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ISSUE: COVID-19 Vaccines – mRNA Vaccine Translation structure, lab tests, characteristics and storage

IF ASKED

Batch release, lab testing and specifications

- Batch release of vaccines is recognised by the World Health Organization (WHO) as a necessary function of a stringent regulatory authority and is a critical part of the regulatory oversight of vaccine quality.
- 'TGA batch release' involves review of the manufacturing and testing documentation for specific batches and may also include the TGA Laboratories performing multiple tests for identity, composition and strength, purity, and integrity.
- Although batch release does not necessarily require TGA testing every batch of vaccine, all batches of COVID-19 vaccines have been assessed and tested by the TGA through the batch release program, except 4 batches that were part of the Pfizer employee vaccination program – however Official Control Authority Batch Release (OCABR) 4 certificates were received and assessed for these batches.
- All batches released to date have complied with required specifications at release. Details of the Batch release assessment of COVID-19 vaccines are published on the TGA website at www.tga.gov.au/batch-release-assessment-covid-19-vaccines.
- To 30 September 2024, there have been 429 batches and 240.9 million doses released.
    - Spikevax mRNA vaccine (Moderna) - 58 batches - s47 [redacted]
    - Comirnaty mRNA vaccine (Pfizer) - 154 batches - s47 [redacted]
    - Nuvaxovid protein vaccine (Novavax/Biocelect) - 11 batches - s47 [redacted] s47 [redacted]
    - Vaxzevria viral vaccine (AstraZeneca) - 206 batches - s47 [redacted]

Batch release pathways for COVID vaccines

Pathway 1 - Release based on overseas certification

- Independent overseas certification from a recognised National Control Laboratory (NCL), such as the OCABR process in Europe.
- The OCABR process involves laboratory testing by a recognised overseas laboratory and an assessment of the manufacturing documentation (summary protocol review). The laboratory testing covers potency, identity and appearance based on a product specific guideline, e.g. mRNA vaccine.
- Once the sponsor provides evidence that the batch to be supplied in Australia has passed OCABR testing, the TGA can release that batch of vaccine without conducting a manufacturing protocol assessment. Although they are released on OCABR certification, the TGA Laboratories still tests these as part of its batch release program.
- The sponsor must still supply samples, batch details and evidence of the maintenance of adequate shipping conditions for the batch under this pathway.
- The availability of an OCABR certificate for vaccine batches entering Australia can depend on many factors, including the final global distribution of a batch. In cases where OCABR certification is not available, we use Pathway 2.

Pathway 2 - Release based on TGA assessment

- This pathway is used when no OCABR certificate is available.

- Release of the vaccine using Pathway 2 is based on an assessment by the TGA of the manufacturing documentation (summary protocol review), shipping information and testing in the TGA Laboratories.

BACKGROUND & DATA

Characteristics and Structure of mRNA and Spike Protein

N1-Methyl-Pseudouridine: Both COVID-19 mRNA vaccines include N1-Methyl-Pseudouridine mRNA, which replaces uridine, and is used to improve:

- Amounts of S protein produced by the cells; and
- Stability and safety of the vaccine.

Consecutive stop codons are used as a fail-safe mechanism that prevents changes occurring if reading of the first stop codon fails.

Repeat dose toxicity studies in animal species with the vaccines at doses many times the human dose indicated no vaccine-related safety risks except for local inflammatory reactions, which are common effects of vaccines.

Spike Protein: The viral spike (S) protein of SARS-CoV-2 is reported in the literature as having a molecular weight of 143kDa, in its deglycosylated form. There is inherent variability in the molecular weight due to the incorporation of host derived glycans, resulting in an acceptable weight) range of 120–200kDa. For mRNA vaccines, an *in vitro* translation (methionine labelling) test is performed to confirm the mRNA active ingredient produces the SARS-CoV-2 S protein. The translated protein must be within the acceptable molecular weight range of ±10% before its release for supply.

Proline substitution: Numerous published studies and submitted data have shown that 2 proline substitutions stabilise the spike protein in its pre-fusion form. COVID-19 vaccines were designed to induce antibodies targeting the pre-fusion form of the spike protein to block the virus from attaching and entering human cells.

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Claims about the Quality of the COVID-19 Vaccines

ARGUMENT	EVIDENCE (QoNs ETC)
The mRNA vaccines are **contaminated with DNA**	• The first biotechnology products using recombinant DNA technology were marketed globally in the early 1980s. Residual DNA in these products has been a topic of international regulatory discussions since at least the 1990s. • Since 1996, the WHO, European Pharmacopoeia, and regulators including the US FDA and TGA have provided guidance on acceptable limits of residual DNA in medicines. All mRNA vaccines registered in Australia comply with these limits. • DNA is an approved starting material for biotechnology products, including recombinant proteins such as insulin, growth factors, cancer medicines, monoclonal antibodies, and vaccines. • Manufacturers take steps during the manufacturing process to digest and filter out DNA. • Residual DNA is present in small fragments in the final mRNA COVID-19 vaccines, in very small quantities (less than 10 ng per dose as recommended by the WHO, FDA, and other regulatory agencies). The limit is set for fragments over 200 base pairs to significantly reduce the chance that active genes are present. • The safe use of biological medicines in millions of patients for over 40 years shows that this technology is safe, and that residual DNA presents a low safety risk. • The plasmid DNA used to make mRNA vaccines does not contain oncogenes (genes that promote cancer). • The effectiveness of the manufacturing process to degrade and remove DNA is well established, with controls in place to monitor this from batch to batch. • All batches of mRNA vaccines supplied in Australia have met the established acceptable limits of residual DNA. This is confirmed as part of the vaccine batch release process prior to the release of the batch. Additionally, the TGA Laboratories has independently tested 13 recent batches of Spikevax (Moderna) and 14 recent batches of Comirnaty (Pfizer) COVID-19 mRNA vaccines for residual DNA. All batches tested to date have met the approved specification for residual DNA. **Previous responses (14)** SQ23-001075 – New Moderna bivalent vaccine SQ23-001111 – Kevin McKernan and batch testing results SQ23-002047 – COVID “vaccines” adulterated with plasmid DNA or similar substance SQ23-002048 – Pfizer Application Adulteration SQ23-002050 – Pfizer ‘vaccine’ clinical trial manufacture – (*refers to other QoNs).* SQ23-002051- Detection of plasmid DNA and SV40 sequence SQ23-002232 – SV40 promoter in production of vaccine SQ23-002089 – DNA and Covid-19 vaccine SQ24-000188 – DNA contamination *(includes response to particulate contamination)* SQ24-000206 – Presence of SV40 and other genes being in the DNA plasmid templates that were used to make the Pfizer Covid-19 vaccine SQ24-000245 – COVID-19 vaccines – Acceptable Safe Levels of DNA for Encapsulated DNA SQ24-001501 – PCR Tests SQ24-001497 – DNA toxicity and safety testing IQ24-000067 – Viral infection and genetic therapy products (DNA/RNA vaccines)

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Residual DNA: **Broadbent** letter to the PM	On 20 September 2024, Mr Russell Broadbent MP sent a letter entitled "Australians Deserve Answers" to the Prime Minister, with copies to Minister Butler, the TGA, and the Human Rights Commission. The letter alleges that mRNA vaccines have higher levels of residual DNA than the "TGA safety limit." Dr Julian Fidge commissioned this work from Dr. David Speicher via PJ O'Brien & Associates and requested testing using: • **qPCR** (the gold standard test) • **Fluorometry**, a test that does not comply with ICH Q2(R2) Validation of Analytical Procedures for specificity. The fluorometry method is unsuitable for detecting residual DNA because the fluorescent dye binds with both mRNA and DNA, resulting in an overestimation of DNA. Dr Speicher attempted to reduce the noise in this assay by using RNase, an enzyme that digests RNA, but did not perform validation studies to prove it is specific for DNA and not mRNA. Issues with the Speicher Testing: • **Results Interpretation**: The Broadbent letter claims that DNA levels are 145 times the TGA safety limit, based on the non-specific fluorometry method. Dr Speicher performed 18 runs of the qPCR test, showing the Moderna vial passed each run, while 6 of the runs on the Pfizer vials passed, 2 were marginal fails, and 4 failed. • **Small Sample Number**: Only two vials of Pfizer and one open, used vial of Moderna were tested. All vials had expired in mid-2022. • **Unknown Vial Provenance**: The affidavit includes only 4 hours of chain of evidence information (from FedEx). It is unknown where the vials were sourced or their location outside of those 4 hours and while they were being tested. Regulatory testing is conducted within tightly controlled frameworks to ensure traceability and certainty about the integrity and provenance of test samples. • **No Cold Chain**: The samples were shipped on dry ice, which had evaporated before arrival. There were no temperature loggers in the shipment. • **Unvalidated Method**: Methods for testing medicines are evaluated and approved by regulatory authorities, requiring evidence that the methods are suitable for their intended purposes. The guidelines used to assess test methods are *ICH Q2(R2) Validation of Analytical Procedures*, developed by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), which provide performance criteria that a test method must meet to demonstrate reliable and accurate results. These are some of the requirements used by the TGA and other regulators to assure the quality of results used to manufacture and release pharmaceutical products. • **Inappropriate Reference Material**: The reference material was not characterized. • **Laboratory Status**: The accreditation status of Dr Speicher's laboratory is unknown. This means his laboratory appears not to have either Good Manufacturing Practice certification, required by laboratories to perform approved testing of pharmaceuticals, nor accreditation to ISO 17025, the international standard for testing and calibration laboratories. Other Studies: • The TGA is aware of the studies linked in Mr Broadbent's letter. These studies have similar quality issues: incorrect and unvalidated methods

	used, and unknown sample provenance. The German publication used the incorrect fluorometry method. The other 2 articles have been pre-prints for more than 12 months, including the McKernan paper from the US. Pre-prints are papers that have not yet been peer-reviewed and have not been accepted for publication in a journal. The Canadian article is also a preprint but used qPCR, which showed that all vials had DNA below 10 ng per dose.
Residual DNA: **integration** into the human genome Paper by Alden et al 2022	SQ23-001077 – Genotoxicity tests on the Covid-19 vaccine SQ22-000355 – Genotoxicity studies performed on the vaccine SQ24-000224 – COVID-19 Vaccines – Testing *(includes a response to the Alden paper).* IQ24-000067 – Viral infection and genetic therapy products (DNA/RNA vaccines)
COVID vaccines are contaminated with the **SV40 virus**	The DNA plasmid template for the Pfizer vaccine contains the promoter gene from SV40. It does not contain the virus. SQ23-002051 – Detection of Plasmid DNA and SV40 Sequence SQ23-002232 – SV40 promoter in production of vaccine *(refers to SQ23-002051)*
COVID vaccines are contaminated with **particles**	The mRNA is contained in lipid nanoparticles. Contamination with other particles addressed in SQ24-000188 SQ23-001108 – Page 18 Pfizer nonclinical report Range of LNP size.
Covid-19 vaccines are contaminated with **endotoxin**	Endotoxin is bacterial cell wall fragments that cause adverse symptoms depending on the dose. The internationally accepted limit for endotoxin is 5 endotoxin units (EU) per kg for a parenteral product. Both mRNA manufacturers have set endotoxin limits lower than the recommended amount. TGA has tested every batch released in the government program for endotoxin and every batch has passed – the batches are lower than the limit of detection in our assay. SQ23-002231 – Validation data for the endotoxin LAL assay *(LAL is limulus amoebocyte assay - blood of the horseshoe crab).* SQ24-001566 – Batch testing for Pfizer and Moderna COVID-19 vaccines IQ24-000082 – Unsafe levels of endotoxin in COVID vaccines
Covid-19 vaccines are contaminated with **E. coli.**	All prescription medicines that are required to be sterile undergo a sterility evaluation prior to approval. SQ24-001566 – Batch testing for Pfizer and Moderna COVID-19 vaccines IQ24-000086 – Pfizer tested vaccine
Pfizer process 1 and process 2 / Commercial process Regulators waived through the change from the clinical scale to the commercial scale, introducing risks such as contamination with E. coli and endotoxin.	Previous responses (9) SQ23-001076 – Testing and quality control of manufacturing techniques. SQ23-002050 – refers to other answers SQ23-002091 – Pre-clinical and animal studies SQ23-002116 – Clinical trial and manufacturing of mRNA vaccines used by Pfizer SQ23-002225 – Placebo group participants who received the Process 2 vaccine SQ24-000143 – Pfizer testing SQ24-000144 – Indemnity to Pfizer for the manufacturing process of Covid vaccine SQ24-000229 – Linearised plasmid *(refers to other QoNs).* SQ24-001492 – Linearised plasmid DNA *(refers to other QoNs).*

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Pfizer employee vaccination program Either the Pfizer employees got "better" batches or the Pfizer employees were put at risk if these batches were not assessed by TGA	Pfizer requested permission from the Department and TGA to use small quantities of vials leftover after order fulfillment to vaccinate their own employees. There was no difference in manufacturing process between the batches used for the Australian rollout and the Pfizer employee program. Three batches were used in both programs. SQ23-001115 – batches not tested SQ23-001199 – Batch FD0927 - Testing SQ23-002114 – COMIRNATY – batch release assessment
The Covid-19 vaccines contain **tromethamine**	SQ22-000198 – Introduction of tromethamine to the Pfizer vaccine SQ23-001120 – Tromethamine risks
Batch release Pathway 1 and pathway 2	TGA really did test all batches (except 4 for the Pfizer employee vaccination program – however OCABR certificates were received and reviewed for these). SQ23-002145 – Batch testing of COVID-19 vaccine SQ24-001464 – Batch release assessment of COVID-19 vaccines.
Shelf life: extension and storage	• The TGA can only extend a shelf life if the sponsor of the product applies to the TGA and provides evidence demonstrating that the product remains stable and is of acceptable quality until the end of the new proposed shelf life. • The TGA's expert evaluators review the methods and materials used to produce the vaccines, as well as the testing methods and results used to determine the quality of the vaccine. The supporting stability testing data needs to demonstrate that the vaccine is stable and remains within approved specifications for the proposed extended shelf life and storage conditions. Evidence of stability and remaining within specifications means that the vaccine retains its safety characteristics. • The protocols Stability *testing for prescription medicines: 14.4 Biological medicines: specific requirements* are available publicly on the TGA website at: 14.4 Biological medicines: specific requirements | Therapeutic Goods Administration (TGA). • Additional testing after the initial expiry date is not conducted because the manufacturer must provide evidence to support both the initial shelf life and for any proposed extensions. SQ22-000118 – Extending the shelf life of vaccines SQ22-000591 – COVID-19 vaccine expiration dates SQ23-000344 – mRNA shelf-life extensions
FOI 4558 TGA is hiding testing data	Refer to the QoN: SQ23-001969 – Follow up to SQ22-000539 and FOI 4558 SQ23-002093 – (refers to SQ23-001969)
The Covid-19 vaccines are gene therapy	SQ23-000306 – TGA Act, Section 30C for advice from the Office of Gene Technology SQ23-002053 – Gene therapy mRNA products SQ23-002106 – Office of Gene Technology Regulator (OGTR) discretion and responsibility to conduct safety tests on COVID vaccine
Batch consistency	SQ23-001124 – mRNA contaminants and batch testing
Independent Testing	SQ21-001180 – COVID vaccine manufacturing SQ22-000155 – Contents of the Pfizer and AstraZeneca vaccine SQ22-000604 – Independent testing of vaccines
mRNA integrity	**RNA integrity**: COVID-19 mRNA vaccines have specifications in place for RNA integrity which includes limits on mRNA impurities and the requirement for a minimum amount of full-length mRNA be present to make the spike protein. In batch release studies where the vaccine is placed on cells, the amount of S protein produced has met specifications for every batch. No truncated or toxic proteins

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	were found. In animal toxicity studies using commercial vaccines no safety concerns were raised. SQ22-000274 – Variance between intact RNA and degraded mRNA SQ22-000539 – Batch testing and contamination/degradation

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Shelf Life – Current Fully and Provisionally Registered mRNA COVID-19 Vaccine

Product	Indication	Shelf life/ Conditions
Pfizer – COMIRNATY		
Full registration (Monovalent ONLY) and provisional registration (Bivalents)		
COMIRNATY (tozinameran) COVID-19 VACCINE 30 micrograms/0.3 mL concentrated suspension for injection vial *(PBS or TRIS formulations)* **– PBS formulation DEREGISTERED – TRIS formulation to be DEREGISTERED on expiry of all batches distributed**	12 years of age and over	Unopened vial: • **24 months at -90°C to -60°C.** • May be received frozen at -90°C to -60°C or at -25°C to -15°C. • Frozen vaccine can be stored either at -90°C to -60°C or 2°C to 8°C upon receipt. • Protect from light. • Once removed from frozen storage, the unopened vial may be stored refrigerated at 2°C to 8°C for a single period of up to 10 weeks within the 24-month shelf life. • Once thawed, COMIRNATY should not be re-frozen.
COMIRNATY (tozinameran) COVID-19 VACCINE 10 micrograms/0.2 mL concentrated suspension for injection vial **– To be DEREGISTERED on expiry of all batches distributed**	5 years to less than 12 years of age	
COMIRNATY (tozinameran) COVID-19 VACCINE 3 micrograms/0.2 mL concentrated suspension for injection vial **– To be DEREGISTERED on expiry of all batches distributed**	6 months to less than 5 years of age	
COMIRNATY ORIGINAL/OMICRON BA.1 (tozinameran/riltozinameran) COVID-19 VACCINE 15/15 micrograms/0.3 mL suspension for injection vial **– To be DEREGISTERED on expiry of all batches distributed**	BOOSTER ONLY 18 years of age and over	
COMIRNATY ORIGINAL/OMICRON BA.4-5 (tozinameran/famtozinameran) COVID-19 VACCINE 15/15 micrograms/0.3 mL suspension for injection vial	12 years of age and over	
COMIRNATY ORIGINAL/OMICRON BA.4-5 (tozinameran/famtozinameran) COVID-19 VACCINE 5/5 micrograms/0.2 mL concentrated suspension for injection vial	5 years to less than 12 years of age	
COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE 30 micrograms/0.3 mL suspension for injection multidose vial	12 years of age and over	
COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE 30 micrograms/0.3 mL suspension for injection single dose vial	12 years of age and over	
COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE 10 micrograms/0.2 mL concentrated suspension for injection multidose vial	5 years to less than 12 years of age	

COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE 10 micrograms/0.3 mL suspension for injection multidose vial	5 years to less than 12 years of age	
COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE 10 micrograms/0.3 mL suspension for injection single dose vial	5 years to less than 12 years of age	
COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE 3 micrograms/0.3 mL concentrated suspension for injection multidose vial	6 months to less than 5 years of age	
COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE 3 micrograms/0.2 mL concentrated suspension for injection multidose vial	6 months to less than 5 years of age	
COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE 30 micrograms/0.3 mL suspension for injection prefilled glass syringe	12 years of age and over	Unopened prefilled syringe: • **8 months at 2°C to 8°C.** • Store in original container. • Protect from Light. • Do not freeze refrigerate.
COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE 30 micrograms/0.3 mL suspension for injection prefilled plastic syringe	12 years of age and over	Unopened prefilled syringe: • **12 months at -90°C to -60°C.** • Protect from Light.
Moderna – SPIKEVAX		
Full registration		
SPIKEVAX (elasomeran) COVID-19 VACCINE 0.2 mg/mL suspension for injection vial	6 years and over	Unopened vial: • **9 months at -50°C to -15°C.** • 30 days at 2°C to 8°C, protected from light. Should not be re-frozen. • Once thawed should be stored at 2° to 8°C until use. • May be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions. • Do not store below -50°C. Unopened vials and syringes: • **9 months at -50°C to -15°C.** • May be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days. Should not be re-frozen. • May be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions. • Do not store below -50°C.
SPIKEVAX (elasomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection vial	Primary 6 years to <12 years of age Booster 18 years of age and over	
SPIKEVAX (elasomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection pre-filled syringe	BOOSTER ONLY 18 years of age and over	
SPIKEVAX BIVALENT ORIGINAL/OMICRON BA.4-5 (elasomeran/davesomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection vial	BOOSTER ONLY 12 years of age and over	
SPIKEVAX BIVALENT ORIGINAL/OMICRON BA.4-5 (elasomeran and davesomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection pre-filled syringe	BOOSTER ONLY 12 years of age and over	

SPIKEVAX XBB.1.5 (andusomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection vial - single-dose	12 years of age and over	
SPIKEVAX XBB.1.5 (andusomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection - pre-filled syringe	12 years of age and over	
Provisional registration		
SPIKEVAX (elasomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection vial	6 months to < 6 years of age	Unopened vial: • **9 months at -50°C to -15°C.** • 30 days at 2°C to 8°C, protected from light. Should not be re-frozen. • Once thawed should be stored at 2° to 8°C until use. • May be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions. Do not store below -50°C.
SPIKEVAX BIVALENT ORIGINAL/OMICRON (elasomeran/imelasomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection vial	BOOSTER ONLY 18 years of age and over	Unopened vials and syringes: • **9 months at -50°C to -15°C.** • May be stored refrigerated at 2°C to 8°C, protected from light, for a maximum of 30 days. Should not be re-frozen. • May be stored at 8°C to 25°C up to 24 hours after removal from refrigerated conditions. • Do not store below -50°C.

Division:	MDPQD
Cleared by:	
Contact Officer:	
Date:	

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Attachment A to COVID-19 Vaccines Lab Testing

Detailed Summary of COVID-19 Vaccines release through TGA batch release to 30 September 2024

COVID-19 vaccine	*Batches released*
Vaxzevria viral vaccine (AstraZeneca)	**206**
Spikevax mRNA vaccine (Moderna)	**58**
SPIKEVAX (elasomeran) COVID-19 VACCINE 0.2 mg/mL suspension for injection vial	*34*
SPIKEVAX (elasomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection vial	*2*
SPIKEVAX BIVALENT ORIGINAL/OMICRON (elasomeran and imelasomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection vial	*6*
SPIKEVAX BIVALENT ORIGINAL/OMICRON BA.4-5 (elasomeran/davesomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection pre-filled syringe	*10*
SPIKEVAX XBB.1.5 (andusomeran) COVID-19 VACCINE 0.1 mg/mL suspension for injection pre-filled syringe	*6*
Comirnaty mRNA vaccine (Pfizer)	**154**
COMIRNATY (tozinameran) COVID-19 VACCINE 10 micrograms/0.2 mL concentrated suspension for injection vial	*18*
COMIRNATY (tozinameran) COVID-19 VACCINE 30 micrograms/0.3 mL concentrated suspension for injection vial	*101*
COMIRNATY (tozinameran) COVID-19 VACCINE 30 micrograms/0.3 mL suspension for injection vial	*3*
COMIRNATY (tozinameran) COVID-19 VACCINE 3 micrograms/0.2 mL concentrated suspension for injection vial	*3*
COMIRNATY ORIGINAL/OMICRON BA.1 (tozinameran/riltozinameran) COVID-19 VACCINE 15/15 micrograms/0.3 mL suspension for injection vial	*8*
COMIRNATY ORIGINAL/OMICRON BA.4-5 (tozinameran/famtozinameran) COVID-19 VACCINE 15/15 micrograms/0.3 mL suspension for injection vial	*12*
COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE 30 micrograms/0.3 mL suspension for injection multidose vial	*5*

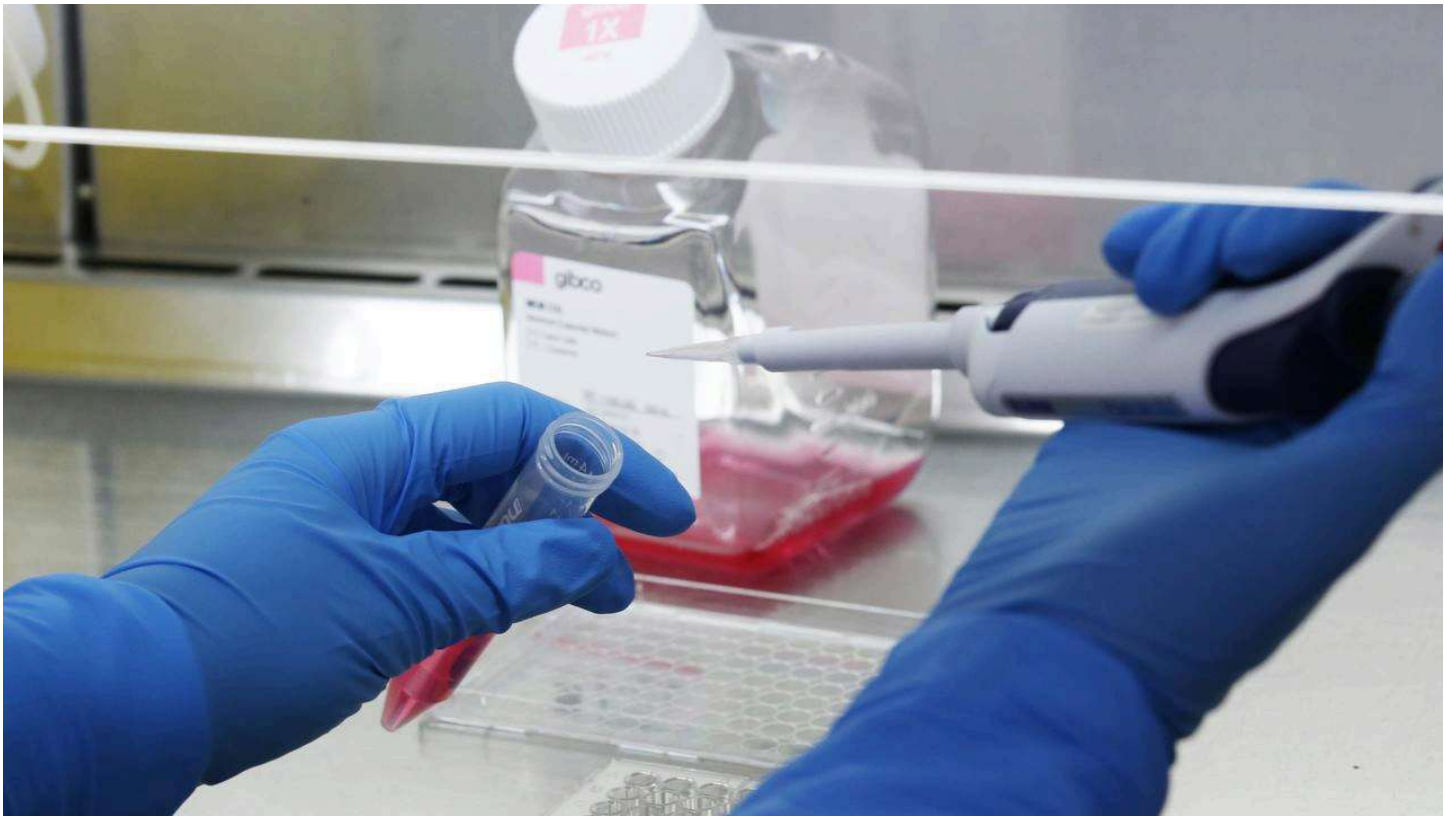
COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE 10 micrograms/0.3 mL suspension for injection multidose vial	*2*
COMIRNATY Omicron XBB.1.5 (raxtozinameran) COVID-19 VACCINE30 micrograms/0.2 mL concentrated suspension for injection multidose vial	*2*
Nuvaxovid protein vaccine (Novavax/Biocelect)	***11***
Totals	***429***

indicates bivalent batches

aap

A Swedish study did not say COVID vaccine changes human DNA

Nik Dirga March 17, 2022



A claim that a Swedish study of COVID-19 mRNA vaccine activity found it changed DNA is false. Image by AAP IMAGES

What was claimed

A university study shows that the Pfizer COVID-19 vaccine enters the nucleus of a human cell.

Our verdict

False. The study authors said this was not the finding of their work, which examined if mRNA from the vaccine could be changed into DNA in liver cancer cells.

A video being shared on social media claims that a recent study from a Swedish university shows that the Pfizer/BioNTech COVID-19 vaccine enters the nucleus of human cells and changes a person's DNA.

The study, however, has been widely misrepresented. The authors of the study made no finding that the vaccine has any effect on a person's genome and genetic researchers elsewhere have said the study is being distorted.

The claim is made In a video interview on a self-described "controversial" US podcast called "Flyover Conservatives", whi Share examines events "through the lens of Conservative, Christian values". The guest, American cardiologist Peter McCullough claims that "... a paper by Alden and colleagues, from Lund University in Sweden, in human hepatic cell lines has demonstr

that in fact the vaccine, the genetic code for the spike protein, doesn't just stay in the cytosol in the rough endoplasmic reticulum, in fact it goes into the human nucleus. And the belief is that it's a permanent installation into human DNA" (video mark 2min 8sec).

Dr McCullough has been repeatedly fact checked by other media over the sharing of COVID misinformation. He was sued by a former employer for using their name while continuing to promote controversial COVID theories.

The Lund University study, titled Intracellular Reverse Transcription of Pfizer BioNTech COVID-19 mRNA Vaccine BNT162b2 In Vitro in Human Liver Cell Line, explores how the Pfizer/BioNTech COVID vaccine could affect human liver cancer cells in petri dishes in laboratory conditions. The introduction of the study states that the authors "aim to examine the effect of BNT162b2 (also known as the Pfizer-BioNTech vaccine for COVID) on a human liver cell line in vitro and investigate if BNT162b2 can be reverse transcribed into DNA through endogenous mechanisms."

Reverse transcription is the process in cells through which an enzyme makes a copy of DNA (the molecule which carries genetic instructions in living organisms) from RNA (a similar molecule that can perform various tasks in regular genetic function or disease). For example, HIV uses reverse transcription to convert its RNA into viral DNA.

Endogenous means produced within an organ and cell line refers to cells specifically used for research purposes. Huh7, the cell line used in this study, derives from liver cancer tissue taken from a Japanese man in 1982.

The Pfizer vaccine uses messenger RNA (mRNA) technology. The mRNA vaccines cause the body to make a "spike protein" that triggers an immune response, according to the US Centers for Disease Control and Prevention (CDC). They do not alter your DNA, the Australian Department of Health and many other health authorities have repeatedly stated.

Experts point out that mRNA cannot enter the nucleus of a cell where DNA is stored. Claims about the Lund University study since its publication in late February have quickly been shared around the internet by organisations including the Epoch Times and then amplified on other sites.

A sentence that has been taken from Section 4 of the study and shared repeatedly online states: "Our study shows that BNT162b2 can be reverse transcribed to DNA in liver cell line Huh7, and this may give rise to the concern if BNT162b2-derived DNA may be integrated into the host genome and affect the integrity of genomic DNA, which may potentially mediate genotoxic side effects". The phrase "genotoxic side effects" has been highlighted in bold font.

The viral posts omit the next sentence, which explicitly states, "At this stage, we do not know if DNA reverse transcribed from BNT162b2 is integrated into the cell genome."

Dr Rhys Parry, a research fellow at the University of Queensland who studies viral evolution, said the study has been misinterpreted.

"The claim made on social media is false, and distorts the findings from the study," he said in an email to **AAP FactCheck**.

"The Lund study does not show that the vaccine mRNA enters the human nucleus at all. It only shows that reverse transcription of the mRNA has happened."

Two authors of the Lund University study, Associate Professor Yang de Marinis and Professor Magnus Rasmussen, have also released a Q&A in response to the attention their work has generated on social media.

"The results have in many cases been misinterpreted," they said.

"This study does not investigate whether the Pfizer vaccine alters our genome," de Marinis confirmed.

Prof Rasmussen also stated: "There is no reason for anyone to change their decision to take the vaccine based on this study."

The study was conducted in a laboratory on cells in a petri dish, which is not the same as a study on human subjects because "cell lines differ from cells in living organisms," Rasmussen wrote.

Dr Parry also said the Huh7 cell line is very different from healthy human cells.

"Huh-7 is an immortal, tumorigenic cell line," he said. "This is barely an appropriate system to make any claims of in healthy persons."

Other medical experts took issue with the Lund study's limited scope and results, including use of the Huh7 cell line, in an interview with the ABC.

Dr Parry said the study did seem to show that DNA was converted from the vaccine through reverse transcription into the liver cancer cell line system samples but it did not present evidence of it entering the cell nucleus as Dr McCullough claims in the video.

False claims that the COVID vaccines change DNA have been circulating for some time, and several have been previously debunked by **AAP FactCheck** here, here and here.

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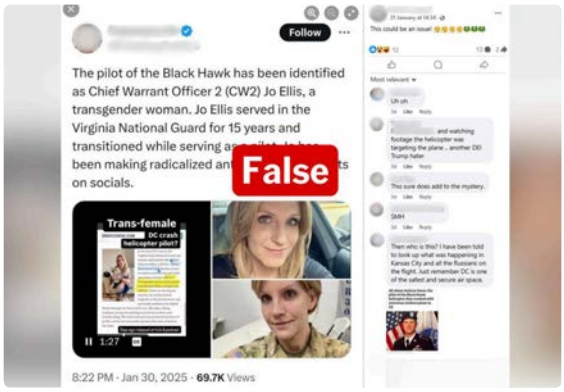

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There are no genetically modified organisms in the COVID-19 mRNA vaccines; no evidence these vaccines modify our DNA

CLAIM

Unapproved genetically modified organisms in the COVID-19 mRNA vaccines could permanently change our DNA

VERDICT

INACCURATE

DETAILS

Factually inaccurate: There are no genetically modified organisms in the COVID-19 mRNA vaccines.
Inadequate support: The studies cited to support the claim that vaccine mRNA can modify the human genome are unrelated to vaccination or didn't actually find any DNA modification. There's no reliable evidence showing that DNA in vaccines integrates into our DNA or increases the risk of cancer. In fact, several vaccines predating COVID-19 vaccines contain DNA, such as the chickenpox vaccine. These have been shown to be safe.

KEY TAKE AWAY

Concerns over the potential health effects of residual DNA in biological products like vaccines aren't new or unknown to regulatory agencies. Regulatory agencies like the U.S. Food and Drug Administration have recommended specific limits on the amount of residual DNA in a vaccine. DNA-containing vaccines, such as the chickenpox vaccine—a live attenuated vaccine containing a DNA virus—have also been widely used before the pandemic and have been shown to be safe.

