# Bio Terror Bible

## EXPOSING THE COMING BIO-TERROR PANDEMIC

**BIOTERRORBIBLE.COM:** In the aftermath of man-made bio-terror generated pandemic, the government and media will be feeding the public any number of different scapegoats allegedly responsible for the pandemic that will likely kill millions.

While some scapegoats (see below) are indeed plausible, it is much more likely that the live pathogens or agents responsible for the pandemic will likely be dispersed via A) chemtrails by government airplanes or drones, B) by the U.S. Postal Service via Tide detergent samples, C) by the government and medical establishment via tainted vaccines, or by D) the portable petri dish commonly known as the Trojan condom.

**Bio-Terror Scapegoats:** Africa, Agriculture (Food & Animals), Airports & Air Travel, Al Qaeda, Bio Labs, Bio-Terrorism Is Easy, Bio-Terrorists (Bio-Hackers), Black Market, Bugs & Insects, Censorship / Lack Thereof, Domestic Terrorists, Exotic Animals (Zoonosis), Government Ineptitude, Mail-Order DNA, Mexico, Missile Shield Failure, Mutation, Natural Disaster, No Clinical Trials (Vaccines), and The Monkeys.

**Title:** Mail-Order Molecules Brew A Terrorism Debate
**Date:** July 17, 2002
**Source:** UCLA

**Abstract:** The orders arrive by fax and e-mail 24 hours a day from pharmaceutical companies, government agencies and academic scientists. And every day at Integrated DNA Technologies, an army of machines responds by producing hundreds of batches of microscopic merchandise: custom-designed snippets of genetic material.

Until recently the Coralville, Iowa, company prospered in quiet anonymity, spewing out for scientists round the world various made-to-order pieces of DNA, the molecular code upon which so much biotechnology research depends today.

But last week's announcement that scientists in New York had used the company's mail-order molecules to make polioviruses from scratch has prompted questions about whether the DNA synthesis industry deserves closer scrutiny, and whether strategies for preventing the proliferation of biological weapons need to be rethought.

For decades the United States and other nations have sought to limit the risk of biological warfare and bioterrorism by placing controls on the cultivation and shipment of dangerous microbes. The new work threatens to undermine that approach by proving for the first time that potentially deadly viruses can be built from the ground up.

If infectious agents can be made from off-the-shelf smidgens of DNA that are individually benign, then government regulators, law enforcement agencies and even DNA synthesis companies may have no way of knowing when someone is building a biological bullet.

"The customer gets to design the sequence they want manufactured and there is a limited ability for us to know what people are going to do with it," said Roman Terrill, vice president of legal and regulatory affairs at Integrated DNA Technologies.

Indeed, Terrill said, with perhaps $10,000 and a few months time, motivated scientists could manufacture the genetic components of a deadly virus. "You could buy your own used DNA synthesizer," he said, "and make whatever you want in the comfort and privacy of your own garage."

Integrated DNA is one of about a half-dozen major U.S. manufacturers of small DNA strands, which are known in the trade as oligonucleotides or "oligos." The bigger companies, including Qiagen Operon of Alameda, Calif., Invitrogen of Carlsbad, Calif., and Sigma-Genosys of Woodlands, Tex., make thousands of customized oligos each day.

Each oligo typically consists of about 25 or 30 units of DNA, representing a tiny fraction of an organism's entire genome (a full viral genetic code can be tens of thousands of units long or more). Scientists generally use the oligos as molecular tools to help them find genes in various organisms or to trigger biological chain reactions that allow them to mass produce DNA strands in test tubes.

Because they are so small, most individual oligos lack any "fingerprint" that might identify them as part of something dangerous. But it was just such oligos that Eckard Wimmer and two colleagues at the State University of New York in Stony Brook painstakingly stitched together into a full length, 7,741-unit poliovirus genome, which spontaneously began making infectious polioviruses.

The feat arguably fell short of creating life from scratch because most scientists maintain that viruses are not truly alive. But the implications were clear.

"If you can go from a viral DNA sequence on paper to an infectious agent using things you can order out of catalogues, obviously that has big implications for bioterrorism," said Mildred Cho of the Center for Biomedical Ethics at Stanford. Two years ago Cho chaired an expert panel on the implications of creating novel life forms.

In fact, it was the Department of Defense that funded the three-year research effort as part of a program to devise protections against "unconventional pathogens." In a statement, the department said Friday it did not believe that the techniques could be used to build viruses with greater bioterror potential, such as smallpox. But others disagreed.

