Nerve agent attack on spy used ‘Novichok’ poison

Chemical weapon used in U.K. assassination attempt was developed by Soviet Union during Cold War

By Mark Peplow, special to C&EN

Chemical weapons experts have identified the nerve agent used in the attempted murder of a former Russian double agent living in the U.K. It is part of a family of compounds known as Novichok agents that were developed in a Cold War-era weapons program in the former U.S.S.R. Russia now faces questions about its involvement in the attack, and indeed whether it has violated the Chemical Weapons Convention.

The nerve agent was used against Sergei Skripal, previously a Russian military intelligence officer who was convicted of leaking secrets to the U.K. He was released in 2010 and settled in Salisbury, England, where he and his daughter Yulia were poisoned on March 4.

“It is now clear that Mr. Skripal and his daughter were poisoned with a military-grade nerve agent of a type developed by Russia,” U.K. Prime Minister Theresa May said on Monday, March 12, citing work by investigators at the U.K.’s Defence Science & Technology Laboratory at Porton Down. May said that it was “highly likely that Russia was responsible”, although Russia has denied any involvement in the attack.
Novichok agents are organophosphorus compounds, similar to sarin and VX, which inhibit the enzyme acetylcholinesterase and cause a biochemical logjam that cripples the nervous system. Symptoms range from sweating and twitching to seizures and an inability to breathe. The U.K. has not disclosed the specific Novichok agent used against the Skripals.

“The U.S.S.R. is the only country to have developed and produced these [Novichok] agents,” says Jean Pascal Zanders, an independent consultant who was previously a senior research fellow at the European Union Institute for Security Studies. “It’s almost as though the Russians are sending a message to the West that they can reach anywhere, whenever they like.”

The newcomers

Much of what is publicly known about Novichok agents comes from Vil Mirzayanov, an analytical chemist who worked for the State Research Institute of Organic Chemistry and Technology (GosNIIOKhT), a notorious chemical weapons laboratory. Mirzayanov developed methods to detect nerve agents created and tested in the U.S.S.R.’s chemical weapons facilities. His techniques would be used to monitor the environment for any traces of the agents that might reveal the labs’ activities to foreign intelligence services.

In the late 1980s, Mirzayanov’s analytical techniques revealed that nerve agents were befouling the air and water around one of these facilities, posing a major health risk. So he went public, revealing details of the U.S.S.R.’s chemical weapons program to Moscow News in 1992. Officials arrested and imprisoned Mirzayanov, but eventually dropped the case against him. In 1995, he immigrated to the U.S., where he subsequently wrote a book about his experiences, titled “State Secrets: An Insider’s Chronicle of the Russian Chemical Weapons Program.”

The book documents the U.S.S.R.’s search for new chemical weapons—the “Foliant” program—from the early 1970s until the early 1990s. That program had several goals. It aimed to develop nerve agents that could not be stopped by the chemical protective gear available to NATO soldiers at the time. It also looked for chemical agents that were safer to handle and undetectable in conventional analytical tests. One of the key approaches
used to achieve the safety and evasion goals involved so-called binary agents—chemical weapons that could be produced immediately before they were deployed, by combining simple and innocuous precursors. “They would have used precursors more frequently present in the chemical industry,” says Ralf Trapp, a consultant chemist and toxicologist who previously worked for the Organisation for the Prohibition of Chemical Weapons (OPCW).

According to writings by Jonathan B. Tucker, a chemical weapons expert, the first binary formulation developed under Foliant was used to make Substance 33, also known as VR. This compound is very similar to the more widely known VX, differing only in the alkyl substituents on its nitrogen and oxygen atoms. “This weapon was given the code name Novichok,” Tucker wrote in “War of Nerves: Chemical Warfare from World War I to Al-Qaeda.” Novichok is the Russian word for ‘newcomer’.

In “State Secrets,” Mirzayanov tells that the program also developed a range of compounds based on the phosphorus-oxygen-fluorine core of older nerve agents like sarin and soman. By substituting the O-alkyl group in these compounds for an amidine, Foliant scientists created a molecule dubbed A-230. Some five to eight times more poisonous than VX, it was subsequently adopted as a chemical weapon by the Soviet Army. Further variations on this theme produced A-232, which had a similar toxicity to Substance 33 but was much more volatile; and its ethoxy analogue, A-234.