FULL CLAIM: "Australian GP sues Pfizer and Moderna over unapproved GMOs in mRNA Covid vaccines. Dr Julian Fidge is seeking an injunction to stop the distribution of the mRNA Covid vaccines. But the human genome could already be permanently altered."; "In tests conducted on the mRNA monovalents and bivalents, genomics expert Kevin McKernan found dangerously excessive levels of DNA contamination"

REVIEW

In November 2023, Gentry Gevers, host of the Break Away USA podcast, posted a screenshot of a tweet (https://perma.cc/JL3Y-VLEU?type=image) by journalist Rebekah Barnett on Instagram that read "Australian GP sues Pfizer and Moderna over unapproved GMOs in mRNA Covid vaccines". It also claimed "the human genome could already be permanently altered".

The tweet is a brief summary of an article (https://web.archive.org/web/20231115131239/https://news.rebekahbarnett.com.au/p/australian-gp-sues-pfizer-and-moderna) published by Barnett in July 2023 on her blog Dystopian Down Under, revolving around a lawsuit (https://www.wangarattachronicle.com.au/health-news/local-gp-takes-vaccine-query-to-court) brought against Pfizer and Moderna by Australian primary care physician Julian Fidge. Fidge seeks to stop further distribution of the vaccines in Australia, alleging that the vaccines contain "unapproved GMOs". Both companies have challenged the injunction (https://www.wangarattachronicle.com.au/health-news/pfizer-moderna-challenge-wangaratta-doctors-injunction-on-medications).

Fidge has promoted ivermectin as a COVID-19 treatment (https://www.ausdoc.com.au/news/racgp-presidential-candidate-defends-proivermectin-campaign/), despite the lack of reliable clinical evidence (https://www.factcheck.org/2022/03/scicheck-evidence-still-lacking-to-support-ivermectin-as-treatment-for-covid-19/) to support this, and has posted (https://perma.cc/C3S8-VFEC) claims (https://perma.cc/VGS9-WMJ4) on social media suggesting that COVID-19 vaccines are

deadly. Fidge was banned from prescribing certain drugs of dependence in December 2022, after the Medical Board of Australia found his practice had enabled a patient's drug dependence, although this ban has been suspended following a temporary stay granted by an appeals court (https://www.perthnow.com.au/news/crime/gp-allowed-to-continue-prescribing-drugs-despite-ban-c-10475207).

In this review, we discuss a few of the primary claims present in the Barnett article and demonstrate why they are inaccurate and misleading.

There are no GMOs in COVID-19 mRNA vaccines

Health Feedback reached out to the Therapeutic Goods Administration, Australia's regulator for pharmaceutical products, regarding Fidge's claim about GMOs in the COVID-19 mRNA vaccines.

In an email, a spokesperson for the Office of the Gene Technology Regulator stated that:

> *"COVID-19 mRNA vaccines do not meet the definition of a GMO in the Gene Technology Act 2000 so do not require a licence from the Gene Technology Regulator. The vaccines do not contain a GMO."*

Australia's Office of the Gene Technology Regulator defines a GMO (genetically modified organism) as (https://www.ogtr.gov.au/about-ogtr/what-are-genetically-modified-organisms-gmos):

> - *"a plant, animal or other organism that has been modified using gene technology*
> - *an organism that has inherited modified traits from a GMO."*

COVID-19 mRNA vaccines don't contain organisms. As such, the claim that they contain "unapproved GMOs" is inaccurate. One example of a COVID-19 vaccine that *does* contain a GMO and is regulated as such (https://www.ogtr.gov.au/gmo-dealings/dealings-involving-intentional-release/dir-180) is the AstraZeneca-Oxford COVID-19 vaccine, as it uses a modified adenovirus vector to deliver the genetic material of the spike protein into cells.

While gene technology is also involved in making the COVID-19 mRNA vaccines, notably recombinant bacteria as we will explain below, the vaccines don't contain the bacteria themselves.

The role of GMOs in COVID-19 mRNA vaccine production

Developing certain desirable traits in plants and animals, such as seedless fruits and intelligence in working dogs, is a human practice that has spanned centuries. Before gene technology was developed however, humans relied on selective breeding (artificial selection) to achieve this aim.

Apart from making it easier and faster to achieve certain traits in plants and animals, gene technology has been indispensable to medical advances. For instance, large-scale production of human insulin (a sugar-regulating hormone) (https://www.yourhormones.info/hormones/insulin/) is possible thanks to such technology. Insulin is critical for people with type I diabetes (https://www.cdc.gov/diabetes/basics/what-

is-type-1-diabetes.html), whose bodies are unable to produce enough of the hormone. Type I diabetes can lead to fatal consequences (https://medlineplus.gov/ency/article/000305.htm) if untreated.

An article (https://diabetes.org/blog/history-wonderful-thing-we-call-insulin) by the American Diabetes Association explains that before this was possible, insulin from the pancreas of cattle and pigs was used for such patients, which occasionally led to allergic reactions.

Nowadays, we can obtain recombinant human insulin by inserting the genetic material encoding human insulin into a plasmid (a circular DNA molecule) (https://www.genome.gov/genetics-glossary/Plasmid), and then inserting the plasmid into the bacterium *Escherichia coli* or baker's yeast (*Saccharomyces cerevisiae*)[1]. The bacterial or yeast cells carrying the plasmid will then produce insulin.

The manufacturing process for COVID-19 mRNA vaccines shares some similarities with the process for making recombinant human insulin. The Pfizer vaccine manufacturing process was detailed in a New York Times article (https://www.nytimes.com/interactive/2021/health/pfizer-coronavirus-vaccine.html), explaining that the genetic material for the SARS-CoV-2 spike protein is mass-produced by inserting it into a plasmid, which is then inserted into *E. coli*.

E. coli divides every 20 minutes, provided laboratory conditions are optimal, allowing very large amounts of plasmid to be generated relatively quickly[2].

The DNA is then harvested from the bacteria and cut to isolate the segment containing the spike protein's genetic material. This segment is then transcribed into mRNA.

Because of the manufacturing process, a certain amount of DNA still gets left behind in the vaccine. Regulatory agencies, like the U.S. Food and Drug Administration (https://www.fda.gov/media/78428/download), have recommended limits on the amount of residual DNA in biological products like vaccines, as they are aware of potential health concerns related to residual DNA (https://twitter.com/anders_hviid/status/1716324269402038626).

However, Barnett's claim that there is a "dangerously excessive" level of residual DNA in COVID-19 mRNA vaccines, citing the findings of "genomics expert Kevin McKernan" as evidence, is inaccurate.

McKernan's findings about residual DNA were examined in two (https://healthfeedback.org/claimreview/claim-covid-19-mrna-vaccines-dna-contaminants-study-unknown-provenance-no-evidence-covid-19-mrna-vaccines-alter-dna-people/) reviews (https://healthfeedback.org/claimreview/regulatory-agencies-knew-residual-dna-covid-mrna-vaccines-no-evidence-health-concern/) from Health Feedback—in both reviews, we concluded that while McKernan and colleagues may have detected DNA in the vaccines, they offered no reliable evidence that the amount of DNA had exceeded the limits recommended by regulatory agencies. In fact, one of the tests performed by McKernan actually found that residual DNA levels in the Pfizer and Moderna vaccine vials tested were well below recommended limits, as we pointed out in this review (https://healthfeedback.org/claimreview/regulatory-agencies-knew-residual-dna-covid-mrna-vaccines-no-evidence-health-concern/).

No evidence that COVID-19 mRNA vaccines modify our DNA

Misinformation surrounding the presence of DNA in vaccines has existed long before the COVID-19 pandemic, as an early Health Feedback review (https://healthfeedback.org/evaluation/article-claiming-vaccines-cause-autoimmunity-and-autism-due-to-fetal-dna-contaminants-found-unsupported-and-implausible-theresa-deisher/) documented. Like early iterations of such misinformation, Barnett's article plays up fears that COVID-19 vaccine mRNA can modify our DNA, citing various studies that purportedly support this claim.

She cited a study allegedly showing the "Pfizer Covid vaccine mRNA is able to enter the human liver cell line and reverse transcribe into DNA in vitro". However, this study (https://doi.org/10.3390/cimb44030073), conducted by Alden *et al.*[3] at Lund University in Sweden, comes with major caveats, which Health Feedback reported on in March 2022 (https://healthfeedback.org/claimreview/study-lund-university-didnt-show-covid-19-mrna-vaccines-change-dna-epoch-times/).

Experts pointed out that the experimental system used was artificial, as the researchers used a liver cancer cell line, which is more likely to overproduce an enzyme used for reverse transcription (making DNA from RNA) compared to healthy cells. The researchers also used much higher doses of vaccine in the experiment than the dose administered to adults.

Furthermore, the study didn't find reverse-transcribed DNA entering the nucleus, much less integrating into the cells' DNA.

Barnett also went on to cite two other studies purportedly supporting the claim. But a closer reading of these studies indicates that neither study shows vaccine mRNA modifying the human genome. In fact, one is a preprint (https://www.biorxiv.org/content/10.1101/2022.09.27.509633v1.full) (a research paper that hasn't yet been peer-reviewed) showing spike mRNA in the nucleus of human cells *during infection*, not vaccination.

The other study (https://doi.org/10.1371/journal.ppat.1010830) found that mice could inherit certain immunological traits from their parents that had been injected with lipid nanoparticles[4]. This type of nanoparticle is used to encase vaccine mRNA.

However, the researchers didn't find that the lipid nanoparticles had modified the mice's DNA. Instead, they proposed that this was the result of DNA methylation:

> *"The mechanism of inheritance also remains to be determined. Likely, it is partially mediated through DNA methylation changes that interferons and other inflammatory cytokines might have induced in this case. DNA methylation-based mode of inheritance has recently been proposed with the transgenerational inheritance observed with pre-exposure to different pathogens."*

DNA methylation (https://www.genome.gov/genetics-glossary/Methylation) involves a reversible chemical change to the DNA strand and is an example of epigenetics. Epigenetics affect how our genes work, without changing the underlying sequence of our DNA (https://www.cdc.gov/genomics/disease/epigenetics.htm). In the case of methylation, methyl groups are added to the DNA strand. The methyl groups typically block proteins that are needed for gene expression, thus turning the gene "off".

Although these changes don't affect the underlying DNA sequence, epigenetic changes can still be transmitted from parent to child. In fact, these changes have been proposed as an explanation for the increased risk of certain metabolic diseases in children (https://www.nytimes.com/2018/01/31/science/dutch-famine-genes.html) born to women who experienced poor nutrition in pregnancy. Notably, studies of people (https://www.ohsu.edu/school-of-medicine/moore-institute/dutch-famine-birth-cohort) affected by the Dutch famine at the end of World War II greatly advanced this aspect of our understanding of epigenetics and its role in health[5,6].

No evidence that the level of residual DNA in vaccines poses a health risk

Even if residual DNA were to make it into our cells, there's no evidence indicating this would integrate into our genes. As the Vaccine Education Center of the Children's Hospital of Philadelphia explained here (https://www.chop.edu/centers-programs/vaccine-education-center/vaccine-ingredients/dna), for DNA to integrate into our genome, the DNA would not only have to enter the nucleus, the enzyme called integrase is also needed, which isn't present.

There are also other obstacles. Marc Veldhoen (https://scholar.google.co.uk/citations?user=7vG1jLIAAAAJ&hl=en), an immunologist and professor at the University of Lisbon, took to X/Twitter to explain why DNA in COVID-19 mRNA vaccines doesn't trigger concerns about health.

He highlighted the fact that there are already a number of vaccines in use that contain DNA (https://twitter.com/Marc_Veld/status/1715321287017431064), such as the COVID-19 adenovirus vector vaccines, as well as the chickenpox vaccine (the virus for chickenpox is a DNA virus). There's no evidence that these vaccines are associated with a greater risk of developing cancer.

He added:

> *"Like DNA or RNA vaccines, vaccines using attenuated or killed pathogens work from a similar principle. The DNA/RNA gets into your cells, and protein from the pathogen is made. Important(sic), DNA/RNA vaccines cannot amplify nor do they generate infectious material."*

In all these cases, DNA would make it into our cells. However, our cells have multiple ways to detect foreign DNA and destroy it (https://journals.physiology.org/doi/full/10.1152/physiol.00022.2019), since our immune system sees foreign DNA as a sign of infection[7-9]. This would eventually lead the affected cells to die by programmed cell death (apoptosis) (https://www.genome.gov/genetics-glossary/apoptosis) and the removal of the cell, proteins, DNA, and RNA left behind.

"So no, even with scare stories about SV40 enhancers, the DNA or RNA does not get into the nuclei, it certainly does not integrate, the cell dies. It detects DNA or RNA, and it dies. It makes foreign protein, and it dies, i.e.; no matter what, the cell dies," Veldhoen concluded (https://twitter.com/Marc_Veld/status/1715321399173075254).

It is also worth keeping in mind that if exposure to DNA alone were sufficient to produce DNA changes, then gene therapy (altering people's genes to cure a disease) would be a lot easier to accomplish than it actually is

(https://learn.genetics.utah.edu/content/genetherapy/challenges).

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COVID-19 (https://healthfeedback.org/tag/covid-19/) DNA (https://healthfeedback.org/tag/dna/) GMOs (https://healthfeedback.org/tag/gmos/) Vaccine (https://healthfeedback.org/tag/vaccine/)

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Contrary to viral claim, regulatory agencies knew of residual DNA in COVID-19 mRNA vaccines; no evidence this poses health concern

CLAIM

Regulatory agencies didn't know of residual DNA contamination in COVID-19 RNA vaccines; residual DNA could integrate into our DNA and cause cancer

VERDICT

INACCURATE

DETAILS

Factually inaccurate: Health Canada stated that it was aware of residual DNA in COVID-19 mRNA vaccines before the vaccines were authorized. A dossier submitted by BioNTech to the European Medicines Agency in 2020 also showed that data on residual DNA was made known to the regulator.

Unsupported: There's no reliable evidence showing that DNA in vaccines integrates into our DNA or increases the risk of cancer. There are, in fact, several vaccines predating COVID-19 vaccines containing DNA, such as the chickenpox vaccine. These have been shown to be safe.

KEY TAKE AWAY

Concerns over the potential health effects of residual DNA in biological products like vaccines aren't new or unknown to regulatory agencies. In fact, recommended guidelines for acceptable levels of residual DNA were already established by the World Health Organization and the U.S. Food and Drug Administration prior to the COVID-19 pandemic. Vaccines containing DNA, such as the chickenpox vaccine—a live attenuated vaccine containing a DNA virus—have also been widely used before the pandemic and have been shown to be safe.

FULL CLAIM: "You can now sue the mRNA COVID vaccine manufacturers for damages and the FDA is required to take the COVID vaccines off the market. Why? Adulteration. The plasmid bioactive contaminant sequences were NOT pointed out to the regulatory authorities."; "Health Canada on Thursday confirmed the presence of DNA contamination in Pfizer COVID-19 vaccines and also confirmed that Pfizer did not disclose the contamination to the public health authority"

REVIEW

A preprint (https://archive.md/yVHQL) posted on 20 October 2023 to the OSF preprint server claimed that DNA fragments were present in certain lots of the Pfizer and Moderna COVID-19 vaccines. It also claimed the amount of residual DNA correlated with the number of serious adverse events associated with particular vaccine lots, suggesting that the adverse events may have been caused by residual DNA.

This is the latest spin on an earlier claim that DNA contamination in COVID-19 mRNA vaccines posed a cancer risk, which went viral in June 2023. This claim was based on an April 2023 preprint (https://archive.ph/wXc78), claiming to show that the Pfizer COVID-19 mRNA vaccines contained a DNA sequence from the SV40 virus. SV40 virus has been found to cause cancer in some animals like hamsters. The April preprint was already discussed at length in an earlier review (https://healthfeedback.org/claimreview/claim-covid-19-mrna-vaccines-dna-contaminants-study-unknown-provenance-no-evidence-covid-19-mrna-vaccines-alter-dna-people/). Based on the available evidence, Health Feedback concluded the claims were unsubstantiated.

Incidentally, an Epoch Times article (https://perma.cc/H3YA-RCW6?type=image) that appeared just one day before the October 2023 preprint claimed that the Canadian drug regulator Health Canada "says Pfizer did not disclose the presence of the Simian Virus 40 (SV40) DNA sequence",

citing the claims from the April preprint. The Epoch Times has published misinformation about COVID-19 and vaccines (https://open.feedback.org/Media/DY) on numerous occasions.

The two preprints, combined with the Epoch Times article, renewed discussions on social media about the potential implications for residual DNA in vaccines.

Unsurprisingly, social media posts from individuals and groups known to be opposed to vaccination—such as this tweet (https://web.archive.org/web/20231023021942/https://twitter.com/stkirsch/status/17158208385 by entrepreneur Steve Kirsch (https://www.mcgill.ca/oss/article/critical-thinking/steve-kirsch-and-seduction-simplicity), this article (https://web.archive.org/web/20231022005202/https://childrenshealthdefense.org/defender/ca dna-contamination-pfizer-covid-vaccine/) by Children's Health Defense (https://www.npr.org/sections/health-shots/2021/06/08/1004214189/anti-vaccine-film-targeted-to-black-americans-spreads-false-information), and this article (https://web.archive.org/web/20231020233329/https://www.rebelnews.com/health_canada_s_s by Rebel News (https://www.theguardian.com/australia-news/2022/feb/11/avi-out-the-uncomfortable-relationship-between-rebel-news-and-australias-anti-vaccine-protesters)—seized on the article to claim that residual DNA contamination wasn't disclosed by vaccine manufacturers and imply that the residual DNA in the COVID-19 vaccines was harmful. Some related (https://web.archive.org/web/20231023042300/https://twitter.com/jesslovesmjk/status/171496 posts (https://web.archive.org/web/20231023130116/https://twitter.com/FreeWCH/status/1714637440 were tagged with the hashtag #PlasmidGate—implying that the preprint's findings about residual DNA in COVID-19 vaccines were revelatory and a scandal.