"With a little more advancement in technology you could probably make something more complex than polio," said Jim Cornette, a retired Air Force colonel with a doctorate in biochemistry who served in the Defense Intelligence Agency and was involved in biodefense planning during Operation Desert Storm. "Smallpox is probably just two or three years down the road, maybe less," said Cornette, who now lives in Florida. "Then what about the things that are 'none of the above?' Something dangerous but totally new?"

Several scientists said in interviews they would be reluctant to see new layers of oversight slapped on oligo makers, which have become to the biotechnology industry what silicon chip makers are to the computer industry. But many suggested the time was ripe for a public discussion about how best to prevent nefarious use of the science.

Today most biodefense efforts focus on disease-causing organisms themselves, rather than the genetic instructions for making them. Federal regulations restrict shipments of dangerous microbes and toxins listed by the government as "select agents," but those rules do not apply to shipments of their DNA components, at least within the United States.

DNA exports are more strictly regulated, with the Commerce Department requiring licenses for overseas shipments of DNA deemed a threat to national security. But those rules are open to interpretation and are easily flouted, scientists inside and outside the government said.

When Terrill of Integrated DNA wanted to learn more about the export rules last year, he went to the Commerce Department's Bureau of Exchange Administration (renamed in April the Bureau of Industry and Security), which oversees and enforces export rules for "dual-use" technologies, including microbial DNA strands. He learned that the bureau restricts exports of genetic sequences "associated with pathogenicity," which means the ability to cause disease.

"The problem is the bureau has not released those sequences, so ... we would have to decide for ourselves whether a sequence is associated with pathogenicity," Terrill said. "But how pathogenic? And what does 'associated' mean? The phrase is difficult to get a grasp on. It's not really a scientific term. It's a lawyer's term."

Moreover, Terrill learned, the 370-person agency has only one microbiologist on staff to deal with the hundreds of biological export applications the agency receives annually.

That employee was away and not available to be interviewed this week. But another Commerce Department official, speaking on condition of anonymity, confirmed that it is "the responsibility of the exporter" to determine if a genetic sequence falls under the bureau's rules.

The official said the bureau engages in "outreach activities" to educate academic and commercial scientists about the export restrictions. But the official also acknowledged that many scientists -- especially university-based researchers -- have a tradition of sharing DNA freely through the mail, making enforcement difficult.

In any case, scientists said, rules that focus on "pathogenic" DNA sequences are meaningless in an era when manufacturers can make pieces of DNA that are individually benign yet can pose a serious threat if properly assembled.

"I don't know how you could overcome that problem," the Commerce Department official said. "You could get one part [of the sequence] from one company and another part from another company and completely circumvent the law."

Some experts have begun to consider whether manufacturers themselves should be brought under some kind of oversight. "We propose that ... those companies that produce the oligos should be asked to routinely check the sequences against those of known pathogens," said Wimmer, the scientist who led the polio project.

Several computer programs, most notably one known as BLAST, can quickly scan the genetic sequence of a large piece of DNA and report whether it is similar to other known sequences, such as ones encoding parts of a virus or toxin. But company officials said they were not enthusiastic about taking on the cost or legal responsibility of fingering potential perpetrators.

In any case, said Garry Merry, corporate vice president of genomic services at Qiagen Operon, a scientist could evade BLAST's eyes simply by ordering DNA components small enough to be completely generic, then assembling them later. "You could do it," Merry said, "and we couldn't tell."

As an alternative, some are calling for extra layers of institutional review for researchers who, like Wimmer, propose combining genetic components to make viruses or other dangerous entities.

"I would argue there needs to be more oversight in terms of getting approval," said Arthur Caplan, a University of Pennsylvania ethicist who sat on Mildred Cho's expert panel. "Are we going to be seeing this kind of thing done in a science fair soon? I'm in favor of tighter controls."

Craig Venter, president of the Center for the Advancement of Genomics in Rockville who last week called the polio work "irresponsible science," said the nation might need a special advisory committee to publicly review all such studies in advance, just as a National Institutes of Health panel reviews proposed gene therapy experiments as a way of watching for trouble and reassuring the public. Without such openness, Venter said, "this kind of work can set science back in the public eye."

But while institutional or government review may bring more oversight to legitimate research, others said, it's unlikely to deter those who wish to keep their work secret. And with the biotech revolution now 30 years old -- and trade in aftermarket equipment burgeoning -- deterrence may be difficult.

"You can buy an old synthesizer and some raw ingredients and no one would have any idea what you're doing or what you're making," said Terrill of Integrated DNA. With an old machine, he said, "it might take you a week longer. They're big and clunky. But a week isn't that long" (UCLA, 2002).

