

Doubts About Novichok

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Introduction

In view of the seriousness of the rapidly worsening relations between the West and Russia, and the quickly evolving military events in the Middle East, especially Syria, we have taken the step to publish relevant evidence-based analysis with respect to the Skripal incident of 4 March 2018. This update to our [earlier briefing note](#) covers new material that has become available. We welcome comments and corrections which can be sent to [Piers Robinson](#) or provided on this [site](#).

Summary

Official statements from the UK government claim that the “military grade nerve agent” detected in Salisbury was “part of a group of nerve agents known as Novichok” that the Russian chemist Vil Mirzayanov alleged had been developed in the Soviet Union in a secret programme. The structures of these compounds, labelled A-230, A-232, A-234, A-242 and A-262, were published by Mirzayanov in a book in 2008, twelve years after he emigrated to the US.

Other than Mirzayanov’s story, there is no evidence that these compounds were ever synthesized in either the Soviet Union or Russia, or that the “Novichok” programme ever existed. The use of the term “Novichoks” to describe this A-230 series of compounds, which are real chemical structures, is therefore tendentious. An account by another Russian chemist Vladimir Uglev, often cited as corroboration of Mirzayanov’s story, appears on close examination to be about the development of a class of nerve agents denoted GV which have been studied in several countries including Czechoslovakia and the US.

The UK government has not revealed the identity of the compound detected in Salisbury, but the Russian ambassador has stated that the Foreign Secretary told him that the compound detected was A-234. Russian experts have revealed that the mass spectrometry profile of this compound was submitted to a public database by a researcher in the US Army’s Edgewood Chemical and Biological Center around 1998, indicating that Edgewood has synthesized and studied this compound.

There is also evidence that the US government has concealed what it knows about the A-230 series of compounds. Edgewood’s entry for compound A-234 in the public database has been deleted. Furthermore, US diplomatic cables from 2009 show that the US and UK governments sought to discourage discussion of Mirzayanov’s story at the OPCW and the Australia Group (an informal grouping of US-allied countries set up in 1985 to control the export of precursors for chemical weapons).

It has been suggested that the A-230 series of compounds have a different mode of action to that of classic organophosphates. To ensure that all relevant information is available to the doctors caring for the victims of the Salisbury poisoning, the UK government should without further delay reveal the identity of the compound detected, and should request urgently that all labs that have undertaken toxicity studies on such compounds make their results publicly available.

Detailed Discussion

Did a “Novichok” programme ever exist?

The word “Novichok” comes from a Russian chemist named Vil Mirzayanov, who emigrated in 1995 after alleging that a secret programme to develop a new class of nerve agents had existed in the Soviet Union and had continued in Russia. In 2008, Mirzayanov published a book containing structures of five compounds that he alleged had been developed in this programme: they were labelled A-230, A-232, A-234, A-242 and A-262. We shall refer to these as the A-230 series of compounds, without taking any position as to whether they were developed in Russia as “Novichoks”.

The UK government has added to this story with this [statement](#) from the Foreign and Commonwealth Office:-

The Foreign Secretary revealed this morning that we have information indicating that within the last decade, Russia has investigated ways of delivering nerve agents likely for assassination. And part of this programme has involved producing and stockpiling quantities of Novichok.

The wording “we have information indicating” suggests that this is [raw human intelligence](#) rather than the “finished” evaluation for use by policy makers, for which wording of the form “[we have assessed](#)” would be used.

The Russian government denies that a Novichok programme ever existed. The Russian envoy to the UN, Vasily Nebenzya [stated on 15 March that](#):

No research, development or manufacturing of projects codenamed Novichok has ever been carried out in Russia, all CW programmes were stopped back in 1991-92_

In a [television interview](#) the Foreign Ministry spokeswoman Maria Zakharova gave a comprehensive denial:-

Never on the territory of the USSR in Soviet times or in the times of the Russian Federation on its territory have there been studies conducted under the code name Novichok. It was neither patented, nor used as a symbol or a code. Once more, as this is the key thing: the word Novichok has never been used in the USSR or in Russia as something related to chemical weapons research. This word was introduced and used for poisonous materials in the West.

