarded. Stanley had fired Kit and offered Toni a full-time job. For that, she would always owe him cast-iron loyalty. She was fiercely determined to repay his trust.

And life had improved. Stanley quickly promoted her from Head of Security to Facilities Manager and gave her a raise. She bought a red Porsche.

When she mentioned, one day, that she had played squash for the national police team, Stanley challenged her to a game on the company court. She beat him, but only just, and they began to play every week. He was very fit, and had a longer reach, but she was twenty years younger, with hair-trigger reflexes. He took a game from her now and then, though in the end she usually won. And she got to know him better. He played a shrewd game, occasionally taking an unexpected risk that usually paid off. He was highly competitive by nature, but managed to be good-humoured about losing. Their relationship continued to be combative, but her quick mind was a match for his brain, and she enjoyed the

P37

KF: Notes from Winnipeg web site.

- The key pad is on a freestanding post, not let into the wall
- Scientists wear white lab coats
- Biohazards suits are bright blue with a soft hood and transparent faceplate
- Blue gloves, blue overalls, white shower caps
- Entrance has a big heavy door like a safe, opened by turning a four-spoked wheel like a ship's wheel
- Yellow air hoses
- Plastic drawer stacks

HEPA means High Efficiency Particulate Air filtration. It filters all particles known to cause disease, and particles 85 times smaller than that (?).

cut-and-thrust. On top of feeling grateful to him, and needing to justify his trust in her, she began to like him.

So her regret at having let him down was like a physical pain. All she could do to ease it was try to understand how Mark had done it and make sure it could never happen again.

On the monitor, she showed him Mark arriving at the main gate and presenting his pass. "The date and time are on the bottom of the screen," she said. "It was fourteen twenty-seven." She tapped the keyboard, and the car park camera showed a green Volkswagen Golf pulling into a space. A slight man of about thirty got out and took a duffle bag from the trunk. "Watch that bag," Toni told Stanley.

"Why?"

"There's a rabbit in it."

"How did he manage that?"

"I don't know for sure, but I guess it's tranquillised, and probably wrapped up tightly. Remember, he's been dealing with laboratory animals for years, he knows how to keep them calm."

The next shot showed Mark presenting his pass at reception. A pretty Pakistani woman of about forty came into the Great Hall. "~~Razia~~ ^{Monica} Ansari," said Stanley.

"Yes. She was his buddy." Because of the two-person rule, Michael had needed someone to be in BSL4 with him. Dr Ansari was a biochemist, and presumably she had wanted to do a couple of hours' work on Sunday afternoon.

They walked along the same corridor Toni and Stanley had taken, but went past the turning for the control room and continued to the end. The corridor was closed by an air-lock. Dr Ansari went through first. She swiped a plastic pass through a card reader, then pressed





GK: Unfortunately, there are no rabbit models for Ebola viruses or Ebola-like viruses. Rabbits would not normally be used for this. The only animal models that currently exist are monkeys and mice. The virus that is used for mice had to be specially adapted through serial passage in baby mice, then older mice. If you want this to be scientifically credible, you will somehow have to build into your novel that their scientists had spent quite some time developing a rabbit model for the virus. This can also be part of the demonstration that this biotech company was very good at what they do - novel lethal rabbit model in addition to the anti-viral drug

P38

SE: Rabbits would not be housed in biosafety cabinets. They would be housed in conventional rabbit racks. The rack would be kept in a flexible isolator with HEPA filters. See image.

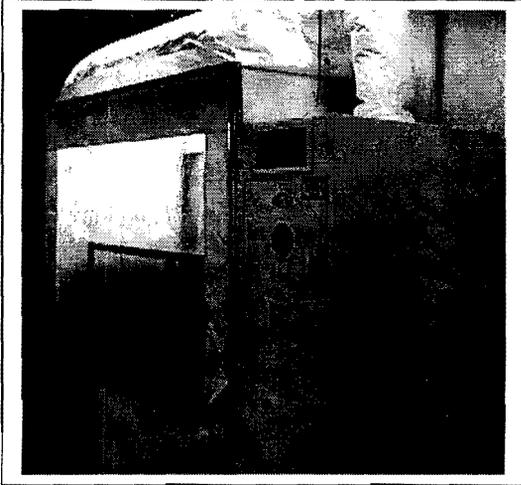
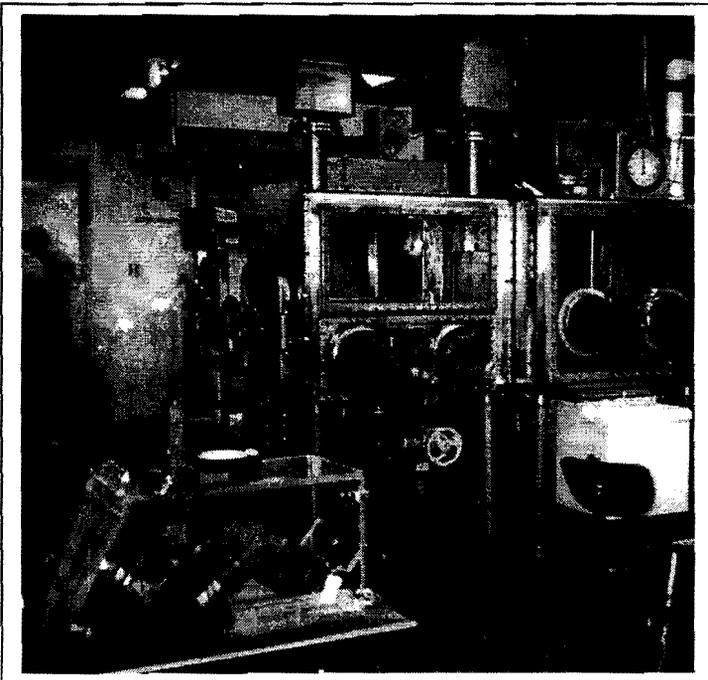


Image of soft-sided isolator with HEPA filters and fan motor assembly. This image just has a stainless steel cart in it, which is also used to stow animal cages (mice, rabbits, etc.)