To help readers understand whether these claims are supported by the evidence, this review will discuss the work performed in the October 2023 preprint, the implications of its findings, and whether there's reason to believe residual DNA in the vaccines poses a significant health concern, as some social media posts implied.

What did the authors of the October 2023 preprint do?

The October 2023 preprint was a follow-up of the results reported in the April 2023 preprint by McKernan *et al.* It set out to measure the level of DNA in several vials of Pfizer and Moderna COVID-19 vaccines, belonging to different lots used in Canada.

Residual DNA present in the COVID-19 mRNA vaccine is a result of the process used to make the vaccine. The Pfizer COVID-19 mRNA vaccine is manufactured (https://www.nytimes.com/interactive/2021/health/pfizer-coronavirus-vaccine.html) by mass producing the genetic material for the SARS-CoV-2 spike protein in the bacterium *Escherichia coli*. This is accomplished by placing the spike protein's genetic material into a plasmid, which is a circular DNA molecule (https://www.genome.gov/genetics-glossary/Plasmid), which is replicated by *E. coli*.

E. coli divides every 20 minutes (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6015860/), provided laboratory conditions are optimal, meaning that very large amounts of plasmid can be generated in a relatively short amount of time[3].

The DNA is then harvested from the bacteria and cut so that the segment containing the spike protein's genetic material is isolated so that it can be transcribed into mRNA.

The authors of the preprint used two different methods for measuring DNA levels: quantitative PCR—which is also the gold standard (https://www.knoxnews.com/story/news/health/2020/10/26/pcr-tests-scientific-gold-standard-covid-19/3712380001/) for detecting SARS-CoV-2 infection—and fluorometry, which uses fluorescent markers that bind to nucleic acids like DNA. The main findings of the preprint centered on the measurement of the spike protein DNA inserted into a plasmid, as well as the DNA marking the origin of replication (https://teaching.ncl.ac.uk/bms/wiki/index.php/Origin_of_replication) (*ori*) on the plasmid.

The authors also wanted to explore the question of whether residual DNA levels correlated with the number of adverse events in the U.S. Vaccines Adverse Event Reporting System.

Per the preprint's Method section, they collected VAERS data related to the vaccine lots that they had analyzed, although they limited the reports to only those from outside the U.S. The reason given for limiting their analysis only to reports outside the U.S. was that they wished to reduce the level of confounding as a result of differences in adverse event reporting rate due to potential underreporting and mandatory reporting requirements within and outside the U.S. No reason was given for why the authors considered data from outside the U.S. to be less affected by differences in reporting rate.

The preprint didn't find concerning levels of residual DNA in COVID-19 vaccines

One of the preprint's key takeaways is that the levels of residual DNA detected in the vaccine vials using qPCR were actually *well below* the World Health Organization (https://www.who.int/docs/default-source/biologicals/vaccine-quality/69-molecular-methods-final-mtg-report-april2005.pdf) and U.S. Food and Drug Administration (https://www.fda.gov/media/78428/download)'s recommended limit of 10 ng DNA/dose. The preprint acknowledged this, stating that "qPCR residual DNA content in all vaccines were below [guidelines set by FDA and WHO of 10 ng/dose]".

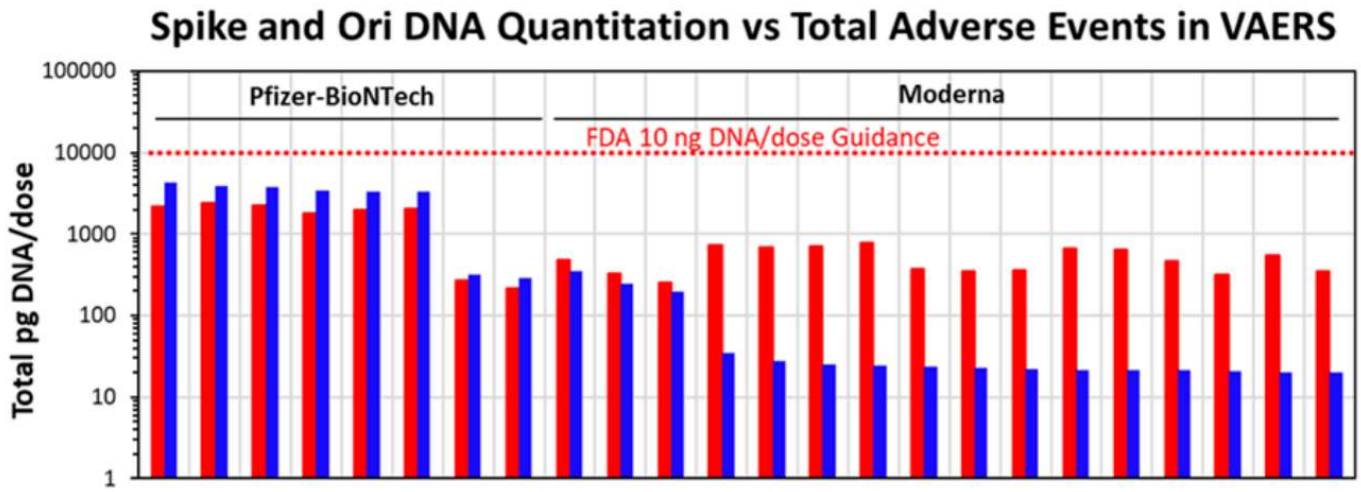

Figure 1 *– The quantity of spike DNA (red) and plasmid DNA (blue) corresponding to the origin of replication* (https://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1008320) *(the region on the plasmid where DNA replication begins) in each of the vials tested. One picogram (pg) is a thousandth of a nanogram. Note that the y-axis is on a log scale, not a linear scale.*

However, the measurement of DNA levels using fluorometry seemed to greatly contrast with the findings of the qPCR tests. The authors reported that this method showed the quantity of DNA in the vaccines exceeded the WHO and FDA guidelines by more than 188 to 509 times.

While this seems alarming, the caveat here is that fluorometry is less specific than qPCR, as the fluorescent marker (https://biotium.com/product/accugreen-high-sensitivity-dsdna-quantitation-kit/) that the authors used can also bind RNA as well as DNA (https://biotium.com/faqs/how-specific-is-the-quantitation-to-dsdna/). This limitation is important to account for, given that the vaccine vials contained a mix of DNA and RNA.

In this article (https://www.respectfulinsolence.com/2023/10/21/vaers-and-plasmid-dna-contamination-of-covid-19-vaccines-the-nonsense-continues/), David Gorski (https://cancerbiologyprogram.med.wayne.edu/profile/dz8037), a surgical oncologist and cancer researcher at Wayne State University, pointed out that the vaccine samples had to be treated with high heat at 95°C before DNA quantification. The heat would have disrupted the lipid nanoparticles encasing the RNA, releasing the RNA into the solution. "When there is a lot more RNA than [double-stranded DNA], even a highly selective assay could be affected by the RNA," he concluded.

Mikael Niku (https://researchportal.helsinki.fi/en/persons/mikael-niku), a senior university lecturer at Helsinki University who studies host-microbial interactions, wrote to Kevin McKernan, one of the preprint's authors, on X/Twitter, raising the same issue: "The fluorometry kit you used is NOT specific for DNA. Biotium tech support says it's only '10X or more selective' for DNA over RNA and you should use it for *clean* dsDNA preparations".

One of the preprint's authors, Kevin McKernan, responded to this criticism (https://archive.md/U9EXb) by pointing to how Pfizer had used fluorometry to measure RNA levels in their vaccine.

Niku countered that (https://perma.cc/8PSY-9JWK) "Fluorometry is completely valid when you're measuring the concentration of the MAJOR nucleic acid of the solution, which obviously is RNA in [Pfizer's] case".

Simply put, the apparently massive amount of DNA detected by fluorometry could have been due to the high level of free RNA in the sample—as expected in an mRNA vaccine—and not DNA.

Gorski suggested that the authors could have checked to see if this was the case by treating the samples with the enzyme RNase, which breaks down RNA, and then measuring the level of DNA using fluorometry afterwards. But the authors didn't report doing so, thus we cannot rule out this possibility.

Next, the authors' attempt to correlate the number of serious adverse event reports from VAERS with the amount of DNA detected in the vaccine lots tested also raises some questions.

As Gorski pointed out, there were too few data points (four or five in most cases) to draw a reliable correlation in the first place.

For example, the graph showing Pfizer data is interpreted as showing that the proportion of serious adverse events rose with the amount of DNA detected by qPCR, even though one shouldn't trust a correlation with so few data points (Figure 2). But in the case of Moderna,

having more spike DNA is interpreted with a line showing more SAEs, while having more DNA from the plasmid's origin of replication (ori) is interpreted with a line showing fewer SAEs.

So in addition to not being reliable, as they are based on too few data points, these trend lines are inconsistent with one another.

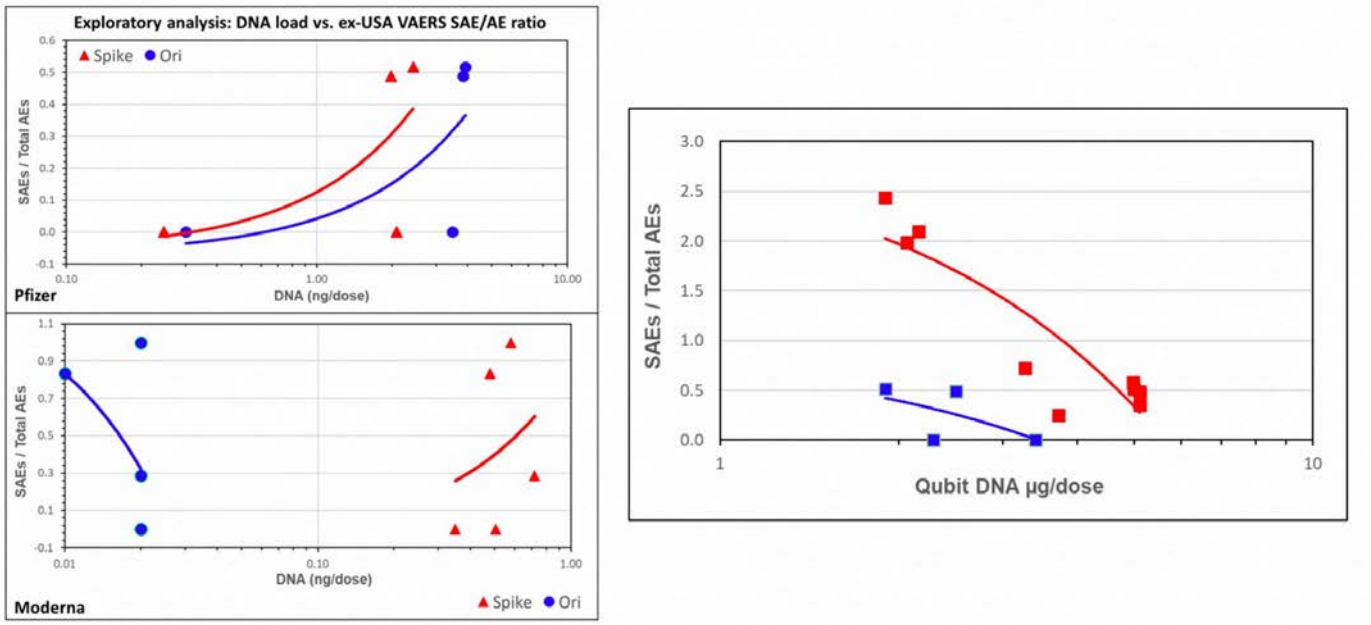

Figure 2 *– Figures allegedly showing correlations of the amount of DNA detected by qPCR (left) and Qubit fluorometric assay (right) with the number of serious adverse events (as a proportion of total adverse events). Left: The red line corresponds to spike DNA while the blue line corresponds to plasmid DNA. The top graph shows results from the Pfizer vaccine and the bottom graph shows results from the Moderna vaccine. Right: The blue line corresponds to Pfizer, the red line to Moderna. Source: Speicher et al.*

And the correlation that used fluorometry-derived DNA measurements suggested that the more the residual DNA present in the vaccine, the *fewer* the serious adverse events. No acknowledgement of this result was made in social media posts that relied on the preprint to claim residual DNA would be harmful.

We reached out to the authors of the preprint with questions about the methods they used via email. In his email response, David Speicher (https://scholar.google.com/citations?user=JurLYgIAAAAJ&hl=en), the corresponding author of the preprint and a senior research associate at the University of Guelph, didn't answer our questions in writing, offering instead to do so via a Zoom call. He added that the authors would "take [our] interesting questions into consideration for clarification in future versions of the manuscript".

Regulatory agencies were aware of residual DNA in COVID-19 vaccines prior to the preprint, didn't find evidence for concern

Despite the assumptions made by certain social media posts, concerns over the potential health effects of DNA in vaccines are neither new nor unknown (https://twitter.com/anders_hviid/status/1716324269402038626) to regulatory agencies, as various (https://www.who.int/groups/global-advisory-committee-on-vaccine-safety/topics/residual-cellular-dna-in-vaccines#cms) publications (https://www.sciencedirect.com/science/article/abs/pii/S0264410X20300396) predating

(https://www.fda.gov/files/vaccines,%20blood%20&%20biologics/published/Guidance-for-Industry--Considerations-for-Plasmid-DNA-Vaccines-for-Infectious-Disease-Indications.pdf) the COVID-19 pandemic demonstrate.

Based on a publicly available document submitted by BioNTech (https://www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-report_en.pdf) to the European Medicines Agency (EMA), dated 19 February 2021, we know that part of the vaccine manufacturing process involves treating batches of the resulting RNA with an enzyme called DNase. This enzyme digests DNA, breaking it into fragments. Thus both BioNTech and the EMA were aware of DNA impurities in the vaccine and of steps taken to reduce this impurity.

It's incorrect to claim that regulatory agencies were unaware of residual DNA in the COVID-19 mRNA vaccines until now, as the same document submitted to the European Medicines Agency indicated that residual DNA was among the impurities quantified by the manufacturer ("Process- and product-related impurities including host cell genomic DNA, RNA, proteins, endotoxins, bioburden and plasmid isoforms, for the plasmid DNA, are routinely quantified").

Emails released by The Epoch Times (https://web.archive.org/web/20231024152802/https://twitter.com/NChartierET/status/1716579 also show that Health Canada was "aware of the presence of residual plasmid DNA as a process-related impurity during review and prior to the authorisation of the mRNA COVID-19 vaccines".

However, this part of Health Canada's response didn't appear in the Epoch Times article, which provided room for the inaccurate claim that regulators were unaware of residual DNA in the COVID-19 vaccines, put about by Kirsch, Children's Health Defense, Rebel News, and others.

In its response to The Epoch Times (https://web.archive.org/web/20231024152802/https://twitter.com/NChartierET/status/1716579 Health Canada also added that "the release testing data for every COVID-19 vaccine lot released into the Canadian market were reviewed and deemed to meet the requirement approved by Health Canada".

In brief, the claim that regulatory agencies like Health Canada hadn't known about residual DNA in COVID-19 vaccines or that vaccine manufacturers didn't disclose the presence of residual DNA in the vaccines is inaccurate.

We reached out to Health Canada and the FDA for comment regarding these claims.

In response to our questions about DNA contamination in the COVID-19 vaccines, Health Canada said in a statement:

> *"As a regulator, Health Canada sets quality standards and requirements for manufacturers to follow, including providing comprehensive and detailed information about the vaccine itself, and about the manufacturing process. In the manufacture of any vaccine, residual elements that are part of the standard manufacturing process may remain. There are strict limits and controls for the presence of these residual fragments to ensure that there is no effect on the safety or effectiveness of the vaccine.*
>
> ***The Pfizer-BioNTech COVID-19 vaccine does not contain simian virus 40 (SV40). The presence of the SV40 promoter enhancer sequence is not the same as the presence of the whole virus itself.***
>
> *The SV40 promoter enhancer sequence was found to be a residual DNA fragment in Pfizer-BioNTech COVID-19 vaccine. The fragment is inactive, has no functional role, and was measured to be consistently below the limit required by Health Canada and other international regulators."*

It also added that "[a]ny claims that the presence of the SV40 promoter enhancer sequence is linked to an increased risk of cancer are unfounded". We have provided Health Canada's full statement at the end of our review.

The FDA informed us via email that our questions had been forwarded to the Center for Biologics Evaluation and Research (CBER), which regulates biologically derived products including vaccines, and would follow up with a response as soon as possible. We will update this review if new information becomes available.

No evidence that residual DNA in COVID-19 mRNA vaccines poses a health risk

Much talk of the potential health effects of residual DNA in the vaccines has revolved around the possibility that the DNA could integrate into our genome and cause diseases like cancer. However, this isn't substantiated by evidence.

Health Canada's response to The Epoch Times (https://web.archive.org/web/20231024152802/https://twitter.com/NChartierET/status/1716579[illegible] stated that "the DNA plasmid used for the Pfizer vaccine production is linearised, degraded, and reduced in quantity through additional steps. There is no peer-reviewed evidence that linearised or fragmented DNA is capable of translocating to the nucleus of cells". This part of the response wasn't included in the Epoch Times article.