GosNIIOKhT researchers then developed a binary formulation that would produce A-232 (or something very close to it) on demand. This was designated Novichok-5. “Both precursor chemicals had legitimate industrial uses,” Tucker wrote, “so they could be produced at plants ostensibly designed to manufacture agricultural fertilizers or pesticides.” In 1993, Foliant spawned another binary—Novichok-7—that was reportedly just as potent.

Mirzayanov writes that the U.S.S.R. produced a few tons of Novichok-5, and tens of tons of Novichok-7. According to Tucker, the U.S.S.R. carried out open-air tests of Novichok-5 in
the early 1990s on the Ustyurt Plateau, a desert area close to the border of present-day Kazakhstan and Uzbekistan. Györgyi Vásárhelyi and László Földi of the National University of Public Service have reported that Novichok-5 and -7 act very rapidly, penetrating the skin and respiratory system.

**Plausible explanations**

Mirzayanov’s account only provides a snapshot of the Foliant program. Indeed, other scientists have proposed many different formulas for Novichok agents, including a series that incorporates a myriad of dihaloformaldoxime groups. Some estimate that over 100 nerve agents were developed under Foliant, although it is unclear how many of them evolved into binary agents.

Novichok agents are not specifically listed in the schedules of the Chemical Weapons Convention (CWC), says Zanders, because “they only became public after the treaty negotiations had been concluded.” But that does not amount to a loophole that would allow their use, because the CWC places a blanket prohibition on the manufacture of any toxic chemical intended to be a weapon. “It covers any toxic chemical, be it past, present, or future,” says Zanders. Russia has been a party to the convention since late 1997, and the Novichok agents “should have been declared to the OPCW, even if they don’t appear in the schedules,” says Zanders.

Prime Minister May has said that there are only two plausible explanations for the attack on the Skripals: “Either this was a direct act by the Russian State against our country, or the Russian government lost control of this potentially catastrophically damaging nerve agent and allowed it to get into the hands of others.” Either of those scenarios would mean that Russia is in breach of the CWC, says Zanders.

May has demanded an explanation from Russia, along with a complete disclosure of the Novichok program to the OPCW. Meanwhile, the executive council of the OPCW is holding a scheduled meeting in The Hague today. Zanders expects that the Novichok attack will be high on the agenda.
CORRECTION: This story was updated on March 15, 2018, to specify when Russia became a party to the Chemical Weapons Convention.

Comments

Bob Rayner  (March 14, 2018 12:41 PM)
This is a great article, and timely too. Thanks!
» Reply

Glen Reeves  (March 14, 2018 3:10 PM)
Being OP compounds, are the Novichok agents treatable by atropine and oximes (and benzodiazepine anticonvulsants)? Do we know the aging periods for AChE binding? Or do they have other pathophysiological mechanisms besides OP effects? I am a physician, and would like to know what medical countermeasures should be given besides airway and ventilator support.
» Reply

J-F Gal  (March 15, 2018 3:50 AM)
When browsing Google Scholar for NOVICHOK for recent articles (from 2010, remove references to barley and tomato...), I saw some papers on toxicology and treatments. As a chemist, I am not able to judge the scientific value of these references. Anyway you may check the following:
* Advances in toxicology and medical treatment of chemical warfare nerve agents, DARU Journal of Pharmaceutical Sciences201220:81
https://doi.org/10.1186/2008-2231-20-81
* Emergency action for chemical and biological warfare agents (book)
CRC Press, Second Edition By D. Hank Ellison
* Organophosphate and Carbamate Poisoning
Emergency Medecine Clinic ; February 2015Volume 33, Issue 1, Pages 133–151
* REVIEW ARTICLE
AGENTS FOR DEFENSE AGAINST CHEMICAL WARFARE: REACTIVATORS OF ACETYLCHOLINESTERASE INHIBITEDWITH NEUROTOXIC ORGANOPHOSPHORUS COMPOUNDS
* A primer on nerve agents: what the emergency responder, anesthesiologist, and intensivist needs to know

Canadian Journal of Anesthesia/Journal canadien d'anesthésie
October 2017, Volume 64, Issue 10, pp 1059–1070
* [BOOK] Nerve agents poisoning and its treatment in schematic figures and tables
etc.
There are several patents and articles in Russian, etc. that I did not check in detail.
Hope this help.
J-F Gal

