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Novichok agent

Novichok (<u>Russian</u>: HOBM40´K, "newcomer") is a series of <u>nerve agents</u> the <u>Soviet Union</u> and <u>Russia</u> developed between 1971 and 1993.^{[a][2][3]} Russian scientists who developed the agents claim they are the deadliest nerve agents ever made, with some variants possibly five to eight times more potent than \underline{VX} ,^{[4][5]} and others up to ten times more potent than soman.^[6]

They were designed as part of a Soviet program codenamed "FOLIANT".^{[7][1]} Five Novichok variants are believed to have been weaponised for military use.^[8] The most versatile was A-232 (Novichok-5).^[9] Novichok agents have never been used on the battlefield. <u>Theresa May</u>, Prime Minister of the United Kingdom, said that one such agent was used in the <u>poisoning of Sergei and Yulia Skripal</u> in England in March 2018.^[10] Russia officially denies producing or researching Novichok agents.^[11]

In 2013, the <u>Organisation for the Prohibition of Chemical Weapons</u> Scientific Advisory Board reported that it had insufficient information to comment on the existence or properties of Novichok agents,^[12] and in 2011 it noted there was no peer reviewed paper on Novichok agents in scientific literature.^[13]

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Design objectives

These agents were designed to achieve four objectives:^{[14][15]}

- To be undetectable using standard 1970s and 1980s <u>NATO</u> chemical detection equipment;
- To defeat NATO chemical protective gear;
- To be safer to handle;
- To circumvent the Chemical Weapons Convention list of controlled precursors, classes of chemical and physical form.

All these objectives were claimed to have been achieved.^[16]

Some of these agents are <u>binary weapons</u>, in which precursors for the nerve agents are mixed in a munition to produce the agent just prior to its use. Because the precursors are generally significantly less hazardous than the agents themselves, this technique makes handling and transporting the munitions a great deal simpler. Additionally, precursors to the agents are usually much easier to stabilize than the agents themselves, so this technique also made it possible to increase the <u>shelf life</u> of the agents. This has the disadvantage that careless preparation may produce a non-optimal agent. During the 1980s and 1990s, binary versions of several Soviet agents were developed and are designated as "Novichok" agents.

Disclosure

The Soviet Union and Russia reportedly developed extremely potent fourth-generation chemical weapons from the 1970s until the early 1990s, according to a publication by two chemists, <u>Lev Fyodorov</u> and <u>Vil Mirzayanov</u> in <u>Moskovskiye Novosti</u> weekly in 1992.^{[17][18][b]} The publication appeared just on the eve of Russia's signing of the <u>Chemical Weapons Convention</u>. According to Mirzayanov, the Russian Military Chemical Complex (MCC) was using defense conversion money received from the West for development of a chemical warfare facility.^{[4][5]} Mirzayanov made his disclosure out of environmental concerns. He was a head of a counter-intelligence department and performed measurements outside the chemical weapons facilities to make sure that foreign spies could not detect any traces of production. To his horror, the levels of deadly substances were 80 times greater than the maximum safe concentration.^{[5][20]}

Russian <u>military industrial complex</u> authorities admitted the existence of Novichok agents when they brought a <u>treason</u> case against Mirzayanov. According to expert witness testimonies that three scientists prepared for the <u>KGB</u>, Novichok and other related chemical agents had indeed been produced and therefore the Mirzayanov's disclosure represented high treason.^[c]

Mirzayanov was arrested on 22 October 1992 and sent to <u>Lefortovo prison</u> for divulging state secrets. He was released later because "not one of the formulas or names of poisonous substances in the *Moscow News* article was new to the Soviet press, nor were locations ... of testing sites revealed."^[5] According to <u>Yevgenia Albats</u>, "the real <u>state secret</u> revealed by Fyodorov and Mirzayanov was that generals had lied—and were still lying—to both the international community and their fellow citizens."^[5] Mirzayanov now lives in the U.S.^[22]