The aerosol would not be delivered into the animal cage. The animal(s) would be transported to a **Class III** biological safety cabinet (aka – Gloveboxes) and the agent would be aerosolized into the cabinet. After the exposure volume/time is complete – the cabinet is evacuated and the animal(s) are removed through a sealed transport device to minimize gross contamination the room. Sometimes a device is used so only the mouth/nose of the animal is exposed – this reduces having fugitive live agent (virus) in the animals fur.



Class III cabinet at USAMRIID (not active).

Note the plexi-glass contraption on the left is a little “device” to hold primates

Cameras are often installed in the Class III (Glovebox) for a number of reasons, including training, monitoring and bio-assurity. These are very custom devices and can also be fitted with refrigerators and freezers to store material.

the forefinger of her left hand to a small screen. There was a pause while the computer checked that her fingerprint matched the information on the microchip embedded in the smart card. This ensured that lost or stolen cards could not be used by unauthorised persons. While she waited, she glanced up at the television camera and gave a mock salute. Then the door opened and she stepped into the airlock. Michael followed the same routine.

Another camera showed them briefly passing through a small lobby and entering separate men's and women's changing rooms. "This is when he took the rabbit out of the bag," Toni said. "If his buddy that day had been a man, the plan wouldn't have worked. But he had Dr Ansari, and of course there are no cameras in the changing rooms."

"But damn it, you *can't* put security cameras in changing rooms!" Stanley said. "No one would work here!"

"Absolutely," said Toni. "We'll have to think of something else. Watch this."

The next shot came from a camera inside the BSL4 laboratory. It showed a line of biosafety cabinets containing rabbits. Toni froze the picture. "What are you doing in this lab, exactly?"

"Our new drug is effective against many viruses, but not all. In this experiment it was being tested against Madoba-2, a variant of the Ebola virus that causes a lethal hemorrhagic fever in both rabbits and humans. Two groups of rabbits were subjected to the virus, introduced into their cages in aerosol form. One group has been injected with the drug."

"What did you find?"

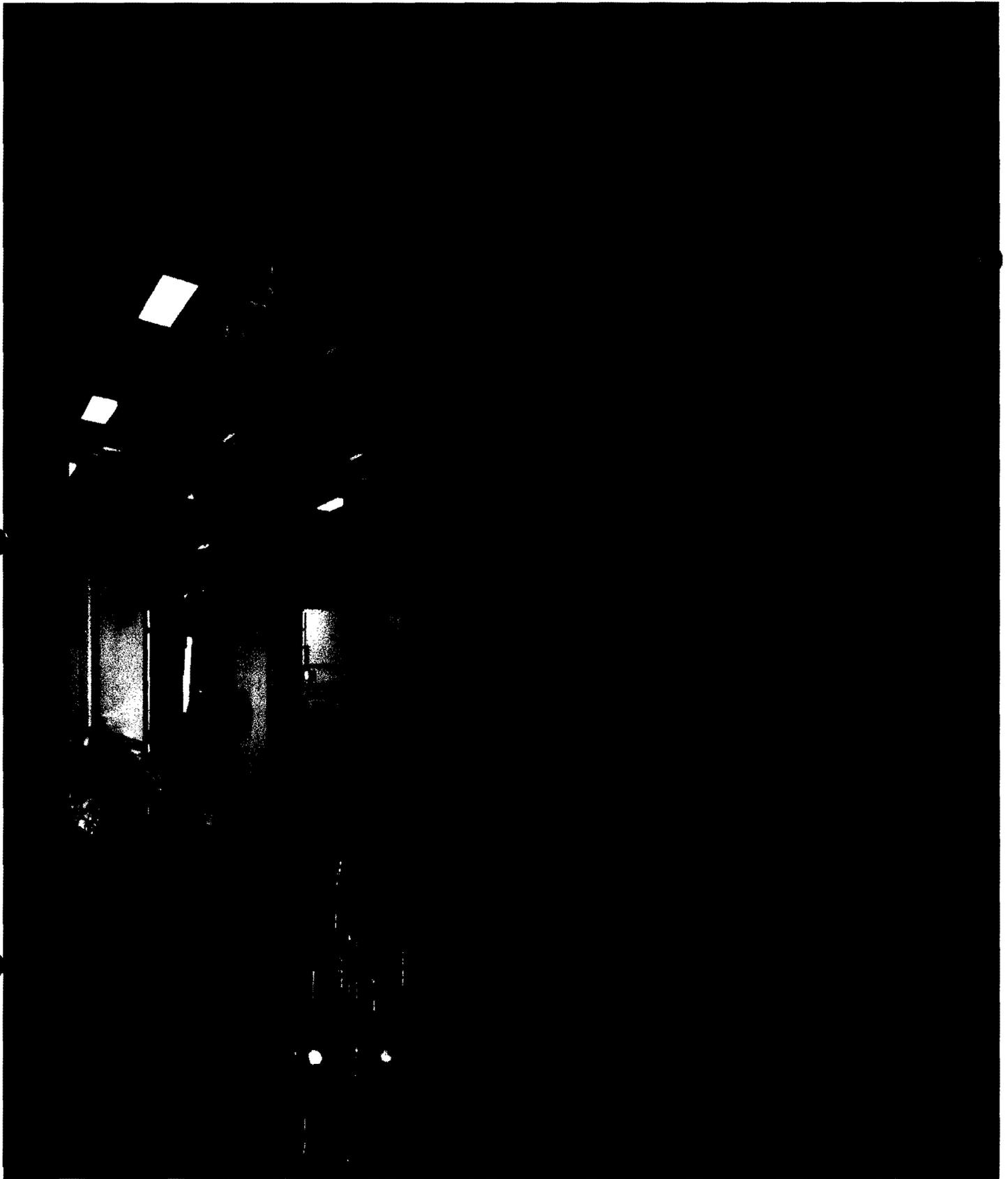
"The drug doesn't work against Madoba-2 in rabbits. So it probably won't work in humans, either."

"But sixteen days ago, you didn't know that."