**Title:** Synthetic Bioterror
**Date:** July 18, 2002
**Source:** UCLA

**Abstract:** Nobody who studies viruses and their genomes seemed surprised last week when researchers announced that they had synthesized a polio virus by using publicly available genetic information and chemical sequences ordered by mail. Even so, the feat points to yet another avenue that sophisticated terrorists might take to threaten unprotected civilians. The danger should not be exaggerated -- it is not imminent -- but the fact that bio-weapons might eventually be synthesized from off-the-shelf chemicals suggests the need for additional safeguards against malicious use of biotechnology.

> The scientists, based at the State University of New York at Stony Brook, created their synthetic virus by modeling it on the genetic sequence for the polio virus, which can be obtained from a public database on the Internet. They ordered short stretches of DNA in the proper chemical order from a commercial company, stitched those chunks together and transformed them into a polio virus that could reproduce itself and paralyze mice.
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> The Pentagon sponsored the research as part of a program to develop countermeasures against bio-weapons. Although the work has been criticized as an irresponsible stunt, it sounds a useful warning and should cause no great harm. Most experts agree that polio would not make a good terrorist weapon. Much of the American population has been protected by vaccination, and only a small percentage of unprotected people who are infected become paralyzed or die.
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> The feat raises the question whether terrorists might some day be able to synthesize more lethal viruses. That would be harder to do, as other dangerous pathogens, such as Ebola, are larger and more complex. Terrorists would probably find it far easier to work with a naturally occurring strain than to create the virus from scratch.
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> The chief exception might be smallpox, which is supposed to be held only in the United States and Russia, under guard, and thus might be hard for a terrorist to obtain. But even in that case, it might be easier to modify cowpox or monkeypox than to synthesize the whole smallpox genome, which is one of the largest and most complex.

Synthetic viruses seem less immediate a worry than another anthrax attack or an attack with natural pathogens. But the synthesis of polio underscores how fast biotechnology is progressing, for good or potential ill. It is not too soon for leaders of science and industry to start pondering whether steps can be taken to keep the chemical ingredients of dangerous pathogens out of the hands of terrorists (UCLA, 2002).

**Title:** Feds Asked To Watch DNA Shipments
**Date:** July 19, 2002
**Source:** UCLA

**Abstract:** The Iowa company that unknowingly supplied bits of genetic material used by scientists to make their own polio virus from scratch said it had recently asked the government to take steps to oversee the shipment of such DNA supplies.

Last week's stunning announcement by researchers at State University of New York at Stony Brook that they had made the virus in their lab raised a new set of fears about bioterrorism.

It was the first time a virus had been synthetically produced, and it was done with a genetic blueprint from the Internet and DNA material provided by a mail-order supplier.

The supplier was Integrated DNA Technologies, or IDT, of Coralville, a suburb of Iowa City. An official of the company said Wednesday that IDT wrote the Defense Department on May 13 about the possible terrorist use of such biomedical material, but never got a response.

"We had submitted a proposal to the Defense Department, ironically, suggesting that (DNA) sequences

ordered by suppliers like ourselves be screened and then reported to federal agencies for the purposes of identifying orders or parts of orders that would be perhaps investigated, questioned, double-checked or whatever," said Roman Terrill, vice president of legal and regulatory affairs for IDT. "The inquiries that we sent weren't really responded to."

Defense Department spokesmen declined to answer questions and only provided a statement about the department's involvement in the SUNY project.

Terrill said IDT only became aware that its supplies were used by the SUNY scientists when they made their announcement of the polio virus in the journal Science last week.

The Defense Department said it funded the project to research protections against unconventional biological agents. SUNY research team leader, Dr. Eckard Wimmer, said the creation of the virus was an attempt to show the reality of the bioterrorist threat.

The fear is that a terrorist or government might attack by spreading a harmful virus or deadly bacteria. Most of the concern so far has focused on security at labs that have supplies of germs or on finding treatments or vaccines to thwart such an attack.

But the SUNY project demonstrated for the first time that deadly diseases could be made synthetically in a lab.

"This approach has been talked about, but people didn't take it seriously," Wimmer said last week. "Now people have to take it seriously."

Terrill said the project illustrates an ethical dilemma: "DNA can be used to cure a virus or to help develop cures. On the other hand, DNA can be used for more nefarious purposes."

IDT is one of a handful of companies across the country that supplies about 15,000 customers with short fragments of DNA used in medical research. These strands, called oligonucleotides, are basic tools in all genetics labs.