Further disclosures followed when Vladimir Uglev, one of Russia's leading binary weapons scientists, revealed the existence of A-232/Novichok-5 in an interview with the magazine *Novoye Vremya* in early 1994.^[23]

Development and test sites

Stephanie Fitzpatrick, an American geopolitical consultant, has claimed that the Chemical Research Institute in <u>Nukus</u>, <u>Soviet Uzbekistan</u>,^[24] produced Novichok agents and <u>The New York Times</u> has reported that U.S. officials said the site was the major research and testing site for Novichok agents.^{[25][26]} Small, experimental batches of the weapons may have been tested on the nearby <u>Ustyurt plateau</u>.^[26] Fitzpatrick also writes that the agents may have been tested in a research centre in <u>Krasnoarmeysk</u> near Moscow.^[24] Precursor chemicals were made at the Pavlodar Chemical Plant in <u>Soviet Kazakhstan</u>, which was also thought to be the intended Novichok weapons production site, until its still-under-construction chemical warfare agent production building was demolished in 1987 in view of the forthcoming Chemical Weapons Convention.^{[27][28]}

Since its independence in 1991, <u>Uzbekistan</u> has been working with the government of the United States to dismantle and decontaminate the sites where the Novichok agents and other chemical weapons were tested and developed.^{[24][26]} Between 1999^[29] and 2002 the <u>United States Department of Defense</u> dismantled the major research and testing site for Novichok at the Chemical Research Institute in Nukus, under a \$6 million <u>Cooperative</u> Threat Reduction program.^{[25][30]} Novichok agent - Wikipedia

Hamish de Bretton-Gordon, a British chemical weapons expert and former commanding officer of the UK's Joint Chemical, Biological, Radiation and Nuclear Regiment and its NATO equivalent, "dismissed" suggestions that Novichok agents could be found in other places in the former Soviet Union such as Uzbekistan and has asserted that Novichok agents were only produced at Shikhany in Saratov Oblast, Russia.^[31] Mirzayanov also says that it was at Shikhany, in 1973, that scientist Pyotr Petrovich Kirpichev first produced Novichok agents; Vladimir Uglev joined him on the project in 1975.^[32] According to Mirzayanov, while production took place in Shikhany, the weapon was *tested* at Nukus between 1986 and 1989.^[4]

Description of Novichok agents

Mirzayanov provided the first description of these agents.^[20] Dispersed in an ultra-fine <u>powder</u> instead of a gas or a vapor, they have unique qualities. A <u>binary agent</u> was then created that would mimic the same properties but would either be manufactured using materials which are not controlled substances under the <u>CWC</u>,^[22] or be undetectable by treaty regime inspections.^[26] The most potent compounds from this family, Novichok-5 and Novichok-7, are supposedly around five to eight times more potent than <u>VX</u>.^[37] The



Examples of structures claimed as Novichok agents[33][34][35][36]

"Novichok" designation refers to the binary form of the agent, with the final compound being referred to by its code number (e.g. A-232). The first Novichok series compound was in fact the binary form of a known V-series nerve agent, \underline{VR} ,^[37] while the later Novichok agents are the binary forms of compounds such as A-232 and A-234.^[38]

Mirzayanov gives somewhat different structures for Novichok agents in his autobiography to those which have been identified by Western experts. He makes clear that a large number of compounds were made, and many of the less potent derivatives were reported in the open literature as new organophosphate insecticides,^[39] so that the secret chemical weapons program could be disguised as legitimate pesticide research.

The agent A-234 is also supposedly around five to eight times more potent than VX.^{[40][37]}

The agents are reportedly capable of being delivered as a liquid, aerosol or gas via a variety of systems, including artillery shells, bombs, missiles and spraying devices.^[24]

In 2016 Iranian chemists isolated five Novichok agents for analysis and produced detailed mass spectral data which was added to the <u>Organisation for the Prohibition of Chemical Weapons</u> Central Analytical Database. Previously there had been no detailed descriptions of their spectral properties in open scientific literature.^[41]