In a tweet (https://archive.ph/Qbct1), McKernan suggested that even small bits of DNA from regulatory elements, like the SV40 promoter, could still pose a risk of DNA integration, citing FDA guidance (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2847045/pdf/nihms162389.pdf)[4]. However, this misses significant context given in the guidance:

> *"In evaluating the potential harm of plasmid integration, it should be noted that the risk of introducing plasmids with strong regulatory regions into the host genome far exceeds that associated with random point mutations […] In this context, sections of DNA as short as 7 bp can affect rates of integration or recombination.* ***Examples include the VDJ recombination signal sequence and related sequences, chi-like elements and minisatellites, ALU sequences, a recombinase signal present in hepatitis B and mammalian genomes, and topoisomerase II recognition sites.****" [emphasis added]*

Several of these given examples all have to do with regulatory elements that are very short to begin with. For example, V(D)J recombination sequences are between seven to nine base pairs long (https://www.nature.com/articles/35014635)[5]. Minisatellites range between 10 to 50 base pairs (https://www.wur.nl/en/article/minisatellites.htm). The SV40 promoter, on the other hand, spans more than 300 base pairs (https://web.archive.org/web/20231025095550/https://www.snapgene.com/plasmids/basic_clc It's doubtful whether it would still retain biological activity after it was broken down into smaller pieces.

Moreover, even if residual DNA were to make it into our cells, there's also no evidence indicating this would lead to integration. Marc Veldhoen (https://scholar.google.co.uk/citations?user=7vG1jLIAAAAJ&hl=en), an immunologist and professor at the University of Lisbon, took to X/Twitter to highlight the fact that there are already a number of vaccines in use that contain DNA (https://twitter.com/Marc_Veld/status/1715321287017431064), such as the COVID-19 adenovirus vector vaccines, as well as the chickenpox vaccine (the virus for chickenpox is a DNA virus). There's no evidence that these vaccines are associated with a greater risk of developing cancer.

He added:

> *"Like DNA or RNA vaccines, vaccines using attenuated or killed pathogens work from a similar principle. The DNA/RNA gets into your cells, and protein from the pathogen is made. Important(sic), DNA/RNA vaccines cannot amplify nor do they generate infectious material."*

In all these cases, DNA would make it into our cells. However, our cells have multiple ways to detect foreign DNA and destroy it (https://journals.physiology.org/doi/full/10.1152/physiol.00022.2019), since our immune system sees foreign DNA as a sign of infection[6-8]. This would eventually lead the affected cells to die by programmed cell death (apoptosis) (https://www.genome.gov/genetics-glossary/apoptosis) and the removal of the cell, proteins, DNA, and RNA left behind.

"So no, even with scare stories about SV40 enhancers, the DNA or RNA does not get into the nuclei, it certainly does not integrate, the cell dies. It detects DNA or RNA, and it dies. It makes foreign protein, and it dies. i.e.; no matter what, the cell dies," he concluded (https://twitter.com/Marc_Veld/status/1715321399173075254).

Health Canada's statement in response to Health Feedback's questions about DNA contamination in COVID-19 vaccines

"Health Canada initially authorized the Pfizer-BioNTech COVID-19 mRNA vaccine in December 2020 and subsequently has authorized updated versions, including the most recent vaccine targeting the XBB Omicron subvariant in September 2023. Each assessment included a determination that the vaccine met the Department's stringent regulatory safety, efficacy and quality requirements for use in Canada.

As a regulator, Health Canada sets quality standards and requirements for manufacturers to follow, including providing comprehensive and detailed information about the vaccine itself, and about the manufacturing process. In the manufacture of any vaccine, residual elements that are part of the standard manufacturing process may remain. There are strict limits and controls for the presence of these residual fragments to ensure that there is no effect on the safety or effectiveness of the vaccine.

The Pfizer-BioNTech COVID-19 vaccine does not contain simian virus 40 (SV40). The presence of the SV40 promoter enhancer sequence is not the same as the presence of the whole virus itself.

The SV40 promoter enhancer sequence was found to be a residual DNA fragment in Pfizer-BioNTech COVID-19 vaccine. The fragment is inactive, has no functional role, and was measured to be consistently below the limit required by Health Canada and other international regulators.

Any claims that the presence of the SV40 promoter enhancer sequence is linked to an increased risk of cancer are unfounded. There is also no evidence to support that the presence of the full SV40 in any vaccine increases the risk of cancer or the acceleration of cancer in individuals.

Health Canada continues to monitor the COVID-19 vaccines to ensure that they continue to meet the highest standards for safety, effectiveness and quality and that their benefits continue to outweigh any potential risks."

UPDATE (28 October 2023):

We updated our review to include responses from the preprint's corresponding author, Health Canada, and the FDA. This information was added to the twenty-seventh and thirty-sixth paragraphs. The full statement by Health Canada was also appended to the end of the review.

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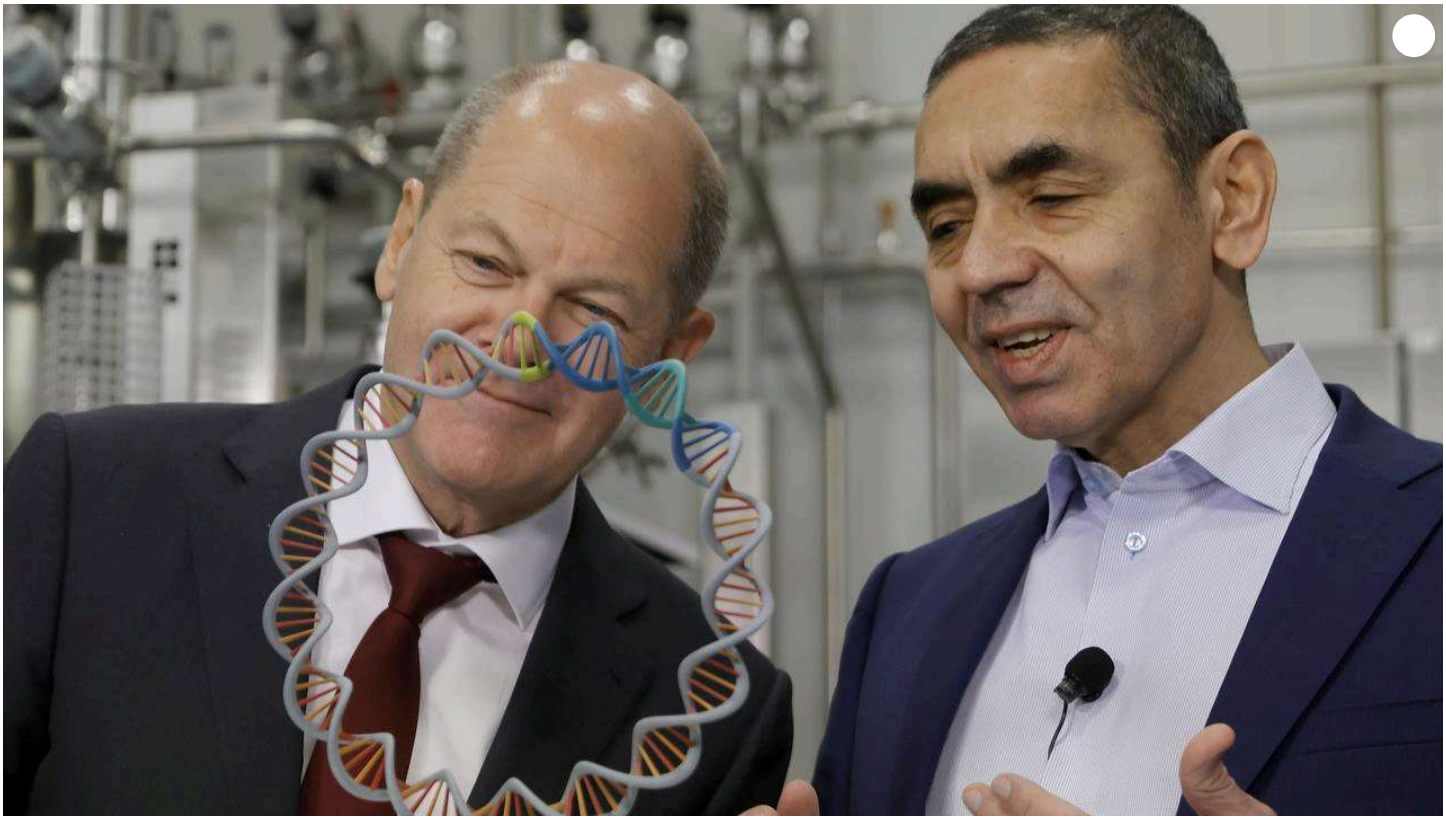
Senate hearing used to propel vaccine DNA fears

David Williams January 08, 2024



A biologist's findings about DNA in vaccines are being misrepresented on social media. Image by EPA PHOTO

What was claimed

A biologist has revealed the Pfizer COVID-19 vaccine contains 200 billion pieces of dangerous DNA.

Our verdict

Misleading. The biologist said any risk of harm is theoretical and untested. Health agencies have said there is no evidence that any DNA in the vaccine causes harm.

It is being claimed a US molecular biologist has revealed the Pfizer COVID-19 vaccine contains 200 billion pieces of dangerous DNA.

This is misleading. The biologists in question said the risk from any residual DNA in the vaccine is only theoretical. Experts and various health bodies have said there is no evidence to link DNA in the vaccines to adverse events.

Various claims relating to "dangerous" DNA in the vaccine have been made in recent months, including in this post (arcl here). Share

"The Pfizer shot contains 200 billion (dangerous) pieces of foreign DNA," the post reads.

It links to a video of a senate hearing in the US state of South Carolina from September 2023, which the post says features molecular biologist Professor Phillip Buckhaults "exposing this monumental crime".

The post links to the professor's senate hearing. (Facebook)

Prof Buckhaults claims the Pfizer vaccine is "contaminated with plasma DNA" (3mins 32secs).

While presenting a slide (13mins 45secs), he says each shot has about 200 billion pieces of plasmid DNA encapsulated in the lipid nanoparticle.

Lipid nanoparticles are an emerging vehicle for gene delivery, which is the way the vaccines are transferred to cells.

Prof Buckhaults also speculates that DNA in the jab could be the cause of rare but serious side effects (4mins 44secs).

He also claims there is a "theoretical risk of future cancer".

However, the molecular biologist makes clear his claims are theoretical and haven't been tested (18 mins).

Prof Buckhaults repeated that point in a post on X, previously Twitter, on September 24, 2023.

"The DNA is real, however the risk of this DNA is theoretical. There is no need to panic about past vaccination," he wrote in the post.

Prof Buckhaults said his senate hearing comments were targeted at regulators and industry experts, not the general public, and had resulted in "totally inappropriate anxiety".

"IMO (in my opinion), these vaccines saved a lot of lives. Far more than the number of people who have had medical events subsequent to vaccine," he added.

Pfizer has said there is zero evidence to support the claim. (Con Chronis/AAP PHOTOS)

"So overall, these vaccines were a win. However, those who experienced harm deserve to have scientists and regulators look carefully at possible causes. Even if the adverse events turn out to have nothing to do with the vaccine..."

In another tweet in October, he said: "I study a scientific mechanism that might explain *rare* events. There are currently no documented cases of the Pfizer vaccine causing cancer. I study the possibility just to make sure that it can't ever happen...do not use my research topic or my video to create fear or panic or anxiety in others just to get attention on social media."

Prof Buckhaults did not respond to a set of questions sent by **AAP FactCheck**.

The European Medicines Agency (EMA) says residual fragments of plasmid DNA used in templates for the mRNA vaccine are supposed to be broken down and removed during the manufacturing process.

"The DNA template is not intended to be part of the final mRNA vaccines; however, very small amounts of residual bacterial DNA fragments may still be present," an EMA spokesperson told **AAP FactCheck** in an email.

However, the European regulator said it had not seen any reliable evidence of an association between mRNA vaccines and adverse events that could be linked to the presence of DNA material.

"Nor are we aware of any scientific evidence showing that the very small amounts of residual DNA that may be present in vaccine batches could integrate into the DNA of vaccinated individuals," the EMA spokesperson added.

The US Food and Drug Administration (FDA) has also said there is no evidence of any risk.

"With over a billion doses of the mRNA vaccines administered, no safety concerns related to the sequence of, or amount of, residual DNA have been identified," the federal vaccine regulator told **AAP FactCheck** in an email.

"While concerns have been raised previously as theoretical issues, available scientific evidence supports the conclusion that the vaccines are safe and effective."

Australia's Therapeutic Goods Administration (TGA) said residual DNA is a "manufacturing impurity" found in very low levels in many medicines and vaccines.

Many millions of Australians have received the Pfizer COVID-19 vaccine. (Albert Perez/AAP PHOTOS)

The regulator said while there is a theoretical possibility the residual DNA may be encased in lipid nanoparticles, it is not aware of any scientific evidence that this occurs in practice.

"There is also no scientific evidence that residual DNA alters the human genome. The safe use of biological medicines in millions of patients for over 40 years shows that this technology is safe and residual DNA presents a low safety risk," a TGA representative told **AAP FactCheck** in an email.

The TGA said the World Health Organization, European Pharmacopeia and regulators including the FDA have provided guidance on the acceptable limits of total residual DNA, and all mRNA vaccines registered in Australia comply with these limits.

Pfizer also told **AAP FactCheck** in a statement that there is "no evidence" to support the claim.

Similar claims have been debunked by other fact-checking organisations here, here, here, here and here.

Leading health bodies told **AAP FactCheck** there is no evidence to support claims residual DNA in the vaccine is dangerous.

Misleading – The claim is accurate in parts but information has also been presented incorrectly, out of context or omitted.

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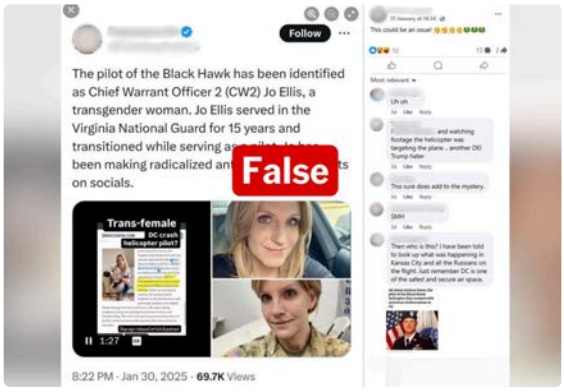

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Claim that COVID-19 mRNA vaccines contain DNA contaminants based on study of vials of “unknown provenance”; no evidence COVID-19 mRNA vaccines can alter DNA in people

CLAIM

DNA in COVID mRNA shots “may have the ability to alter the human genome”; “SV40 has been linked to cancer in humans”; “Regulatory Agencies Knew There Was a Contamination Problem”

VERDICT

MISLEADING

DETAILS

Misleading: While SV40 is known to cause cancer in certain animals like hamsters, epidemiological studies didn’t find an elevated risk of cancer in people who received SV40-contaminated polio vaccine.
Inadequate support: Neither the preprint by McKernan et al. nor the other studies cited in

the article provided evidence for the claim that COVID-19 mRNA vaccines contained significant DNA contamination or that the vaccines can alter DNA in people. The analysis underpinning this claim was performed on vials of unknown origin.

KEY TAKE AWAY

To date, claims that COVID-19 mRNA vaccines can alter DNA in people lack a biologically plausible mechanism to explain how this would happen. A certain proportion of polio vaccine administered between the 1950s and 1960s were contaminated with the virus SV40, which can cause tumors in animals. However, epidemiological studies since then haven't detected a higher risk of cancer in people who received the polio vaccine at that time period.

FULL CLAIM: "SV40 has been linked to cancer in humans"; "The finding of DNA [in COVID-19 mRNA vaccines] means the mRNA COVID shots may have the ability to alter the human genome"; "Cytoplasmic transfection can also allow for genetic manipulation, as the nucleus disassembles and exchanges cellular components with the cytosol during cell division"; "Regulatory Agencies Knew There Was a Contamination Problem"

REVIEW

On 11 June 2023, The Epoch Times republished an article (https://web.archive.org/web/20230616101141/https://www.theepochtimes.com/health/green-monkey-dna-found-in-covid-19-shots_5317587.html) by osteopath Joseph Mercola, which carried the headline "Monkey Virus DNA Found In COVID-19 Shots". The article claims that a group of scientists had found "massive DNA contamination in the mRNA COVID-19 shots, including simian virus 40 (SV40) promoters"; that "SV40 has been linked to cancer in humans"; and that "The finding of DNA means the mRNA COVID shots may have the ability to alter the human genome".

The same article was also republished by the website Discern Report (https://web.archive.org/web/20230614030001/https://discernreport.com/green-monkey-dna-found-in-covid-19-shots/). Both articles together accrued more than 10,000 engagements on social media to date, according to the social media analytics tool CrowdTangle. However, the article's content is misleading and the claims are unsubstantiated by evidence, as we will explain below.

Preprint finding of DNA contamination in COVID-19 vaccine used vials of unknown origin

The article's claims draw heavily on a preprint (https://osf.io/b9t7m/) (a study not yet peer-reviewed) authored by McKernan *et al.*, a group of scientists at Medicinal Genomics, a company that offers nucleic acid sequencing services.