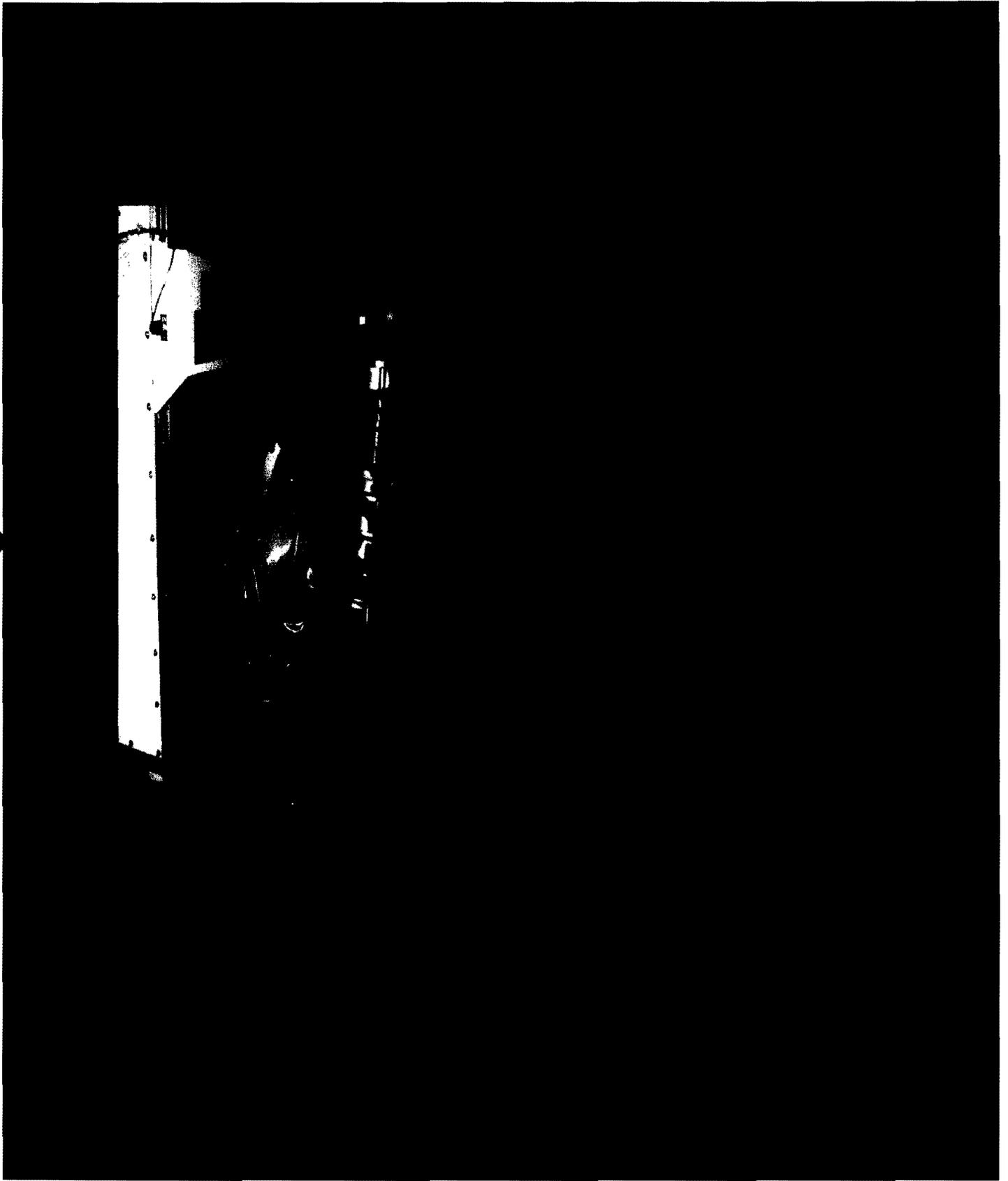
US Army Medical Research Institute for
Infectious Diseases, (USAMRIID) Ft. Detrick
Maryland





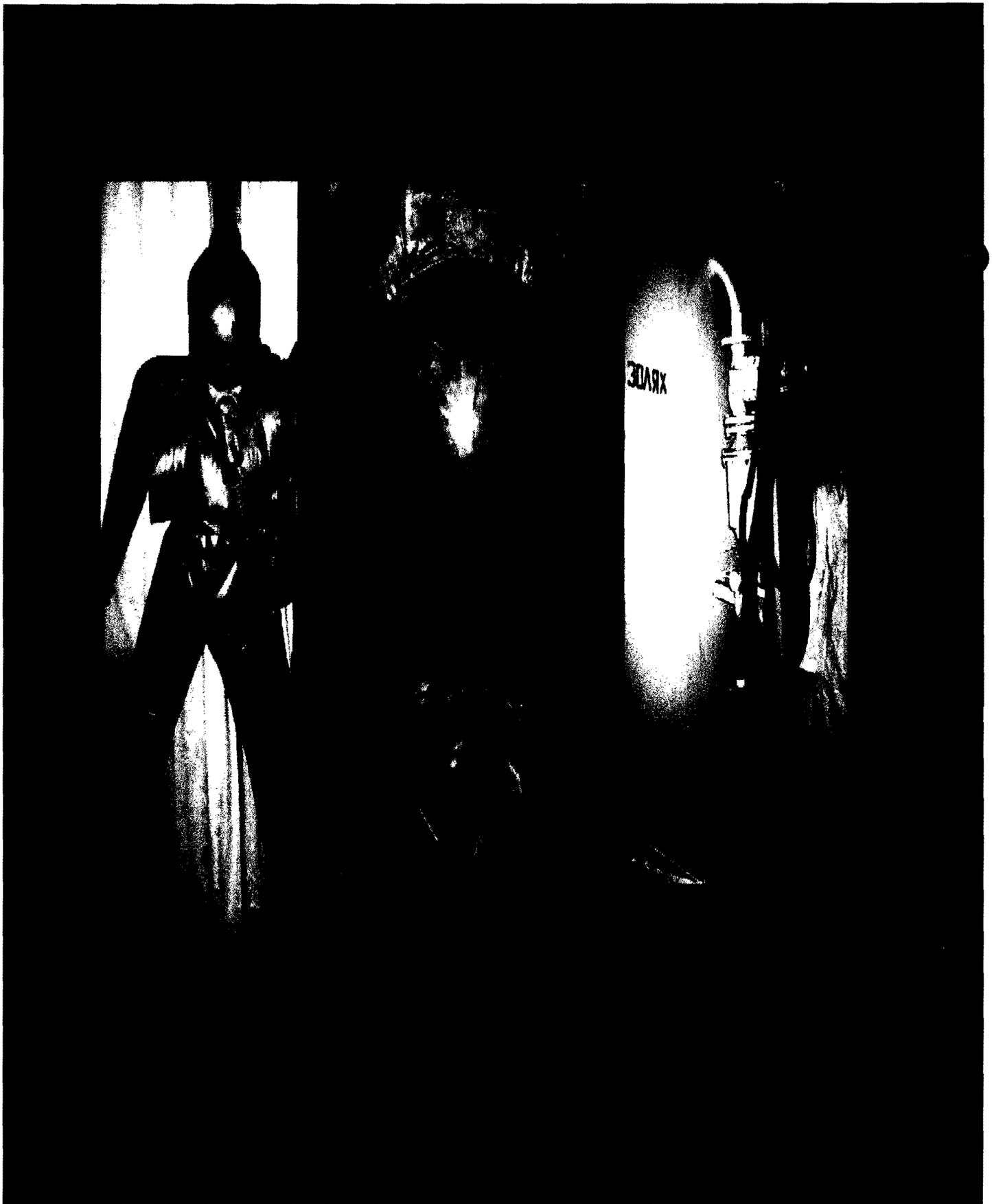
Canadian Science Centre for Human and
Animal Health,
Winnipeg, Manitoba