» Reply

Roman Ivanov (March 14, 2018 3:19 PM)
If Prime Minister May said something, it does not mean it is true. They must present full report
including chemical analyses and comparison with a known standard in order to prove that the
substance is "Novichok". If UK has such a "standard", they must have an exact chemical formula
and therefore they are able to produce this substance in UK. Otherwise, they can speculate who
produced this substance and what is this substance till the end of days. We are scientist and only
scientific method is valid, not what Prime Minister has to say.
» Reply

Cliff Tebeau, PhD analytical, organic chemist (March 15, 2018 11:54 AM)
Dawkins defines Science and Scientific Methods as ultimate TRUTH seekers; a former
Russian defector and his daughter were killed. So much for your speculations!
» Reply

Dave Trapp (March 14, 2018 5:20 PM)
Is it conceivable for a competent chemist who has seen the formula for such a nerve agent to
successfully guess an appropriate binary formula and procedure to make a small amount? If the
raw materials are commercially available, could a chemist working for any of a number of other
military or secret services produce the material?
» Reply

Francis Antoine (March 14, 2018 6:57 PM)
I wonder why we do not hear of the various chemical and biological agents that were also created
by the West during and after the cold war? Is not objective reporting a balanced look at both sides
of a story?
» Reply
John Carpenter (March 14, 2018 9:12 PM)
Francis, the story is about a particular class of chemical agents, said to be used by Russia to kill someone, and said to be developed by Russia. The West is not accused of having recently used a nerve agent to kill someone, so why would you expect this article to address chemical agents previously developed by the West? Russia is accused of having recently violated an international treaty through the use of one of these compounds. The West is not.
» Reply

Cliff M. Tebeau (March 15, 2018 12:38 PM)
John, you expect too much logic from any of the "apologists" commenting here.
» Reply

Herb Skovronek (March 14, 2018 7:51 PM)
Yes, Russia is a prime suspect. This could be, as stated, a warning, just as Putin warned he has nukes that can hit Florida.

But there is at least one other possible source—a third party or country who has reinvented the product on his own using available info. But we also need a motive—for anyone—why would Russia decide to kill these two now after years in England? Why would a third party?

Question 1: How reliable are the tests that were used to identify the toxicant in the British labs?

Question 2: How did Russians do their 'open air tests' to determine toxicity and exposure route? I just wonder who volunteered!!!!
» Reply

George Krepinsky (March 14, 2018 8:43 PM)
These are not complex substances. It is not impossible to imagine that knowing structure any organic chemist would be able to produce it. For instance, when sarin (or tabun?) was used in Tokyo subway in later 20th century, nobody was suggesting that German government of the day was responsible for providing it. Moreover, substances of this kind are not very stable, and while stored in a forgotten corner of a warehouse, after half of a century the containers may contain decomposition products only. So it looks like the "third party" involvement suggested above is a possibility. It may require Hercule Poirot to discover who would have a motive to using it.
» Reply

Cliff M. Tebeau, PhD Chemist (March 15, 2018 12:03 PM)
Like Ivanov comment above, your Russian apologist statements are a poor attempt to DEFLECT from the facts skillfully presented in the CEN report.
» Reply
Istvan Ujvary  (March 16, 2018 3:12 AM)
I am amazed how far reaching conclusions, even verdicts are made based on the scarce information available. Structure(s) have not been disclosed, investigation is still ongoing yet some people claim to know whodunit.

"It is a capital mistake to theorize before one has data. Insensibly one begins to twist facts to suit theories, instead of theories to suit facts."
» Reply

Matthew Perry  (March 15, 2018 2:37 PM)
Most competent chemists could produce these agents without difficulty in a lab I would imagine. Doing so without poisoning oneself would be more challenging. Dosing one to a targeted individual would, I would expect, require a moderately sophisticated device, perhaps akin to a modified asthma inhaler.
» Reply

Istvan Ujvary  (March 16, 2018 12:37 PM)
As a chemist the 'only' thing I do not understand why the agents shown above - and the structures widely circulated elsewhere - are called 'binary' agents. Is it known from the chemical literature what the two apparently stable precursors for these could be?
» Reply
Although Basu said the poison was Novichok, one of a series of chemical weapons developed by Russia, "we are not in a position to say whether the nerve agent was from the same batch that the Skripals were exposed to." Speaking to Parliament on Thursday, Britain’s home secretary, Sajid Javid, connected the new episode to what he called the "reckless" decision taken by the Russian government to deploy a chemical weapon in Salisbury in March. "It is now time," Javid added, "that the Russian state comes forward and explains exactly what has gone on.""The eyes of the world are currently on