In the preprint, the authors claimed that they detected DNA in the Pfizer-BioNTech COVID-19 vaccine and in particular a particular gene sequence originating from the simian virus 40 (SV40) [1]. The gene sequence is known as a promoter, which can enhance expression of a gene that is located after the promoter. The U.S. National Human Genome Research Institute explains more about the role of promoters in this article (https://www.genome.gov/genetics-glossary/Promoter#:~:text=A%20promoter%2C%20as%20related%20to,initiate%20transcription%20c It is this finding that forms the basis for the article's claim that COVID-19 mRNA vaccines could modify DNA and increase cancer risk.

However, one of the most significant limitations is that the vials tested were of "unknown provenance" and the authors explained that the vials had been sent to them "anonymously in the mail without cold packs" but that the vials were "unopened". Simply put, whether the vials were actually of COVID-19 mRNA vaccines and the integrity of the contents is questionable. The Epoch Times article simply glossed over this fact, discussing the preprint findings as conclusive evidence of DNA contamination when this is far from certain.

Michael Imperiale (https://medicine.umich.edu/dept/microbiology-immunology/michael-j-imperiale-phd), a professor at the University of Michigan who studies DNA tumor viruses, told Health Feedback in an email that the results are far from establishing that DNA contamination of COVID-19 mRNA vaccines is widespread. "Since this article has not been peer reviewed, we don't know if there was truly significant DNA contamination," he explained. *[Read Imperiale's feedback in full here.]*

The Epoch Times also asserted that "Regulatory Agencies Knew There Was a Contamination Problem", based on a Substack article (https://web.archive.org/web/20230613083357/https://anandamide.substack.com/p/dsdna-variance-in-pfizer-docs) by the preprint's first author, and that "Data submitted to the EMA by Pfizer shows sampled lots had anywhere from 1 ng/mg to 815 ng/mg of DNA".

It's important to note that the upper limit of 815 ng DNA/mL RNA came from a lot that had been treated with the incorrect DNase stock, as the footnote on the report clearly showed, resulting in more residual DNA left in the vaccine. This fact however, is glossed over by The Epoch Times.

Were we to exclude that value, the highest value would be 211 ng DNA/mL RNA, which is within the "commercial acceptance criterion" of the European Medicines Agency (≤330 ng DNA/mg RNA) stated in the report.

Furthermore, vaccine vials with significant residual DNA levels exceeding that criterion wouldn't be used for vaccination in the first place. This would also be the case in the U.S., Imperiale pointed out.

Others (https://twitter.com/dr_jon_l/status/1666263196116590594) also (https://twitter.com/Debunk_the_Funk/status/1667301119872188417) pointed out that since quantifying residual DNA levels is based on a measurement relative to RNA levels, vials that

weren't stored properly are likely to experience significant RNA degradation. In contrast, DNA would be more stable and less likely to degrade. This could produce spurious results as DNA levels could thus be much higher than RNA levels by the time the analysis was conducted.

No evidence to date that SV40 causes cancer in humans

The claim that SV40 is associated with cancer harkens back to early reports of SV40 contamination in polio vaccines that were used between the 1950s and 1960s. SV40 is a DNA virus that is found in both monkeys and humans, and has been reported to cause cancer in some animals, such as hamsters[2,3].

The U.S. Centers for Disease Control and Prevention (CDC) explains (https://www.cdc.gov/vaccinesafety/concerns/concerns-history.html):

> *"From 1955 to 1963, an estimated 10-30% of polio vaccines administered in the US were contaminated with simian virus 40 (SV40). The virus came from monkey kidney cell cultures used to make polio vaccines at that time. Most of the contamination was in the inactivated polio vaccine (IPV), but it was also found in oral polio vaccine (OPV). After the contamination was discovered, the U.S. government established testing requirements to verify that all new lots of polio vaccines were free of SV40."*

The news of the contamination therefore led to concerns (https://www.science.org/doi/10.1126/science.298.5594.725b) that people who'd received the polio vaccine during that time period could be at a higher risk of cancer.

Several epidemiological studies have since been performed on populations that received the polio vaccine during that time period. These didn't find a heightened risk of cancer in these people[4-7], which is inconsistent with the claim that SV40 increases cancer risk. Health Feedback covered this subject in an earlier review (https://healthfeedback.org/claimreview/claim-that-virus-contaminating-polio-vaccine-between-1955-and-1963-is-cancer-causing-not-supported-by-science/). The Children's Hospital of Philadelphia also addresses this subject in this article (https://www.chop.edu/centers-programs/vaccine-education-center/vaccine-ingredients/sv40).

In 2002, the U.S. Institute of Medicine published a review (https://doi.org/10.17226/10534) on the relationship between SV40 and cancer[8]. In its Executive Summary, it concluded:

> *"Although SV40 has biological properties consistent with a cancer-causing virus, it has not been conclusively established whether it might have caused cancer in humans. Studies of groups of people who received polio vaccine during 1955–1963 provide evidence of no increased cancer risk. However, because these epidemiologic studies are sufficiently flawed, the Institute of Medicine's Immunization Safety Review Committee concluded that the evidence was inadequate to conclude whether or not the contaminated polio vaccine caused cancer."*

There are a few things to keep in mind here. Firstly, the preprint claimed to have found only a fragment of the SV40 genome (the promoter), not the full virus. The preprint's lead author told AP News (https://apnews.com/article/fact-check-COVID-vaccine-monkey-virus-DNA-922368719320) that "that's not the same as finding the full SV40 virus in the shot". And it is the virus that has been associated with cancer in animals, not the promoter fragment alone.

Secondly, the polio vaccine contamination with SV40 was the result of using monkey kidney cells to grow the polio virus used to manufacture the vaccine. The making of the Pfizer-BioNTech COVID-19 mRNA vaccine on the other hand, doesn't involve such cell cultures (https://www.nytimes.com/interactive/2021/health/pfizer-coronavirus-vaccine.html), raising questions about the origin of the alleged SV40 contamination detected by the scientists.

No plausible mechanism for COVID-19 mRNA vaccines to alter DNA

The Epoch Times article cited the preprint's first author Kevin McKernan (https://scholar.google.com/citations?user=WKED1_sAAAAJ&hl=en), formerly the R&D lead for the MIT Human Genome Project and currently chief scientific officer at Medicinal Genomics, who stated that "the concern that people, even at the FDA, have noted in the past whenever injecting double-stranded DNA, is that these things can integrate into the genome". The Epoch Times article also claimed that "the finding of DNA means the mRNA COVID-19 vaccine may alter the human genome".

The claim that COVID-19 mRNA vaccines can alter our DNA is an enduring one that can be traced all the way back to 2020, when the vaccines were under development. Scientists interviewed by Health Feedback explained that there's no known biological mechanism that allows COVID-19 mRNA vaccines to alter DNA; their comments were included in these two (https://healthfeedback.org/claimreview/contrary-to-popular-claim-on-social-media-rna-vaccines-do-not-alter-our-dna/) reviews (https://healthfeedback.org/claimreview/inaccurate-clickbait-headline-forbes-article-used-to-promote-false-claim-that-covid-19-vaccines-change-our-dna/).

The Epoch Times article however offered a new twist to this claim, proposing that it is DNA contaminants in the vaccine, particularly the SV40 promoter, rather than the spike mRNA, that can modify our DNA.

But "there is no evidence that the SV40 promoter can act as a so-called insertional mutagen, i.e., integrate next to a cellular oncogene and activate its expression," Imperiale told Health Feedback.

The Epoch Times article cited microbiologist Sucharit Bhakdi (https://healthfeedback.org/claimreview/unsubstantiated-claims-by-michael-palmer-sucharit-bhakdi-dont-demonstrate-covid-19-vaccines-harm-organs/), who claimed that "cytoplasmic transfection", during which the membrane surrounding the nucleus of the cell (where DNA is housed) is dissembled during cell division (mitosis (https://www.genome.gov/genetics-glossary/Mitosis)), can "allow for genetic manipulation".

However, Imperiale pointed out that "since the vaccine is delivered into muscle, which contains mostly post-mitotic cells, the idea of cytoplasmic-nuclear mixing does not apply". Post-mitotic cells –common examples include nerve cells and skeletal muscle cells– are generally understood to no longer undergo mitosis.

Preprint author's reaction to our request for comment

We reached out to McKernan to ask for clarification regarding his claim that SV40 promoters could integrate into the human genome. McKernan didn't respond to our email, but posted our email on Twitter.

In his Twitter thread (https://perma.cc/TKK8-7ZNT?type=image), McKernan alleged Health Feedback is "obsessed with reducing population levels"; incorrectly claimed that we'd asserted only retroviruses can integrate into the human genome; and cited a PNAS article (https://www.pnas.org/doi/pdf/10.1073/pnas.2105968118) as evidence to support his claim, stating that "If non-retrovirus mRNA can integrate, DNA is even easier".

The PNAS article (https://www.pnas.org/doi/pdf/10.1073/pnas.2105968118) in question, authored by Zhang *et al.*, detected parts of the SARS-CoV-2 genome integrated into the genome of an immortalized human cell line (cells that can proliferate indefinitely like HeLa cells (https://www.hopkinsmedicine.org/henriettalacks/importance-of-hela-cells.html)), following infection by SARS-CoV-2[9].

The authors reported that this integration was facilitated through the LINE-1 retrotransposon system, which is present in the human genome. Health Feedback discussed the LINE-1 retrotransposon system in greater detail in this review (https://healthfeedback.org/claimreview/study-lund-university-didnt-show-covid-19-mrna-vaccines-change-dna-epoch-times/) regarding a claim based on a study by Alden *et al.*

One caveat is that the PNAS study used genetically modified human cells that overexpress LINE-1 (https://www.deplatformdisease.com/blog/reverse-transcription-of-sars-cov-2-into-the-genome-a-brief-update?), whereas normal human cells don't, which raises questions about how likely the effect observed in the study would occur in people.

The PNAS article generated controversy in the scientific community, as other scientists reported being unable to replicate the results[10], raising questions about the generalizability and reliability of the findings.

McKernan also cited a 1999 study by Dean *et al.* (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4152905/), which reported that including certain parts of the SV40 promoter on a plasmid (https://www.genome.gov/genetics-glossary/Plasmid) (a circular extrachromosomal DNA molecule) improved the movement of the plasmid into the nuclei of monkey kidney cells growing in cell culture and led to improved gene expression (https://www.genome.gov/genetics-glossary/Gene-Expression#:~:text=Gene%20expression%20is%20the%20process,molecules%20that%20serve%20o of genes on the plasmid. However, it didn't show the plasmid integrating into the genome of the cells. The study offers no evidence that integration in the context of vaccination occurs.

In brief, McKernan's Twitter thread contained no answers regarding our questions. Instead, he asked Twitter users to "address [our] questions".

It is worth noting that in February 2023, Zhang *et al.* (the authors of the PNAS article cited by McKernan) published a study (https://www.mdpi.com/1999-4915/15/3/629) in the journal Viruses, which followed up on their earlier findings regarding LINE1-mediated SARS-CoV-2 integration into human DNA. They examined both SARS-CoV-2-infected cells and mRNA-transfected cells for signs that SARS-CoV-2 mRNA had integrated into the cells' DNA. The mRNA-transfected cells serve as a model for what happens in mRNA vaccination, albeit imperfectly.

They found that while virus-infected cells showed signs of SARS-CoV-2 integration into the human genome, cells transfected with mRNA from the virus didn't[11].

The authors concluded that "Retrotransposition in virus-infected cells, in contrast to transfected cells, may be facilitated because virus infection, in contrast to viral RNA transfection, results in significantly higher viral RNA levels and stimulates LINE1 expression by causing cellular stress."

A press release (https://wi.mit.edu/news/new-research-supports-finding-explaining-why-some-patients-may-test-positive-covid-19-long) by the Whitehead Institute also pointed out the same finding:

> "*The researchers found that transfection of SARS-CoV-2 mRNA did not lead to genomic integration in the same way that infection did. Infection naturally produces a large amount of viral RNA and causes an inflammatory response in cells. Such cellular stresses increase the level of the reverse transcription machinery. Transfection does not do this, and correspondingly, the researchers found no evidence with TagMap that it led to viral genomic integration by LINE1 in normal cells.*"

Rudolf Jaenisch (https://wi.mit.edu/people/member/jaenisch), a senior author of both the PNAS and Viruses studies and a co-founder of the Whitehead Institute, stated that "our results are consistent with vaccine RNA not integrating", although he cautioned that further research using the actual mRNA vaccine was still needed.

McKernan didn't mention this study in his Twitter thread reacting to our email.

Conclusion

In summary, the Epoch Times article's proposal that DNA contaminants in COVID-19 mRNA vaccines pose a risk of DNA modification and cancer isn't substantiated by sufficient evidence. While a preprint claimed DNA contaminants were present in an alleged vial of Pfizer COVID-19 mRNA vaccine, this finding came from a vial of unknown origin. Yet this fact is glossed over and the preprint finding is discussed as conclusive evidence of contamination despite this significant limitation.

The preprint also offered no evidence that COVID-19 mRNA vaccines cause DNA alterations nor a plausible mechanism for this to occur, and the Epoch Times article's claim that SV40 is associated with cancer is misleading, as studies so far haven't shown that this association is a causal one.

SCIENTISTS' FEEDBACK

Michael J Imperiale (https://cancerbio.medicine.umich.edu/michael-imperiale-phd), Professor, Department of Microbiology and Immunology, University of Michigan:
Let me preface my answer with the caveat that since this preprint has not been peer reviewed,

we don't know if there was truly significant DNA contamination. I am certain that the FDA does not allow the release of lots of vaccine that have such contamination.

There is no evidence that the SV40 promoter can act as a so-called insertional mutagen, i.e., integrate next to a cellular oncogene and activate its expression. Moreover, since the vaccine is delivered into muscle, which contains mostly post-mitotic cells, the idea of cytoplasmic-nuclear mixing does not apply. Next, even if the DNA entered the nucleus, integration of any plasmid into the cell genome would be an extremely rare event. And finally, since these cells are expressing a viral antigen (the SARS-CoV-2 Spike protein), they will be destroyed by the immune system.

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HEALTH

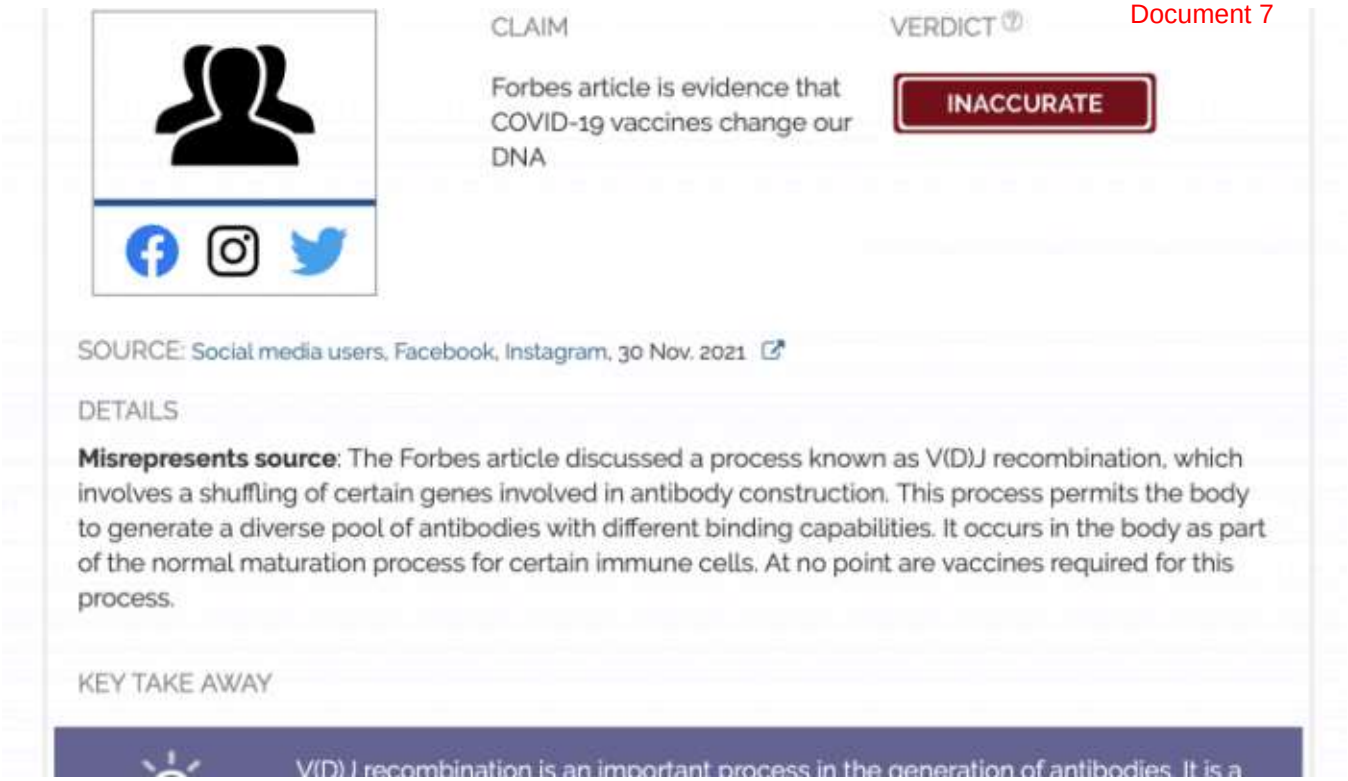
Inaccurate clickbait headline in Forbes article used to promote the false claim that COVID-19 vaccines change our DNA

2021-12-02

KEY TAKEAWAY

V(D)J recombination is an important process in the generation of antibodies. It is a normal part of the maturation of certain immune cell groups. During V(D)J recombination, DNA segments that are involved in antibody production are cut up and rearranged in random fashion to generate a wide range of combinations that serve as unique blueprints for antibody production. This process is behind the diversity of our body's antibody repertoire and helps the immune system to respond to different kinds of disease-causing microorganisms.