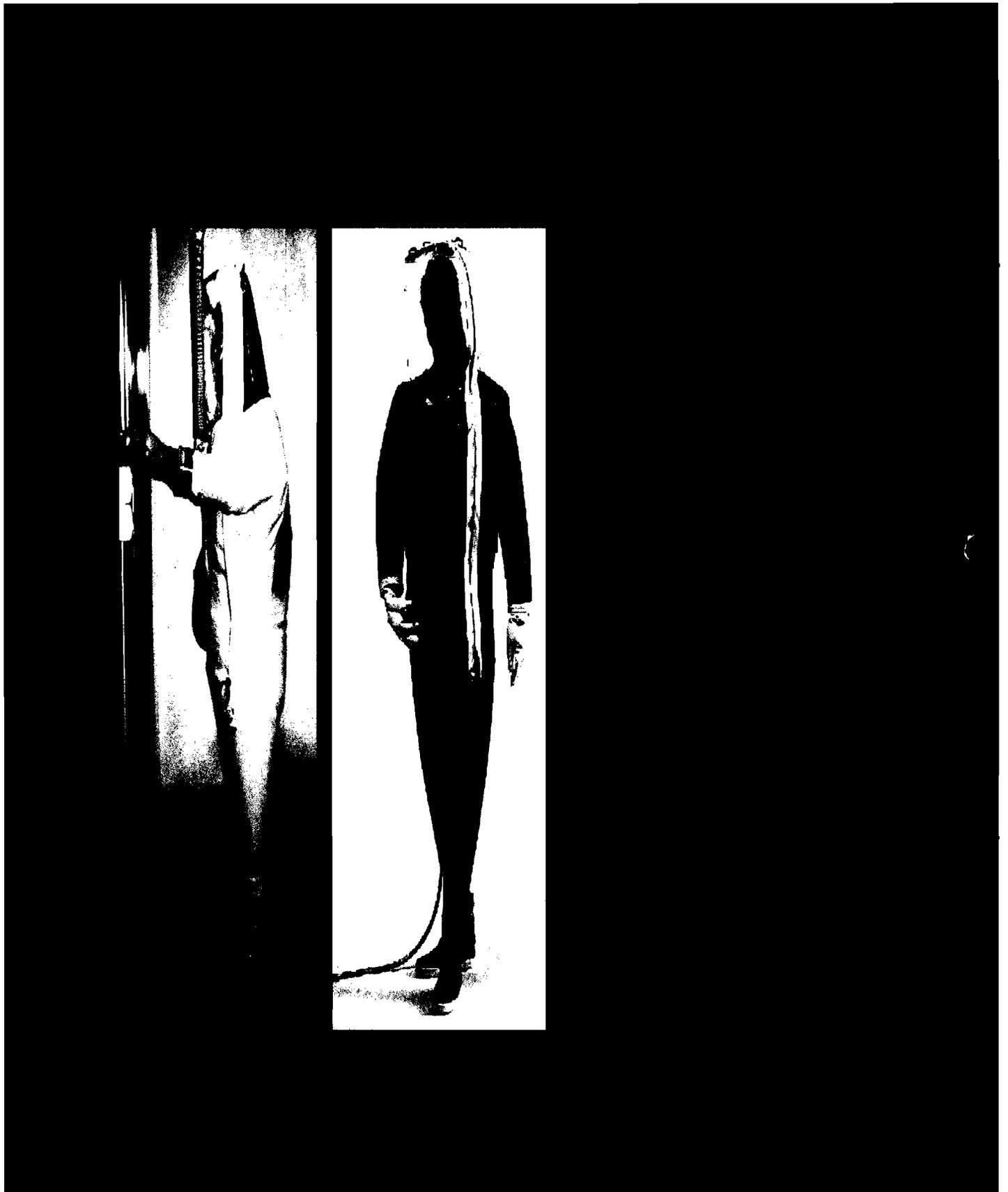
Canadian Science Centre for Human and
Animal Health,
Winnipeg, Manitoba





VECTOR Laboratories,
Novosibirsk, Russia





Foundation Merieux – P4, Lyon, France



p39

GK: The actual act of aerosol challenge of animals involves placing the animals into a specialized aerosol hood line. This type of line is air-tight and the animals are generally exposed either to whole body aerosol, or to a head only aerosol. For the purposes here, you may want to say something like "the rabbits were subjected to the virus in a specialized aerosol generation cabinet, exposing their heads only to the microscopic mist of lethal virus.

“Correct.”

“In that case, I think I understand what Mark was trying to do.” She touched the keyboard to unfreeze the picture. A figure in a light blue space suit stepped into shot. “This is Mark. He changed faster than Dr Ansari, so at the moment he’s in there alone.”

“It shouldn’t happen, but it does,” Stanley said. “The two-person rule is observed, but not minute by minute. Damn.”