A recent [interview with Vladimir Uglev](#) has been often cited as corroborating Mirzayanov’s

account. Uglev describes how he helped to develop a “new class of organophosphorus chemical agents”, but states that the name “Novichok” was not used for these compounds. Uglev states that one of these compounds, obtained from a military laboratory, was used to murder the banker Ivan Kivelidi and his secretary Zara Ismailova in 1995. A [report in the pro-Western magazine Novaya Gazeta](#) includes an image of a page from a document purported to be from the investigation of this murder. This document shows a reconstruction of the molecular structure of the compound from the fragments detected by mass spectrometry. However the reconstructed structure shown is identical to that of a nerve agent known as GV (see Appendix), with what may be the mistaken substitution of an ethoxy group for a fluorine atom. If Uglev’s account is accurate and this document is genuine, this establishes that the new class of nerve agents that he helped to develop was the GV class of agents, which Russia has never denied studying. Because the A-230 series of compounds have structures that are very different from GV-like compounds, Uglev’s story does not corroborate that of Mirzayanov. Mirzayanov’s [account in 1995](#), in which he labels “Substance 33” (the Russian isomer of VX), as a “precursor” (possibly “forerunner” is the intended meaning as Russian VX is not a chemical precursor) of what he called “novichoks” is also consistent with these being GV-type agents. At a [briefing by the Russian Ministry of Foreign Affairs on 21 March](#), Viktor Kholstov, Director of the Centre for Analytical Research on Chemical and Biological Weapon Conventions under the Russian Ministry of Industry and Trade, stated that “Vil Mirzayanov did not have these formulas [the structures given in his 2008 book for the A-230 series of compounds] in the early 2000s”.

In summary, there is ample evidence that the Soviet Union and other countries were developing GV-type agents up to the 1990s. However Mirzayanov’s story that the chemical structures labelled as A-230 to A-262 in his 2008 book were developed in the Soviet Union or Russia remains open to serious doubt.

Was one of the A-230 series of compounds used in the Salisbury poisoning?

The Prime Minister stated to the House of Commons on 12 March that

It is now clear that Mr Skripal and his daughter were poisoned with a military-grade nerve agent of a type developed by Russia. It is part of a group of nerve agents known as Novichok.

On 22 March, the Russian Ambassador to the UK gave a [briefing](#):-

On 12 March, 8 days after the day of poisoning, I was summoned by Foreign Secretary Johnson, who put forward a 24-hour ultimatum to explain the Russian Government’s position by the end of the next day. The question was put like following: either the incident in Salisbury was a direct act of the Russian Government against the UK or the Russian Government had lost control of a nerve agent that the Foreign Secretary identified as A-234, and allowed it to get into the hands of others.

The UK government has not confirmed that the nerve agent was identified as A-234, or that this information was conveyed to the Ambassador by the Foreign Secretary. It is expected that the OPCW investigation will reveal the identity of the agent detected in Salisbury within the next few weeks. For now, it is reasonable to assume that the agent found was one of

the A-230 series of compounds.

Scientific studies of the A-230 series of compounds

In 2016, Iranian scientists [reported](#) bench scale synthesis of a few compounds closely related to those labelled by Mirzayanov as “Novichoks”. They added the mass spectrometry signatures of these compounds studied to the OPCW’s Central Analytical Database. The structure denoted “compound 3” in their paper is similar to A-234 except that it has methyl instead of ethyl groups.

A similar study of the compound later published as A-234 had been undertaken by Dr Dennis Rohrbaugh at the US Army Chemical and Biological Defense Command’s Edgewood Research Development and Engineering Center around 1998. He added the mass spectrometry profile to the 1998-2001 version (NIST 98) of the National Institute of Standards and Technology Mass Spectral Library. This was revealed in a [television interview](#) by Professor Igor Rybalchenko, formerly the head of the Russian chemical weapon detection lab (the Laboratory of Chemical and Analytical Control of the Ministry of Defence). Rybalchenko is a highly-respected scientist who has worked closely with western colleagues on the OPCW Scientific Advisory Board and with international agencies supervising the destruction of the former Soviet chemical weapons stockpiles. Rybalchenko showed a [slide](#) (at 1:11:53 in the recording) and explained:-

As far back as 1998, we looked through a regular edition of the spectral database released by the US National Bureau of Standards [now the National Institute of Standards and Technology], which has spectral data on about 300,000 compounds and is regularly updated, to find an agent that caught our attention as it was an organophosphate chemical. We understood that it must have a lethal effect. Now it has turned out that, judging by the name of that agent, it was “Novichok” A-234.