Chemistry

A wide range of potential structures have been reported. These all feature the classical <u>organophosphorus</u> core (sometimes with the P=O replaced with P=S or P=Se), which is most commonly depicted as being a <u>phosphoramidate</u> or <u>phosphonate</u>, usually fluorinated (cf. <u>monofluorophosphate</u>). The organic groups are subject to more variety; however, a common substituent is <u>phosgene oxime</u> or analogues thereof. This is a potent chemical weapon in its own right, specifically as a <u>nettle agent</u>, and would be expected to increase the harm done by the Novichok agent. Many claimed structures from this group also contain <u>cross-linking agent</u> motifs which may covalently bind to the <u>acetylcholinesterase</u> enzyme's active site in several places, perhaps explaining the rapid denaturing of the enzyme that is claimed to be characteristic of the Novichok agents.

Effects

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As nerve agents, the Novichok agents belong the class organophosphate to of acetylcholinesterase inhibitors. These chemical compounds inhibit the enzyme acetylcholinesterase, preventing the normal breakdown of the neurotransmitter acetylcholine. Acetylcholine concentrations then increase at neuromuscular junctions to cause involuntary contraction of all muscles. This then leads to respiratory and cardiac arrest (as the victim's heart and diaphragm muscles no longer function normally) and finally death from heart failure or suffocation as copious fluid secretions fill the victim's lungs.^[43]

The use of a fast-acting peripheral <u>anticholinergic</u> drug such as <u>atropine</u> can block the receptors where acetylcholine acts to prevent poisoning (as in the treatment for



Synthesis of A230, A232, and A234. Ethanediol modified with up to two methyl groups is reacted with phosphorus trichloride to form a ring structure named as a phospholane analogue. The last chlorine atom is replaced by fluorine (nucleophilic substitution). This compound is then reacted with a phosgene oxime-like chloride to open the ring and create the product flourophosphonate.^[42]

poisoning by other acetylcholinesterase inhibitors). Atropine, however, is difficult to administer safely, because its effective dose for nerve agent poisoning is close to the dose at which patients suffer severe side effects such as changes in heart rate and thickening of the bronchial secretions which fill the lungs of someone suffering nerve agent poisoning, so that suctioning of these secretions and other advanced life support techniques may be necessary in addition to administration of atropine to treat nerve agent poisoning.^[43]

In the treatment of nerve agent poisoning, atropine is most often administered along with a Hagedorn oxime such as <u>pralidoxime</u>, <u>obidoxime</u>, <u>TMB-4</u>, <u>HI-6</u> which reactivates acetylcholinesterase which has been inactivated by <u>phosphorylation</u> by an organophosphorus nerve agent and relieves the respiratory muscle paralysis caused by some nerve agents. Pralidoxime is not effective in reactivating acetylcholinesterase inhibited by some older nerve agents such as <u>soman^[43]</u> or the Novichok nerve agents, described in the literature as being up to 8 times more toxic than nerve agent VX.^[36]

The agents may cause lasting nerve damage, resulting in permanent disablement of victims, according to Russian scientists.^[44] Their effect on humans was demonstrated by the accidental exposure of Andrei Zheleznyakov, one of the scientists involved in their development, to the residue of an unspecified Novichok agent while working in a Moscow laboratory in May 1987. He was critically injured and took ten days to recover consciousness after the incident. He lost the ability to walk and was treated at a secret clinic in Leningrad for three months afterwards. The agent caused permanent harm, with effects that included "chronic weakness in his arms, a toxic hepatitis that gave rise to <u>cirrhosis</u> of the liver, epilepsy, spells of severe depression, and an inability to read or concentrate that left him totally disabled and unable to work." He never recovered and died in July 1992 after five years of deteriorating health.^[45]

Use

Poisoning of Kivelidi

Novichok or another similar classified phosphorus-based nerve agent ^[46] was reportedly used in 1995 to poison Russian banker Ivan Kivelidi, the head of the Russian Business Round Table, and Zara Ismailova, his secretary.^{[47][48][49] [50][51]} According to historians <u>Yuri Felshtinsky</u> and <u>Vladimir Pribylovsky</u>, the murder became "one of the first in the series of poisonings organized by Russia's security services". The <u>Russian Ministry of Internal</u>