Mark went up to a biosafety cabinet. His back was to the camera and, for a few moments, his body shielded the cabinet. Then he stepped away and dropped a towel on a bench.

“Notice anything?” Toni said.

“No.”

“Nor did the security guards who were watching the monitors. But look again.” She went back a couple of minutes and froze the frame just as Mark stepped into shot. “One rabbit in the cabinet.”

“I see.”

“Look harder at Mark. He’s got something under his arm.”

“Yes—wrapped in a towel.”

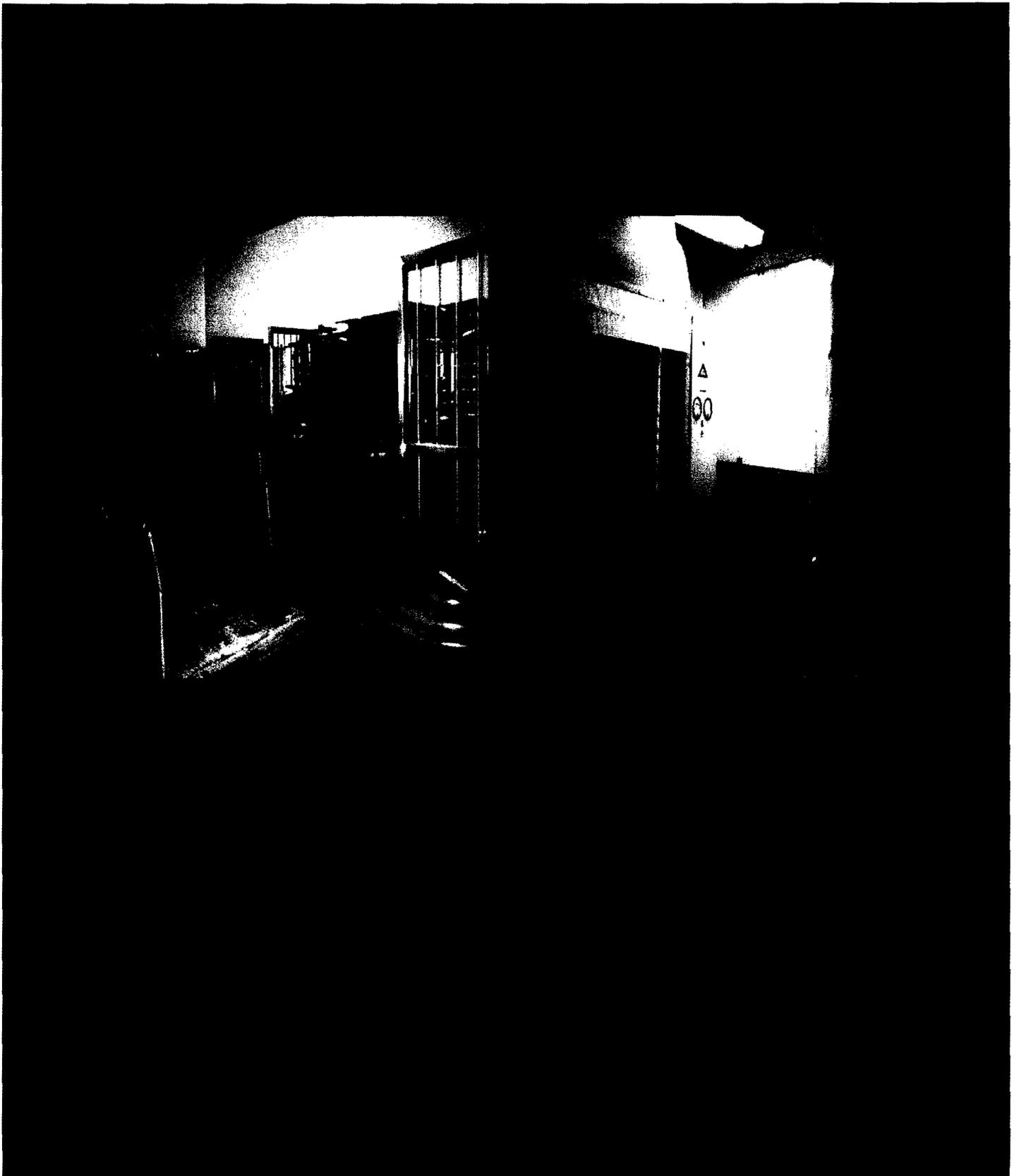
She ran the footage forward, stopping again as Mark stepped away from the cabinet.

“How many rabbits?”

“Two, damn it.”