The image shows a faded printout of a record from NIST 98 for a chemical with formula $C_8H_{18}FN_2O_2P$ named as N-(O-ethyl-fluorophosphoryl)-N'-N'-diethyl-acetamidine, with NIST number 226889. As Rybalchenko notes, this molecular structure corresponds to A-234

Evidence that the US and UK governments are concealing what they know about the A-230 series of compounds

The record submitted by Edgewood for a compound with formula $C_8H_{18}FN_2O_2P$ no longer exists in the [current version](#) of the NIST Mass Spectral Library. As such research is entirely legitimate, it is puzzling that this record should have been deleted.

A [secret cable dated 26 March 2009](#) from a US delegate to OPCW reported that at a meeting of the OPCW Data Validation Group in The Hague a few weeks earlier, “representatives of several countries (Finland, Netherlands, UK) had begun discussing the Mirzayanov book on the margins of the meeting”. The US delegate noted that

U.S. Del understands from OSD that the UK Ministry of Defense has spoken to its counterparts in the Netherlands and Finland, apprised them of the conversation, and asked each country to provide guidance to its del members not/not to raise this issue in the future

The Canadian delegate was also curious, but the US and UK delegates expressed lack of familiarity with and interest in the matter.

On March 25, in a private conversation, Canadian delegate asked U.S. and UK Delreps whether they had heard of the Mirzayanov book "State Secrets: An Insider's View of the Russian Chemical Weapons Program." Canadian Rep added that Mirzayanov now appeared on YouTube. UK Rep acknowledged she had heard of it, but said this was the first time she had heard of "novichoks" and thought the entire discussion was best left to experts in capital. U.S. Delrep indicated a lack of familiarity with the subject matter and indicated no interest in pursuing the discussion further.

The cable requested further "guidance as to how this issue is to be handled if raised by others" for US members of OPCW technical advisory bodies such as the Scientific Advisory Board. The cable was addressed to the CIA, the National Security Council, the Secretary of Defense and the Secretary of State, suggesting that this issue was being discussed at high levels of the US government.

A [subsequent cable](#) on 3 April 2009 from the Secretary of State Hillary Clinton instructed the US delegation to the Informal Inter-Sessional Meeting of the Australia Group (a group of US-allied countries set up in 1985 to control the export of precursors of chemical weapons) that one of five US objectives for the meeting was to:-

- Avoid any substantive discussion of the Mirzayanov book "State Secrets: An Insider's View of the Russian Chemical Weapons Program" or so-called 'Fourth Generation Agents.'

More detailed guidance was provided for the US delegates, echoing the description of how US and UK delegates had responded to the Canadian delegate a week earlier:-

If AG participants raise the issue of Vils Mirzayanov's book "State Secrets: An Insider's View of the Russian Chemical Weapons Program," the Del should:

- Report any instances in which the book is raised.
- Not/not start or provoke conversations about the book or engage substantively if it comes up in conversation.
- Express a lack of familiarity with the issue.
- Quietly discourage substantive discussions by suggesting that the issue is 'best left to experts in capitals.'

These cables establish that the US and UK governments sought to discourage discussion of Mirzayanov's book in 2009. Taken together with the deletion of the record for A-234 submitted by Edgewood to the NIST Mass Spectral library, this suggests that the US and UK governments are concealing what they know about the A-230 series of compounds, for reasons that are not clear.

These cables suggest a reinterpretation of our earlier briefing in which we noted that the OPCW Scientific Advisory Board in 2013 had stated that it "*has insufficient information to*

comment on the existence or properties of “Novichoks”. We had interpreted this as scepticism, on the part of experts who were in a position to know, about whether these compounds were really military-grade nerve agents. From the cables cited above, however, it appears that these experts may have been following the guidance issued earlier that they should “discourage substantive discussions” of the matter.

What is known of the toxicity of the A-230 series of compounds?