REVIEWED CONTENT



Verdict: INACCURATE

Claim: Forbes article is evidence that COVID-19 vaccines change our DNA

Source: Facebook, Instagram, Social media users, 2021-11-30

VERDICT DETAIL

Misrepresents source: The Forbes article discussed a process known as V(D)J recombination, which involves a shuffling of certain genes involved in antibody construction. This process permits the body to generate a diverse pool of antibodies with different binding capabilities. It occurs in the body as part of the normal maturation process for certain immune cells. At no point are vaccines required for this process.

SEE OUR METHOD OF EVALUATION

FULL CLAIM

> Forbes article is evidence that COVID-19 vaccines change our DNA

Review

On 29 November 2021, Forbes published an article written by Steven Salzberg, a professor of biomedical engineering at Johns Hopkins University, bearing the headline "Yes, The Vaccine Changes Your DNA. A Tiny Bit. That's A Good Thing". The article's headline was disseminated on social media by individuals who previously spread vaccine misinformation, viewing the article as mainstream validation for the false claim that COVID-19 vaccines alter DNA (see examples of posts here and here).

Following criticism, Forbes changed the headline later to read "Covid Vaccines Don't Alter Your DNA – They Help Choose Cells To Strengthen Your Immune Response". Nevertheless, the archive of the original article and screenshots of the original headline alone continued to circulate. For some like Dino Veletanlic, who previously spread false claims about election fraud, the change in headline was simply evidence that mainstream media was conspiring to cover up the "truth".

As Health Feedback explained in a previous review, COVID-19 mRNA vaccines don't alter our DNA. One reason is because DNA and RNA are chemically different from each other, which poses a barrier to integration. There were some who claimed that DNA alterations with mRNA vaccines could occur with the help of an enzyme called reverse transcriptase, which converts RNA to DNA. While this may be plausible under artificial conditions like in a laboratory, the likelihood of such an event occurring in the human body is extremely remote, as neither the COVID-19 mRNA vaccines nor human cells carry reverse transcriptase.

The Forbes article didn't provide evidence that COVID-19 vaccines alter our DNA; in fact, the original headline of the Forbes article inaccurately described what was discussed in the article, specifically the process known as V(D)J recombination. This is a normal part of development for certain types of immune cells, specifically B and T cells, and that occurs independently of vaccination, as virologist Angela Rasmussen explained in a Twitter thread.

Document 7

Dr. Angela Rasmussen
@angie_rasmussen · **Follow**

Tell me you don't understand immunology without telling me you don't understand immunology.

Vaccines do not change your DNA, indirectly or "a tiny bit."

He's referring to V(D)J recombination, which occurs normally. It's fundamental to our immune system.

1:09 AM · Dec 1, 2021

1.4K **See the latest COVID-19 information on X**

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The name V(D)J recombination is derived in part from the names of the gene segments that encode the amino acid sequence for different parts of an antibody: V for variable, D for diversity, and J for joining (Figure 1).

Figure 1. The gene segments involved in V(D)J recombination. From the British Society of Immunology website.

Figure 2. A general schematic of the structure of an antibody. The antigen binding site is the area that makes contact with a pathogen. From the University of Arizona's Biology Project.

The process is highly complex, but to put briefly and simply, during V(D)J recombination, the DNA making up these gene segments are cut up and then rearranged in random fashion. As shown in Figure 1, only one gene segment each from the V, D, and J groups make it into the final product. In theory, this process can generate millions of unique combinations that serve as blueprints for antibody production[1]. And the ability of an antibody to bind to a pathogen will vary depending on the combination of these segments. Thus, V(D)J recombination is a key

process that contributes to the body's wide repertoire of antibody diversity that is needed to tackle different pathogens.

At no point does this process involve vaccination. As we explained above, V(D)J recombination is part of the maturation process for B and T cells and takes place all the time; in humans, the process occurs in the bone marrow for B cells and the thymus for T cells. Indeed, Salzberg wrote that "[T]o be more precise, as an immunologist colleague explained to me: the vaccine doesn't change any DNA, even in your immune cells, but it causes the proliferation of certain immune cells that have already undergone genetic rearrangement".

To use an analogy, we can think of V(D)J recombination as the "arms manufacturer" of the body's immune system; vaccination allows the immune system to test out which weapons would be most effective against the enemy (pathogen), and to selectively deploy only those weapons in the event that it encounters the enemy.

In summary, the original Forbes article headline inaccurately described the process of V(D)J recombination, leading many to misinterpret it as a validation of the false claim that COVID-19 vaccines alter our DNA. While the Forbes headline was later corrected, it didn't prevent this false claim from continuing to circulate, and even promoted conspiratorial thinking among others.

Scientists' Feedback

[This comment comes from an evaluation of a related claim.]

Sanjay Mishra
Staff Scientist, Vanderbilt University Medical Center

While there is a theoretical possibility of DNA (or RNA) vaccines causing autoimmunity or that the DNA would integrate into the human genome, pre-clinical testing and careful clinical monitoring have shown DNA vaccines not only do not induce or worsen auto-immunity, they in fact therapeutically benefit in autoimmune diseases such as diabetes mellitus and multiple sclerosis[2,3]. Unlike viral vectors for gene therapy, the nucleic acid vaccines are considered so safe that they do not need

to be evaluated by the National Institutes of Health (NIH) Recombinant Advisory Committee prior to human clinical trials.

Safety studies have concluded that there is little concern for integration of DNA into genomes. mRNA vaccines are even safer and advantageous because RNA itself cannot integrate into genomic DNA without the presence of a retrovirus element (reverse transcriptase and integrase). It is possible that some recipients of an mRNA vaccine might be already infected with a retrovirus (e.g., HIV), where theoretically such integration could happen. But the risk of integration, like a “gene therapy”, is extremely unlikely for mRNA, and is not a significant concern for plasmid DNA. From a regulatory perspective, DNA and mRNA vaccines do not count as gene therapy products.

[This comment comes from an evaluation of a related claim.]

Robert Carnahan
Associate Professor (Pediatrics and Radiology and Radiologic Sciences), Vanderbilt University Medical Center

In many cases, the principle of a given vaccine is to expose the body to a key protein, called an antigen, that leads to the development of a long-term immunity to the pathogen from which the antigen protein originates. In the case of RNA vaccines, rather than directly giving the body the actual protein, an RNA which instructs cells in the body as to how to make the antigen protein is given.

Though these RNA vaccines represent a new innovation, they are based on longstanding, foundational scientific principles. RNA itself is used in all cells in the body as a short-lived blueprint for building proteins within the cells. That is a key safety advantage for using it to provide a message encoding the antigen protein. The cells in the body have innate mechanisms of degrading this RNA and not allowing it to persist. Moreover, though RNA is related to DNA, it is chemically distinct and is not able to integrate into the DNA. This means that these vaccines will not modify the DNA of the cells, and also will not be present for prolonged periods to cause other long-term effects like autoimmune disorders.

CORRECTION (4 DEC. 2021):

The review initially misspelled Salzberg's name. This has since been corrected.

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TAGS: COVID 19 CORONAVIRUS VACCINE

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HEALTH 2025-02-14

Flu vaccine reduces risk of flu-related illness and hospitalization, even though it hasn't eradicated flu

LACKS CONTEXT

Claim: "We've had the flu vaccine for 78 years. We still have the flu."

Source: Threads, Social media user, 2025-02-08

HEALTH 2025-02-11

Infants younger than 6 months had the second highest COVID-associated hospitalization rate for most of the pandemic

MOSTLY ACCURATE

Claim: "Babies under 6 months have the second highest hospitalization rate after the elderly"

Source: Facebook, Social media user, 2025-02-06

HEALTH 2025-02-06

Japanese study misrepresented in posts claiming "heart failure surges among Covid-vaccinated"

INACCURATE

Claim: "Japan sounds alarm as heart failure surges among Covid-vaccinated"

Source: Slay News, TikTok, Facebook, Frank Bergman, Social media users, 2025-01-18

HEALTH

Modified RNA in COVID-19 vaccines isn't linked to cancer development

2024-04-29

KEY TAKEAWAY

The mRNA COVID-19 vaccines contain RNAs with chemical modifications that increase their stability and improve their ability to induce a potent immune response. Some results suggest that such chemical modifications make mRNA-based anti-cancer vaccines less effective. However, it doesn't mean that COVID-19 vaccines increase the risk of cancer. There's no evidence that COVID-19 vaccination increases the risk of cancer.

REVIEWED CONTENT

Verdict: UNSUPPORTED

Claim: A review “has found that COVID-19 mRNA vaccines could aid cancer development”

Source: America's Frontline Doctors, The Highwire, Social media users, 2024-04-16

VERDICT DETAIL

Misrepresents source: The claim originates from the conclusion of a literature review based on a study by Sittplangkoon and colleagues. However, this review didn’t accurately represent the study’s findings. Contrary to the claim, the study didn’t show that modified mRNA like those used in COVID-19 vaccines enhanced cancer development.

Inadequate support: The claim suggested that new results established a link between COVID-19 vaccines and cancer development. However, the scientific publication used to support that claim is a literature review. This form of publication summarizes existing knowledge but doesn't provide any new results.

SEE OUR METHOD OF EVALUATION

FULL CLAIM

> A review “has found that COVID-19 mRNA vaccines could aid cancer development”; “Confirmed: Researchers Reveal COVID mRNA Vaccines Contain Component that Suppresses Immune Response and Stimulates Cancer growth”; “not only could the COVID-19 mRNA jabs aid cancer development, but they could actually cause and worsen cancer, not make it better”

Review

Science Feedback and other organizations have repeatedly refuted unsupported claims and flawed public health data analyses suggesting that the COVID-19 vaccines increase the risk of cancer. We also explained that a predicted increase of new cancer diagnoses in the U.S. in 2024 was unrelated to COVID-19 vaccination and could plausibly be explained by population aging and delayed cancer screening and treatment during the pandemic.

However, the organization America’s Frontline Doctors, known for spreading COVID-19 disinformation, continues to push this narrative. More recently, it claimed that an

April 2024 scientific publication by Rubio-Casillas *et al.* "found that COVID-19 mRNA vaccines could aid cancer development"[1].

The website The HighWire, which has previously published false claims about COVID-19 and vaccines, also wrote that the scientific paper showed that "mRNA vaccines could aid cancer development". The HighWire cited Peter McCullough, a cardiologist known for spreading misinformation about COVID-19 vaccines. McCullough said that "not only could the COVID-19 mRNA jabs aid cancer development, but they could actually cause and worsen cancer, not make it better".

However, this claim is unsubstantiated. The scientific publication presented as evidence for this claim doesn't contain new results that support the claim and it misinterprets results from another study.

THE PAPER BY RUBIO-CASILLAS *ET AL.* DIDN'T FIND ANYTHING NEW

To begin with, this paper by Rubio-Casillas *et al.* isn't a study. It doesn't contain new experimental or clinical results. Instead, the authors conducted a review of already-existing literature.

This is a crucial difference between studies and literature reviews. A study formulates a hypothesis and tests it by conducting experiments, data analysis, and trials, thereby producing new knowledge.

By contrast, a literature review summarizes what is already known and provides a critical analysis of results and competing hypotheses. This can lead to formulating new hypotheses and identifying new avenues of research, but it doesn't in itself demonstrate anything new. New hypotheses that may arise still would need to be confirmed experimentally and clinically. Thus, the claim that this paper "has found" a link between COVID-19 vaccines and cancer isn't correct, because it didn't test that hypothesis with experiments and clinical trials.

RUBIO-CASILLAS *ET AL.* MISINTERPRETED KEY STUDY UNDERPINNING THEIR CLAIM

The main claim of Rubio-Casillas *et al.* was that the mRNA used in COVID-19 mRNA vaccines contained chemical modifications that allegedly "stimulated cancer growth and metastasis", thus "suggesting that COVID-19 mRNA vaccines could aid cancer development".

This refers to modified nucleotides—the building blocks of RNAs and DNAs—used in the COVID-19 mRNA vaccines. More specifically, instead of the nucleotide uridine, the vaccine mRNA contains N1-methyl-pseudouridine.

Unmodified RNAs—using normal uridine—trigger an inflammatory response and are rapidly degraded upon entering a cell. By contrast, modified RNAs using N1-methyl-pseudouridine are able to evade the cell's RNA detection system and don't trigger inflammation[2]. Vaccines using modified RNA are able to induce greater antigen production, are better tolerated due to a lower inflammation, and induce a stronger immune memory[2]. It was the discovery of modified RNA's immunomodulating potential that won Katalin Karikó and Drew Weissman the Nobel Prize in Physiology or Medicine in 2023.

Rubio-Casillas *et al.* heavily relied on a study by Sittplangkoon *et al.* to support their claim that N1-methyl-pseudouridine, although useful for vaccine effectiveness, could also favor the development of cancer[3]. Indeed, Sittplangkoon *et al.* is the only study cited in the review that directly investigates the effect of uridine modifications in cancer immunity.

Furthermore, Rubio-Casillas *et al.* claimed in their abstract that "evidence is provided[...] suggesting that COVID-19 mRNA vaccines could aid cancer development". This sentence refers to the work by Sittplangkoon et al. and has been repeated in several versions of the claim.

However, this is an incorrect interpretation of this study, as we explain below.

It's important to clarify that Sittplangkoon *et al.* didn't investigate whether COVID-19 vaccines enhance cancer development. In fact, their work focused on anti-cancer vaccines, that is, a vaccine boosting immunity against a specific cancer, the same way that COVID-19 vaccines boosts immunity against the SARS-CoV-2 virus.

To do this, the researchers injected mice with melanoma cells (melanoma is a type of skin cancer) producing the protein ovalbumin (a protein abundant in egg whites). At the same time, they immunized the mice with a vaccine containing mRNA containing the genetic information to produce that ovalbumin protein. The objective was to train the mice's immune systems to recognize and destroy ovalbumin-carrying melanoma tumors, just like the COVID-19 vaccine trains the immune system to recognize and destroy the spike-carrying SARS-CoV-2.

From the start, we can see that Sittplangkoon and colleagues were addressing a completely different scientific question from the one that Rubio-Casillas *et al.* tried to address. Rubio-Casillas *et al.* debated whether COVID-19 mRNA vaccines, which contain mRNA for the spike protein to build immunity against a virus, could inadvertently impair our immune defense against naturally-occurring cancers. By contrast, Sittplangkoon *et al.* asked whether modified and unmodified RNAs could be used in a vaccine targeting a specific, artificially-induced cancer.

Sittplangkoon *et al.* found that the anti-cancer vaccines that used unmodified RNAs efficiently boosted immunity against the melanoma. By contrast, the vaccines using modified RNAs didn't improve immunity against melanoma compared to unvaccinated, healthy mice (Figure 1).

Figure 1 – *Effect of anti-cancer vaccines containing either modified or unmodified RNAs on tumor growth. This graph represents melanoma growth in mice that are unvaccinated, or vaccinated with modified or unmodified mRNA. Modified RNA containing N1-methyl-pseudouridine is indicated by "100% m1Ψ". Grey line: Mice vaccinated with unmodified RNA. Blue line: mice vaccinated with modified mRNAs. Red, orange and green lines: mice that haven't been vaccinated. Source: Sittplangkoon et al*[3].

It's important to emphasize that mice vaccinated with modified RNAs didn't fare worse than unvaccinated mice. So, the presence of N1-methyl-pseudouridine didn't hamper the mice's immunity against cancer; it just didn't improve anti-cancer immunity.

In summary, the results of Sittplangkoon *et al.* suggest that anti-cancer vaccines would be more effective if they didn't contain modified RNAs. But they didn't show that the N1-methyl-pseudouridine contained in modified mRNA was detrimental to anti-cancer immunity of our body. In the absence of such a finding, the claim by Rubio-Casillas *et al.* is unsubstantiated and misrepresents the original study by Sittplangkoon *et al.* We reached out to Rubio-Casillas *et al.* to know if they had considered the results from Sittplangkoon *et al.* that we presented here.

The first author, Alberto Rubio-Casillas, replied via email, acknowledging that their publication “is a review article, not an experimental work” and it had been “distorted on social networks”. The authors stood by their conclusions, but didn’t provide new evidence to refute our conclusion that mice immunized with modified RNA had an equivalent or better outcome than non-immunized mice.

In conclusion, Rubio-Casillas *et al.* offered no new data to support the claim that COVID-19 vaccines cause cancer or favor cancer development. This claim strongly relies on a study by Sittplangkoon *et al.* that was unrelated to COVID-19 vaccines and didn’t show what Rubio-Casillas *et al.* claimed it did.

UPDATE (6 May 2024):

We updated our review with comments by Alberto Rubio-Casillas, the first author of the review. This information can be found in the twenty-first paragraph.

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TAGS: COVID 19 CANCER MRNA VACCINE

Published on: 2024-04-29 Editor: Pablo Rougerie

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Flu vaccine reduces risk of flu-related illness and hospitalization, even though it hasn't eradicated flu

LACKS CONTEXT

Claim: "We've had the flu vaccine for 78 years. We still have the flu."