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<u>Affairs</u> analyzed the substance and announced that it was "a phosphorous-based military-grade nerve agent"^[52] "whose formula was strictly classified".^[52] According to Nesterov, the administrative head of Shikhany, he did not know of "a single case of such poison being sold illegally" and noted that the poison "is used by professional spies".^[52]

Vladimir Khutsishvili, a former business partner of the banker, was subsequently convicted for the killings.^[47] According to *The Independent*, "A closed trial found that his business partner had obtained the substance via intermediaries from an employee of a state chemical research institute known as GosNIIOKhT, which was involved in the development of Novichoks. The employee, Leonard Rink, told police he had been storing poisons in his garage and selling them to pay off debts."^[53] However, Khutishvilli was not detained at the time of the trail and freely left the country. He was arrested only in 2006 after returning back to Russia and believing that the ten-year case was closed.^[52] According to Felshtinsky and Pribylovsky, Khutishvilli was framed for the murder by Russia's security services which had access to the chemical agent and used it to organize the murder on the order by a senior Russian state official.^[52]

Poisoning of Sergei and Yulia Skripal

On 12 March 2018, the UK government said that a Novichok agent had been used in an attack in the English city of <u>Salisbury</u> on 4 March 2018 in an attempt to kill former <u>GRU</u> officer <u>Sergei Skripal</u> and his daughter Yulia.^[54] British <u>Prime Minister Theresa May</u> said in Parliament: "Either this was a direct action by the Russian state against our country, or the Russian government lost control of its potentially catastrophically damaging nerve agent and allowed it to get into the hands of others."^[54] On 14 March 2018, the UK expelled 23 Russian diplomats after the Russian government refused to meet the UK's deadline of midnight on 13 March 2018 to give an explanation for the use of the substance.^[55]

After the attack, 21 members of the emergency services and public were checked for possible exposure, and three were hospitalised. As of 12 March, one police officer remained in hospital.^[54] Five hundred members of the public were advised to decontaminate their possessions to prevent possible long-term exposure, and 180 members of the military and 18 vehicles were deployed to assist with decontamination at locations in and around Salisbury. The exact location of the attack has not been released.^{[54][56][57]} Addressing the <u>United Nations Security Council</u>, Vassily Nebenzia, the Russian envoy to the UN, responded to the British allegations by denying that Russia had ever produced or researched the agents, stating: "No scientific research or development under the title novichok were carried out."^[11]

Daniel Gerstein, a former senior official at the U.S. <u>Department of Homeland Security</u>, said it was possible that Novichok nerve agents had been used before in Britain to assassinate Kremlin targets, but had not been detected: "It's entirely likely that we have seen someone expire from this and not realized it. We realized in this case because they were found unresponsive on a park bench. Had it been a higher dose, maybe they would have died and we would have thought it was natural causes."^[58]

See also

- Poison laboratory of the Soviet secret services
- Russia and weapons of mass destruction

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Notes

a. Jonathon B. Tucker writes that approval to commence research into "fourth generation" chemical weapons was given by the <u>Central Committee of the Communist Party</u> and the <u>Soviet Council of Ministers</u> in May 1971. Vil Mirzayanov, the Russian scientist who first alerted the West to the existence of the Novichok agents, states that testing of Novichok-7 was successfully completed in 1993—after the signing of the Chemical Weapons Convention.^[1][2]

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- b. Mirzayanov had made a similar disclosure a year earlier in the 10 October 1991 issue of the Moscow newspaper, *Kuranty*.[19]
- c. "[T]he talk [by Mirzayanov] about binary weapons was no more than a verbal construct, an argument ex adverso, and only the MCC [Russian Military Chemical Complex] could corroborate or refute this natural assumption. By entangling V. S. Mirzayanov in investigation, the MCC confirmed the stated hypothesis, advancing it to the ranks of proven facts."^[21]

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