But Terrill said the DNA supplier has no way of knowing how the genetic fragments it ships will be used.

"It's kind of like a phone number. They're ordering a phone number where we have the equivalent of seven digits. Without an area code, you really can't specify where the call is coming from. You need a longer sequence to identify it," Terrill said.

Besides polio, the genetic maps to anthrax, Ebola and other diseases are readily available to researchers in libraries and on the Internet, he said.

Gary Comstock, coordinator of the bioethics program at Iowa State University, said there is "a clash of values" between society's desire for innovation and new bioengineering technologies and the desire to protect ourselves from those who would abuse the new technologies.

"Given the events of Sept. 11 and since, I think the issue has a particular urgency for us that it may not have had a year or two ago" (UCLA, 2002).

**Title:** New Scientist Investigation Reveals How Easily Terrorists Can Obtain Biological Weapons 'Building Blocks'
**Date:** November 12, 2005
**Source:** Continuity Central

**Abstract:** You might think it would be difficult for a terrorist to obtain genes from the smallpox virus, or a similarly vicious pathogen. Well, it's not. Armed with a fake email address, a would-be bioterrorist could

probably order the building blocks of a deadly biological weapon online, and receive them by post within weeks.

That's the sobering reality uncovered by a New Scientist investigation into the bioterror risks posed by the booming business of gene synthesis. Dozens of biotech firms now offer to synthesise complete genes from the chemical components of DNA. Yet some are carrying out next to no checks on what they are being asked to make, or by whom. It raises the frightening prospect of terrorists mail-ordering genes for key bioweapon agents such as smallpox, and using them to engineer new and deadly pathogens.

Customers typically submit sequences by email or via a form available on a company's website. The companies then construct the specified genes and mail them back a few weeks later, usually spliced into a bacterium such as Escherichia coli. New Scientist approached 16 such firms, identified by a Google search, to ask whether they screened orders for DNA sequences that might pose a bioterror threat. Of the 12 companies that replied, just five said they screen every sequence received. Four said they screen some sequences, and three admitted not screening sequences at all.

The risks posed by gene synthesis first hit the headlines in 2002, when a team from the State University of New York at Stony Brook made infectious polioviruses from synthetic DNA. And just last month, researchers with the US Centers for Disease Control and Prevention in Atlanta, Georgia, said that they had used similar means to recreate the virus that caused the 1918 flu (New Scientist, 8 October, p 16).

In theory, a terrorist group could try to emulate the latter feat, or create a virus such as Variola major, which causes smallpox. However, the Variola genome comprises some 190,000 base pairs of DNA, and while some companies will make sequences 20,000 or more base pairs long, an attempt to order all the genes necessary to launch a smallpox attack would probably arouse suspicion. "That would stand out from a technological point of view," suggests Drew Endy, a bioengineer at the Massachusetts Institute of Technology.

A more realistic risk is that terrorists could order genes that confer virulence to dangerous pathogens such as the Ebola virus, and engineer them into another virus or bacterium. They could also order genes for a hazardous bacterial toxin – although many of these are also available by isolating the microorganisms from the environment.

Virulence genes are typically no more than a few thousand base-pairs long. Their sequences are publicly available, so screening gene-synthesis orders for potential bioweapons shouldn't pose a huge challenge.

Even if they don't routinely perform sequence checks, some companies say that they do investigate their customers. But the scope of these checks varies widely and email addresses are notoriously easy to fake. Even orders from legitimate institutions may not be what they seem (Continuity Centra, 2005).

**Title:** Synthetic DNA Makers Warned Of Bioterrorism Threats
**Date:** October 22, 2010
**Source:** New Scientist

**Abstract:** To make it harder for bioterrorists to build dangerous viruses from scratch, guidelines for firms who supply "custom DNA" are being introduced in the US.

The US and other countries restrict who can work with certain germs, but it might be possible to build some viruses from their genes. A number of firms supply DNA sequences to order. A 2005 investigation by *New Scientist* raised alarms when it found that only five out of 12 of these firms in North America and Europe always screened orders for sequences that might be used in bioweapons.

The US now wants firms to verify a customer's identity and make sure they are not on a list of banned buyers. It also wants them to screen orders for sequences that are unique to Select Agents, a list of microbes the US deems dangerous.

However, scientists commenting on the draft rules earlier this year fear that sequences from microbes other than Select Agents might also be dangerous. The US Department of Health says not enough is known about them to say which ones should arouse a firm's suspicions. Other potential weaknesses include the fact that the rules are voluntary, and that much custom DNA is made outside the US (New Scientist, 2010).