Rybalchenko stated that “All that we know is that all substances of this class are very difficult to overcome in case of injuries, and the antidote therapy will hardly bring about the desired effect”. One [review](#) has stated (without citing a source) that inhibition of an enzyme known as neuropathy target esterase, which can cause delayed nerve damage, “is of primary concern for the Novichok agent”. The consultant treating the victims of the Salisbury poisoning reported on 22 March that they were [“heavily sedated following injury by a nerve agent”](#) and unable to communicate. This prolonged paralysis is not typical of acute poisoning by standard organophosphate agents. To ensure that all available toxicological and medical expertise can be mobilized to help the Salisbury doctors manage the victims, the identity of the agent should be made public without delay. Edgewood and any other laboratories that have studied this compound should reveal the results of any toxicity studies they have done.

Appendix – technical points

This appendix explains some technical points on which there has been confusion.

Why is it necessary to synthesize a new compound before it can be detected by mass spectrometry?

Mass spectrometry identifies compounds by the mass-charge ratio of the ions produced by fragmentation of the compound. These mass-charge ratios, combined with separation by another method such as gas chromatography, are a unique “signature” for the compound. To determine this signature for a new compound, it has to be synthesized and analysed by mass spectrometry to measure the mass-charge ratios, which are then added to databases so that the compound can be detected in future by matching the observed mass-charge ratios with the records in the database.

Is it feasible to synthesize these compounds at bench scale?

The Iranian paper confirms that compounds similar to A-234 can be synthesized at bench scale in any modern university lab. Synthesis at industrial scale for military use would be a different matter, but an assassination would require only bench scale quantities.

Did Porton Down make a definite identification of the agent?

In Mr Justice Williams’s [court judgement](#) on 22 March, the statement from witness CC, described as “Porton Down chemical and biological analyst” was summarized as follows:-

Blood samples from Sergei Skripal and Yulia Skripal were analysed and the findings indicated exposure to a nerve agent or related compound. The samples tested positive for the presence of a Novichok class nerve agent or closely related agent.

This is similar to the form of words that OPCW has used to report positive blood tests for sarin

exposure: [“sarin, or a sarin-like substance”](#). This wording is used because blood tests for nerve agent detect only what is left of the molecule after it has bound to the receptor. The “leaving group” (the rest of the molecule) cannot be identified. For sarin (and presumably for A-234) the leaving group is a fluorine atom, and for VX the leaving group is a thiol.

Although it is possible that the blood test would not be able to identify definitively a molecular structure such as A-234, this inability to determine the leaving group applies only to physiological samples. If environmental samples have tested positive, Porton Down should have been able to identify the original molecule precisely. As noted above, to use the word “Novichoks” for the A-230 series of compounds is tendentious.

The GV agents studied in several countries are not the “Novichoks” described by Mirzayanov

In his authoritative review, Dr Robin Black, former head of the detection laboratory at Porton Down, makes clear that the development of a class of “intermediate volatility agents” (IVAs), [designated “GV agents” by the Czechoslovak chemists Ivan Masek and Jiri Matousek](#) is distinct from Mirzayanov’s unconfirmed story about “Novichoks”:-

Two additional series of nerve agents are worthy of mention. Research on IVAs in several countries led to the analogue known as GV, O-(2-dimethylaminoethyl) N,N-dimethyl phosphoramidofluoridate (Scheme 1.7). The name GV was coined by Czech chemists to indicate properties of both G and V agents.⁶⁵ The US military designator was GP. GV is a hybrid structure incorporating structural features of tabun, sarin and V agent. GV had true intermediate volatility properties (bp 226 °C, volatility 527 mg m⁻³ at 25 °C),⁶⁶ producing sufficient vapour to cause an inhalation hazard, and possessing percutaneous toxicity approaching that of the V agents. GV might have become an important threat agent had it not had very poor storage stability. It has been suggested that a binary version might be feasible.

In recent years, there has been much speculation that a fourth generation of nerve agents, ‘Novichoks’ (newcomer), was developed in Russia, beginning in the 1970s as part of the ‘Foliant’ programme, with the aim of finding agents that would compromise defensive countermeasures.^{67,68} Information on these compounds has been sparse in the public domain,^{30,68-70} mostly originating from a dissident Russian military chemist, Vil Mirzayanov.⁶⁹ No independent confirmation of the structures or the properties of such compounds has been published.

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