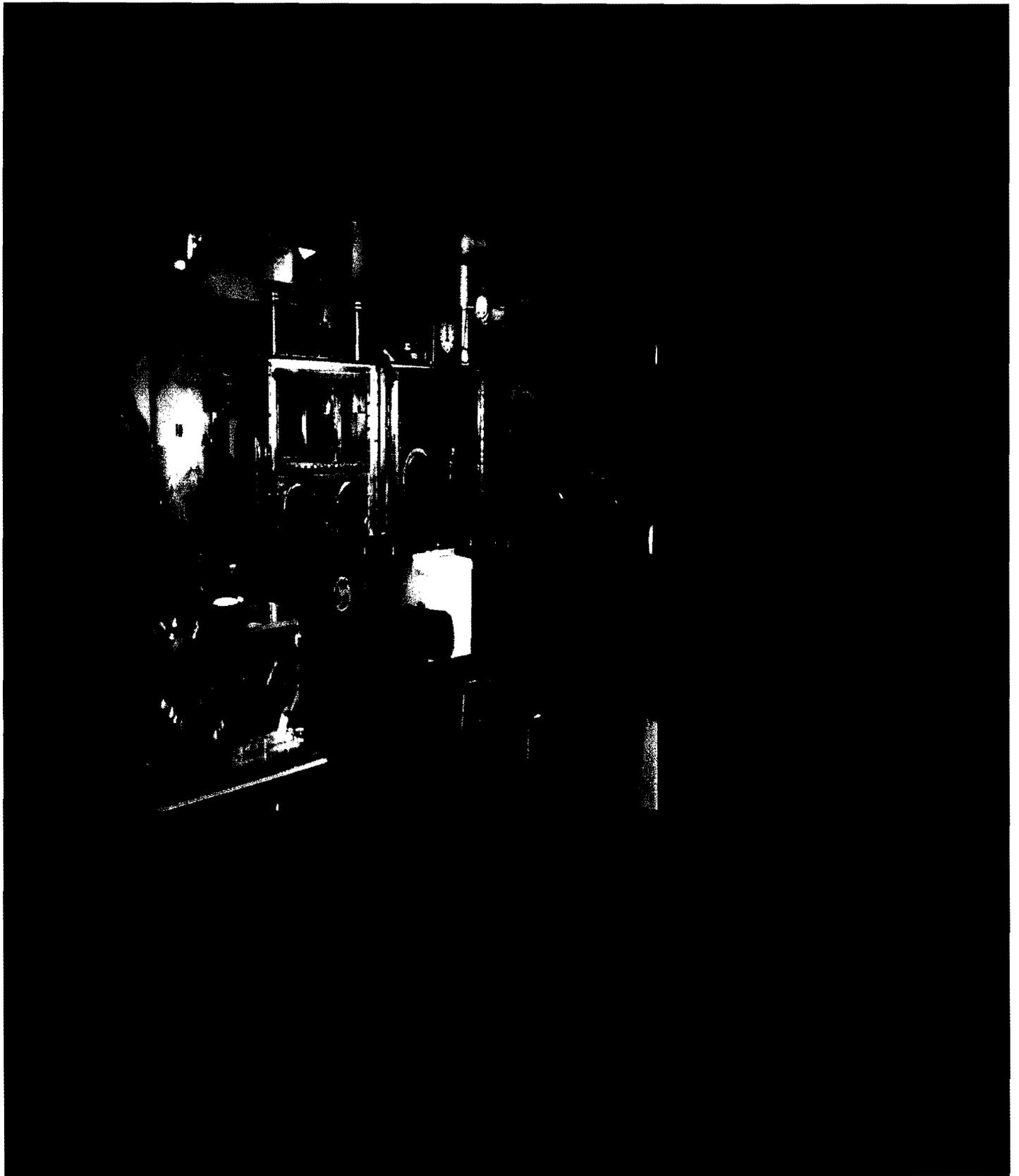
She showed the next few seconds. “And Mark drops a light blue towel on the bench.”

Stanley frowned. “We want to know how he got a rabbit *out of* the lab. You’ve shown him bringing one in!”

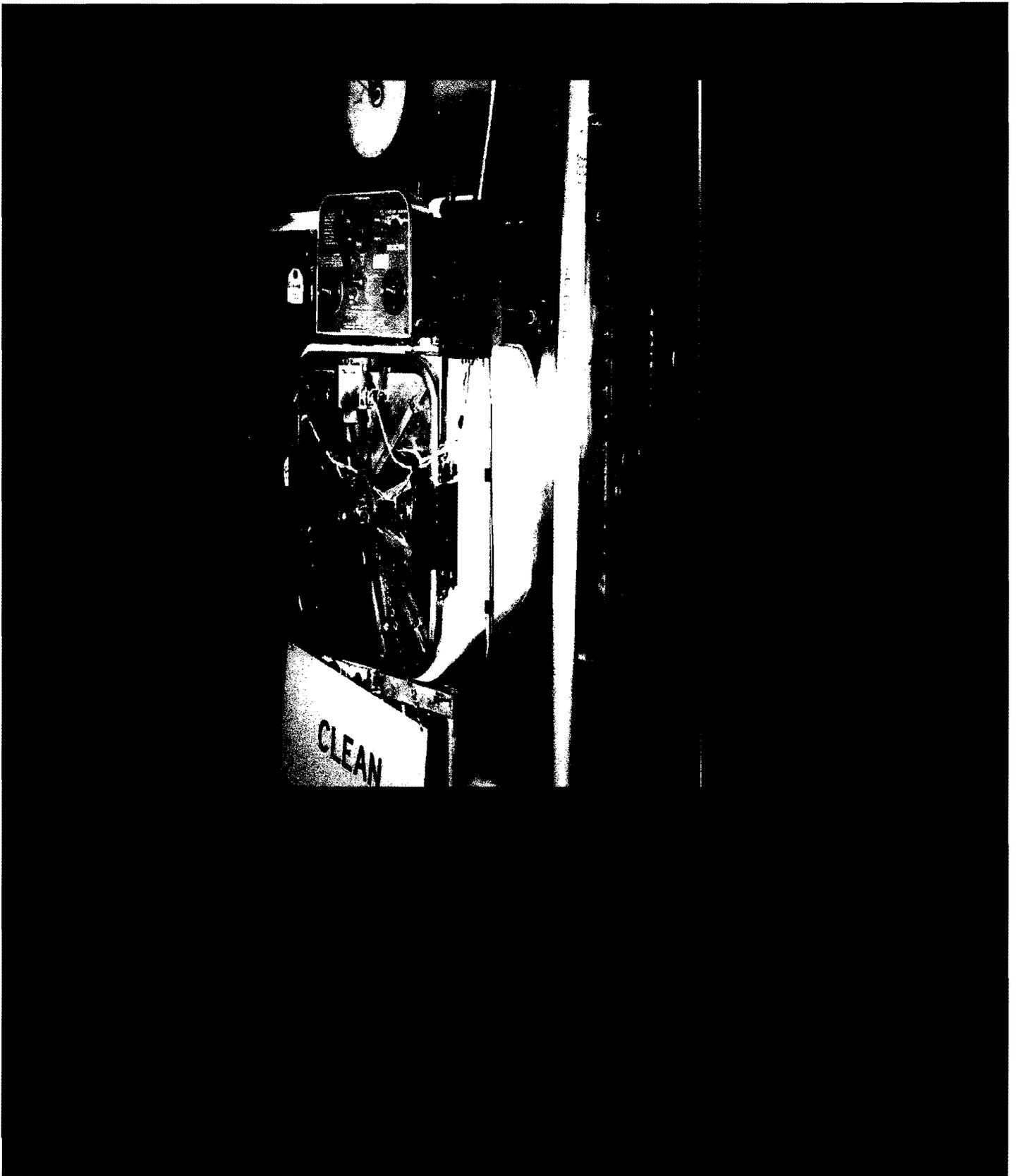


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Maryland



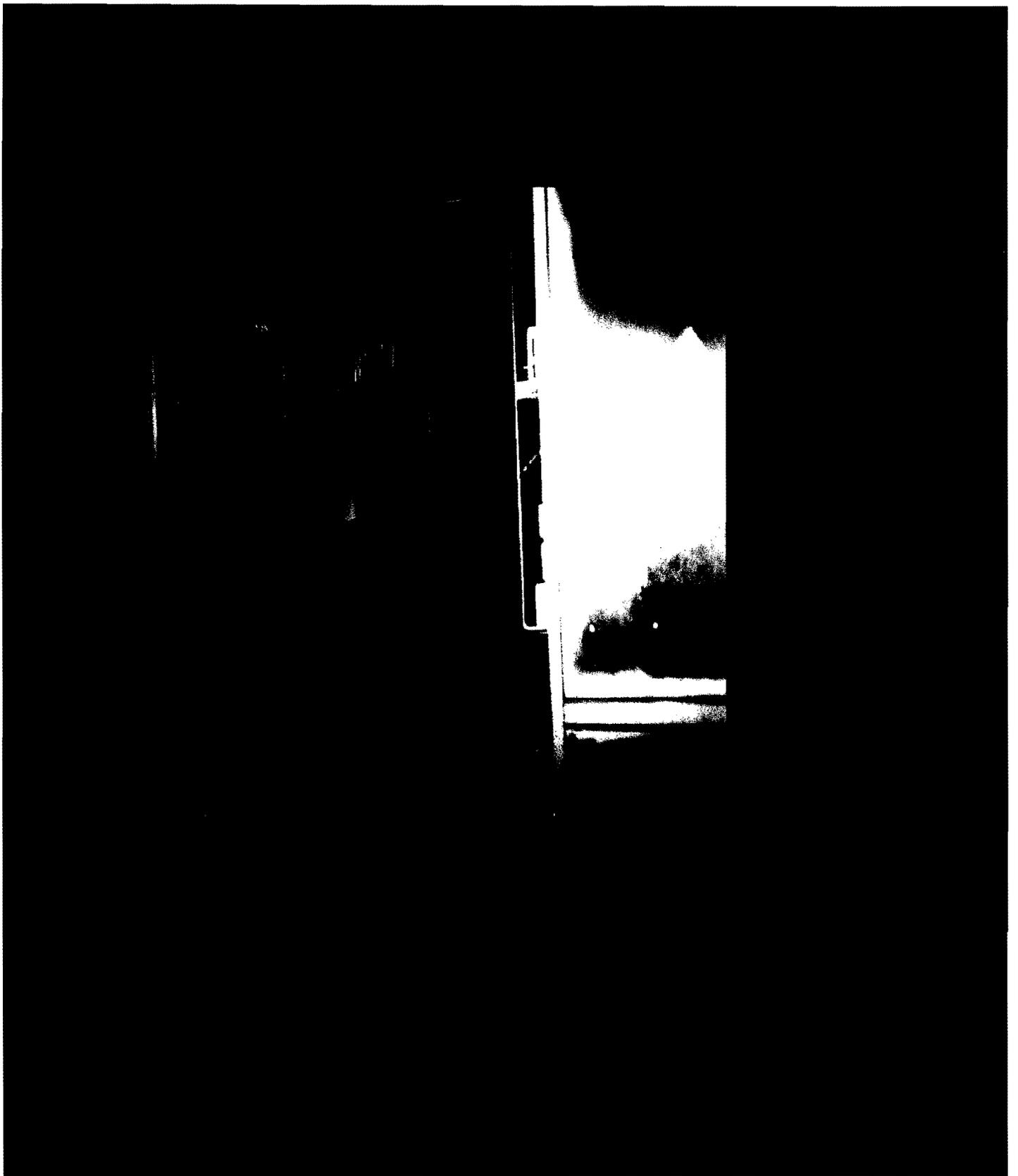


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Maryland



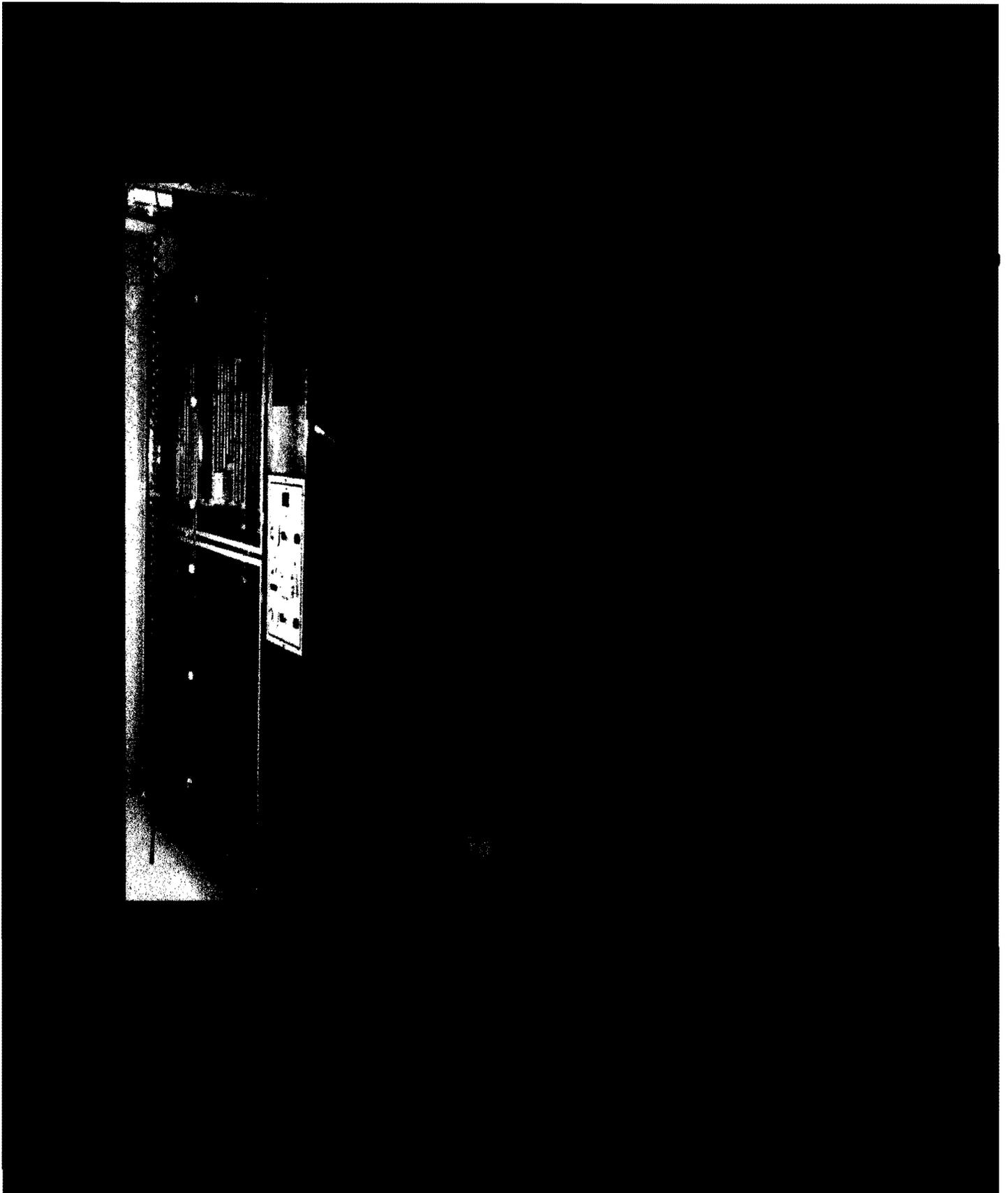
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P40

BF: Why does he take a rabbit in if he loves animals? KF: More discussion of this by Stanley and Toni. He must have developed an affection for a particular rabbit. (Named it, too.)

EF: I'm not clear why he nicked the anti-viral. I'm getting confused between the virus and the anti-viral.

SE: If macaque monkeys are used then it would be rare to have beagles in the BSL4. Typically vaccines are tested on rodents, rabbits and non-human primates (macaques, baboons, etc.). Dogs are usually used for toxicology studies that are not in containment. Tox studies are done to see if the drug or its delivery compound have a negative (toxic) reaction. I'm not exactly a dog lover.....but, puppies?

GK: I do not know of any beagles currently being used in filovirus (Ebola) research. Of course, these dogs may be associated with some other type of work not specific to the fictional virus Madoba-2.

“A substitute. Otherwise the scientists would have known one was missing.”

“Of course.”

“Now he does his chores as usual, checking the food and water in the cabinets, making sure the animals are still alive, ticking his tasks on a checklist. Dr Ansari comes in, but she goes into a side laboratory to work on her tissue cultures, so she can't see him. He goes next door, to the big lab, to take care of the beagle puppies and the macaque monkeys. Now watch.”

Returning to the rabbit lab, Michael went to the safe, a steel cabinet like a large double-door refrigerator, with a combination padlock. He dialled the combination on the lock and opened the door. A security camera inside the safe showed him selecting two doses of the antiviral drug, already measured and loaded into disposable syringes. “The small dose for the rabbit he's going to steal and the larger, presumably, for himself,” Toni said. “The guards could see what he was doing, but they would not have thought it unusual. He is authorised to handle these materials. They didn't know he was taking them home.”

“They might have noticed he didn't write anything in the log.” Inside the refrigerator was a hardback notebook in which every dose used had to be recorded.

“They might have, but remember that one guard is watching thirty-seven screens, and he's not trained in laboratory practice.”

Stanley grunted.

Toni said: “Michael must have figured that the discrepancy wouldn't be noticed until the annual audit, and even then it would be put down to clerical error. He didn't know I was planning a spot check.”

Stanley was watching the screen. “Ah—now he takes the virus.”

P41

GK: The described technology of having a canister with a filovirus ready to aerosolize would also be very, very different from any current technology. All aerosol experiments these days involve very precise delivery techniques that take place inside specialized cabinets called Class III (aerosol hood lines). The virus must be prepared in a liquid form and then sprayed. Viruses such as Ebola must be maintained for long term storage at -70 C or greater, so just taking a canister from a cabinet and spraying like a hairspray would be quite novel (I am not sure that such a device would be possible - but this is fictional).

SE: Reference to dose of Madoba in Aerosolized form. Note storage would not be in aerosolized form, but rather a concentrated culture.

Here is reference to Michael taking the rabbit out through the shower (Chemical Shower). This would be the place to slip the rabbit into the suit...

In terms of dramatic action, it would be good for her to have a goal vis a vis Stanley which either she does or does not attain. (See below first)

Michael picked up a small metal canister labelled with the international biohazard symbol. It contained a dose of the virus Madoba-2 in aerosol form. Then he moved to the cabinet.

Once again, his body concealed his actions from the camera. Toni said: "I think he opens the cabinet and takes out the rabbit he wants to save. He wraps the rescued rabbit in the light blue towel and tucks him under his left arm. With his right hand, he installs the canister of virus aerosol in the biosafety cabinet and twists it to open the nozzle, infecting the new rabbit with the virus. Either now or later, he injects the rescued rabbit with the antiviral drug."

Michael walked out of shot, and Toni killed the image.

"After that he left the lab, taking the rabbit with him through the showers. He put it in the duffle bag. As he exited the building, the guards saw him carrying the same bag he came in with and suspected nothing. He went home. I think the rabbit may have bitten him when he injected it with the drug. Whenever it happened, he injected himself with the larger dose of the same antidote. It didn't work for the rabbit, and it didn't work for him."

"But even if it had worked, what was the point? He would have killed one to rescue one!"

"No doubt he felt the one he rescued was special. Look, he was an awkward young man. He lived alone, he had no family, no girlfriend, few acquaintances. He must have formed an attachment to this rabbit and convinced himself it was different. I know he named it: its food bowl had 'Joe' on the side."

Stanley looked sad. "Poor boy," he said. "Poor, foolish boy."

This is all good information, but it feels a bit flat because there's little that's personal going on between Toni and Stanley. With her staring at him, could she be hopeful that this episode might bring them closer together? Does his physical closeness alongside her at the computer affect her? Is she eager for a word of praise that she made this discovery? Does she admire him in those clothes which she hasn't seen before?