Source: Threads, Social media user, 2025-02-08

HEALTH 2025-02-11

Infants younger than 6 months had the second highest COVID-associated hospitalization rate for most of the pandemic

MOSTLY ACCURATE

Claim: "Babies under 6 months have the second highest hospitalization rate after the elderly"

Source: Facebook, Social media user, 2025-02-06

HEALTH 2025-02-06

Viral copypasta posts mislead about cancer causes and testing, promote unproven cancer remedies such as ivermectin, fenbendazole, alkaline water, and vitamin B17

INCORRECT

Claim: A list of alternative cancer treatments can be "successfully used to treat certain cancers"

Source: Facebook, Social media users, 2025-01-28

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HEALTH

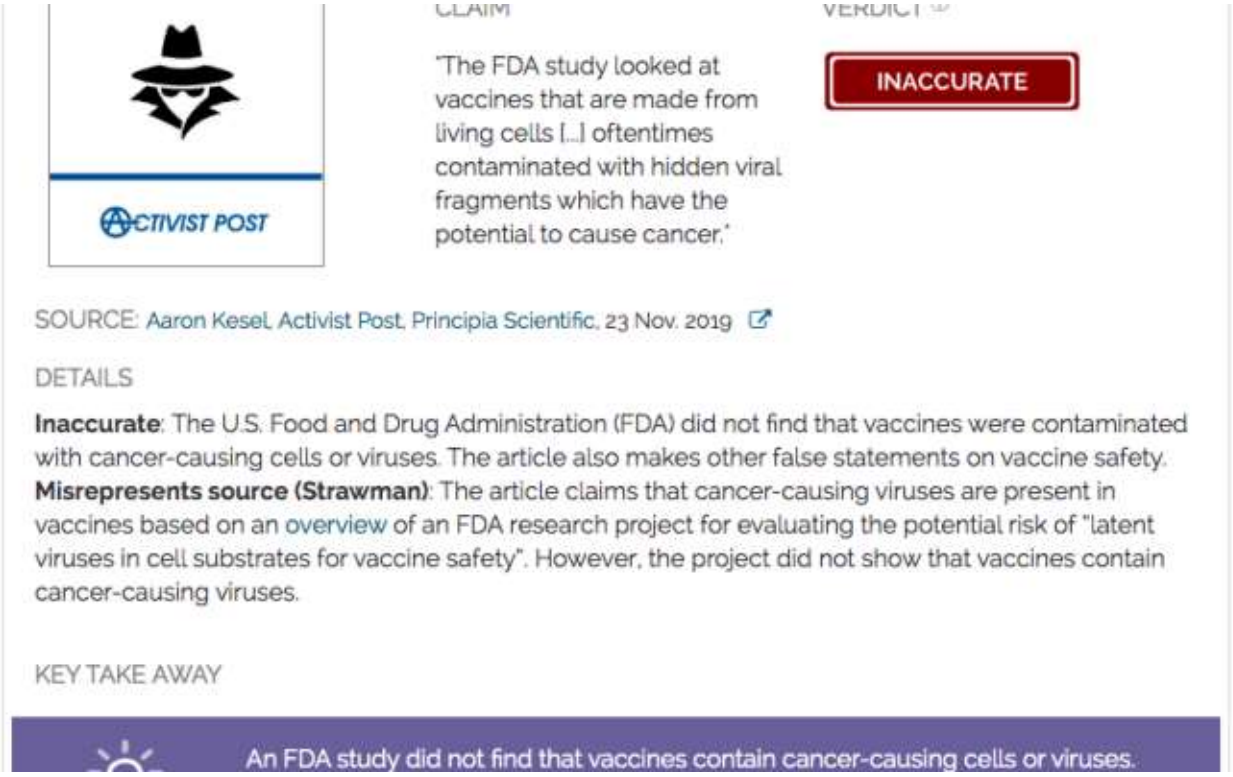
No, an “FDA study” did not find that vaccines contain cancer-causing viruses

2020-01-31

KEY TAKEAWAY

An FDA study did not find that vaccines contain cancer-causing cells or viruses. Vaccines do not increase the risk of cancer.

REVIEWED CONTENT



Verdict: INACCURATE

Claim: The FDA study looked at vaccines that are made from living cells [...] oftentimes contaminated with hidden viral fragments which have the potential to cause cancer.

Source: Principia Scientific, Activist Post, Aaron Kesel, 2019-11-23

Document 9

VERDICT DETAIL

Inaccurate: The U.S. Food and Drug Administration (FDA) did not find that vaccines were contaminated with cancer-causing cells or viruses. The article also makes other false statements on vaccine safety.

Misrepresents source (Strawman): The article claims that cancer-causing viruses are present in vaccines based on an overview of an FDA research project for evaluating the potential risk of "latent viruses in cell substrates for vaccine safety". However, the project did not show that vaccines contain cancer-causing viruses.

SEE OUR METHOD OF EVALUATION

FULL CLAIM

> The FDA study looked at vaccines that are made from living cells, or replicated cell substrates that some manufacturers are investigating to create. According to research, these cells are oftentimes contaminated with hidden viral fragments which have the potential to cause cancer.

Summary

This claim was published in an article in late November 2019 and went viral on Facebook in January 2020, receiving more than 41,000 interactions. The article makes several claims, primarily that vaccines contain cancer-causing viruses.

As addressed in a previous review: vaccines do not cause cancer. This article by the Dana-Farber Cancer Institute, a world leader in cancer research, states that there is no link between vaccines and an increased risk of cancer, and that vaccines can actually protect people from developing certain cancers; the HPV vaccine springs to mind.

The article also falsely claims that "Polio vaccine SV40 is documented on record by the CDC themselves [...] to have cost people their lives and caused cancer." While simian virus 40 (SV40) was found to have contaminated certain batches of the polio vaccine between 1955 and 1963, it has not been found to cause cancer in humans.

The U.S. Centers for Disease Control and Prevention (CDC) has made information about this incident public, which can be found here.

The article also repeats the myth that vaccines cause autism. This has already been disproven in numerous studies in thousands of people, as we reported in an earlier article. The article also repeats other false statements about the safety of vaccine ingredients, specifically aluminium and mercury.

Aluminium is not used in its elemental form in vaccines, but in the form of aluminium salts which act as adjuvants. Adjuvants are used to heighten the immune response upon vaccination and enhance protection during subsequent natural infection. While it is possible for adjuvants to trigger side effects if used in excessive amounts, the levels in vaccines are low and safe.

Mercury in its elemental form, which is toxic, is not used in any vaccine. Another form of mercury called methylmercury, which contaminates seafood, is also toxic, but is not present in vaccines either. The mercury-containing compound called thimerosal is used in vaccines as a preservative and antibacterial. Although the level of thimerosal in vaccines is safe, persistent public concern over thimerosal led to its removal from childhood vaccines in the United States in 2001. Thimerosal is no longer present in most vaccines, with the exception of certain multi-dose influenza vaccines.

Scientists' Feedback

[This comment comes from an evaluation of a related claim.]

Neal Halsey
Professor Emeritus, Johns Hopkins Bloomberg School of Public Health

Every vaccine that is approved by the FDA has undergone extensive safety testing and been found to be safe and effective.
Thimerosal is a mercury-containing preservative that is only used in some of the many different influenza vaccines that are available today. In the late 1990s and early 2000s, thimerosal was removed as a preservative from all pediatric vaccines with the exception of some influenza vaccines. Thimerosal-free influenza vaccines are

available for children and pregnant women upon request in virtually all settings where these vaccines are given.

All of us are exposed to substances that are potentially toxic when we are exposed to high concentrations for long periods of time. None of the substances in vaccines are considered to be “toxic” in the concentrations that are in vaccines.

[This comment comes from an evaluation of a related claim.]

James D. Cherry
Professor (Pediatrics), David Geffen School of Medicine, University of California Los Angeles

There is aluminum salt present in killed vaccines, such as the present DTaP and Tdap vaccines, but it’s a very good adjuvant and it’s been in killed vaccines from the very beginning. The amount and the actual aluminum salt may vary with vaccines. The key thing is that too much aluminum would give you abscesses at the site of vaccination, but no present killed vaccine has excessive amounts. In live vaccines there’s no aluminum at all.

Mercury is really interesting. Ethylmercury, which is from thimerosal, is very safe, and it degrades so that there’s no problem whatsoever. The problem is that regular mercury is very toxic. Methylmercury, which contaminates fish for example, is also toxic. But ethylmercury acts as a preservative and also as an antibacterial, so it prevents vaccines from being contaminated with bad bacteria. The confusion of roles [between ethylmercury and methylmercury] – and this happened with people who should have known better – created the push to get mercury out of vaccines. There was thimerosal in the DTP vaccine and also later when the hepatitis B vaccine came along, which we gave right at birth. Although the amount of mercury appeared to exceed the EPA level, that level is for methylmercury, not ethylmercury. Nevertheless, that prompted the move to take mercury out of vaccines, and so our present killed vaccines have no mercury in any of them, with the possible exception of multidose vials of some influenza vaccines.

The whole idea was wrong from the beginning. Ethylmercury is incredibly safe and we know that because back before we had antibiotics, it was given in an attempt to treat serious infections, in large doses – a thousand times bigger than what’s in any vaccine. And of course in any live vaccine, there’s no mercury whatsoever.

[This comment comes from an evaluation of a related claim.]

Michael J Imperiale
Professor, Department of Microbiology and Immunology, University of Michigan

While it is true that many individuals may have been inadvertently exposed to SV40, there is no reliable evidence that SV40 contributes to cancer in humans. This is one scientific review that speaks to this issue[1].

From the review's abstract:

> *"Reports of the detection of SV4o DNA in a variety of cancers have raised serious concerns as to whether the inadvertent inoculation with SV4o has led to the development of cancer in humans. However, inconsistent reports linking SV4o with various tumor types has led to conflicting views regarding the potential of SV4o as a human cancer virus. Several recent studies suggest that older detection methodologies were flawed, and the limitations of these methods could account for most, if not all, of the positive correlations of SV4o in human tumors to date. Although many people may have been exposed to SV4o by polio vaccination, there is inadequate evidence to support widespread SV4o infection in the population, increased tumor incidence in those individuals who received contaminated vaccine, or a direct role for SV4o in human cancer."*

[This comment comes from an evaluation of a related claim.]

Angéline Rouers
Senior Research Fellow, A*STAR Infectious Diseases Labs

The estimation that 100 million persons were inoculated between 1955 and 1963 in the United States with the poliovirus vaccine containing a small amount of the SV40 virus is correct. However, the link between SV40 virus and the development of cancer in humans is still unclear and has created a huge debate since the last 60 years.

In 2001, the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH) in the United States convened an independent expert

group, which worked over 3 years in an objective manner on the eventual adverse effects of the administration of contaminated batches of poliovirus vaccine. The committee published their report in 2003[2] which clearly addressed the question: "Can SV40 cause cancer in humans under conditions of natural exposure?"

From a mechanistic point of view, SV40 has the capacity to be tumorigenic (to generate tumors) and studies have shown that the virus can lead to tumor development in animal models. However, the experts also highlighted that "data on the association between SV40 and human tumors are inconsistent". Several studies have shown the presence of SV40 DNA in tumors. The report emphasized the fact that this does not demonstrate a causal relationship: even if the virus is present, it does not prove that the virus caused the cancer.

The committee then addressed this important question: "Is Contamination of the Polio Vaccine with SV40 Responsible for SV40 Infection in Humans?" Since the source of exposure to SV40 can be diverse (animal-to-person, person-to-person or laboratory exposure) and because animal models show preferential infection of neonates and not older ones like in this context (vaccination was mostly for school-aged children, adolescents and adults), the experts finally concluded that "the biological evidence is moderate that SV40 exposure from the polio vaccine is related to SV40 infection in humans".

All the studies sustaining a link between SV40 and human cancer are based on the detection of SV40 in patients' tumor. However, two recent reviews[1,3] reveal that the technique for detecting SV40 was not optimal in the previous studies published, mostly due to the cross-reactivity with other polyomaviruses (known as BKV and JCV). More recent studies conducted with improved techniques failed to reproduce the results of previous studies reporting the presence of SV40 in human tumors. The possibility that contamination with laboratory plasmids in detection assays is also proposed as a reason for false positives in previous studies.

Overall, it is accurate to say that SV40-contaminated poliovirus vaccines were used to vaccinate people, however, this issue was addressed and resolved as soon as it was raised. None of the existing data allow us to link SV40 contained in the vaccine to cancer development later.

READ MORE

The Children's Hospital of Philadelphia published a fact-sheet addressing concerns about SV40 contamination in polio vaccines and cancer. AFP and Snopes also published fact-checks which examined similar claims.

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2 – Institute of Medicine. (2003) Immunization Safety Review: SV40 Contamination of Polio Vaccine and Cancer. Washington, DC: The National Academies Press.
3 – Shah KV. (2006) SV40 and human cancer: A review of recent data. International Journal of Cancer.

TAGS: CANCER POLIO VACCINE

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LACKS CONTEXT

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Claim: A list of alternative cancer treatments can be "successfully used to treat certain cancers"

Source: Facebook, Social media users, 2025-01-28

HEALTH 2025-02-06

Japanese study misrepresented in posts claiming "heart failure surges among Covid-vaccinated"

INACCURATE

Claim: "Japan sounds alarm as heart failure surges among Covid-vaccinated"

Source: Slay News, TikTok, Facebook, Frank Bergman, Social media users, 2025-01-18

COVID-19 Vaccines Have Not Been Shown to Alter DNA, Cause Cancer

By Kate Yandell

Posted on October 26, 2023

THIS ARTICLE IS AVAILABLE IN BOTH ENGLISH AND ESPAÑOL English

SciCheck Digest

Small amounts of DNA from the manufacturing process may remain in the mRNA COVID-19 vaccines. Purification and quality control steps ensure any leftover DNA is present within regulatory limits. There isn't reason to think that this residual DNA would alter a person's DNA or cause cancer, contrary to claims made online.

How do we know vaccines are safe?

Full Story

The COVID-19 vaccines made by Pfizer/BioNTech and Moderna are produced with help from DNA templates, which include instructions for making the mRNA that encodes the spike protein. Manufacturers take steps to purify the final vaccine components, cutting up and removing the DNA, although there could be a very small amount of DNA left.

Past research and mechanistic logic indicate that any DNA remaining after these purification and quality control steps is likely inconsequential. However, in recent months unsubstantiated theories have spread online that DNA remaining in mRNA vaccines could integrate into a person's own DNA and cause cancer, or even that the vaccines are already causing cancer.

A spokesperson from the U.S. Food and Drug Administration told us in an email that "no safety concerns related to residual DNA have been identified." The spokesperson added that "with regard to the mRNA vaccines, while concerns have been raised previously as theoretical issues, available scientific evidence supports the conclusion that the minute amounts of residual DNA do not cause cancer or changes to a person's genetic code."

A spokesperson for the European Medicines Agency — which helps regulate medical products in the European Union — told us via email that the agency "can confirm that we have not seen any reliable evidence of residual DNA exceeding approved/safe levels" for the Pfizer/BioNTech or Moderna COVID-19 vaccines. Nor is the EMA "aware of scientific evidence showing that the very small amounts of residual DNA that may be present in vaccine batches could integrate into the DNA of vaccinated individuals," the spokesperson continued.

Various experts also told us that it is unlikely that residual DNA in the vaccines could integrate into DNA or cause cancer, even in theory. And as we have previously written, there isn't evidence to date that the vaccines cause cancer or have led to an increase in cancer.

Marc Veldhoen, an immunologist at the Instituto de Medicina Molecular João Lobo Antunes in Portugal, told us via email that residual DNA would be expected, but he refuted the idea that it could cause cancer. "Yes, there would be some fragments, but within the limit this is allowed and without any clinical consequence," he said.

This family of claims was originally inspired by a preprint posted in April, which said there was "DNA contamination that exceeds" the EMA and FDA regulatory limits in Moderna and Pfizer/BioNTech vaccine vials sent anonymously to the authors in the mail without cold packs. This led to other reports of DNA in mRNA vaccine vials, including a second preprint that analyzed largely expired vaccine vials obtained at pharmacies in Canada. None of this work has been published in peer-reviewed journals, and many elements of it have been criticized.

We reached out to Kevin McKernan, an author on both preprints, to better understand his views. Rather than replying to our email, he posted a screenshot of it on X, formerly known as Twitter, and included responses there. McKernan, who has an undergraduate degree in biology, is the founder of Medicinal Genomics, a company that markets test kits and genomics-related services to the cannabis, hemp and mushroom industries.

Some of the alleged concern has focused on the possibility, raised in the original preprint, that some of the residual DNA in the Pfizer/BioNTech vaccine is from a monkey virus called SV40. The EMA confirmed to us that the plasmid, or DNA template, used to make the Pfizer/BioNTech vaccine contains some short sections of DNA from this virus. A Pfizer spokesperson also told us via email that "specific, non-infectious parts of the SV40 sequence, which are commonly used in the pharmaceutical industry are present in starting material used by Pfizer and BioNTech."

But none of the sequences identified in the preprint are known to cause cancer, contrary to recent social media posts that say "SV40, a cancer causing sequence" was "put in the Covid Vaccine."

Experts say there isn't reason to think that any small pieces of leftover DNA, including SV40 DNA, in the vaccines would be harmful.

"It is very unlikely that any residual DNA would integrate into a person's genome and if it did it would be even much less likely to cause cancer," Barry Milavetz, a molecular biologist who studies SV40 at the University of North Dakota, told us in an email.

South Carolina Senate Committee Meeting Amplifies DNA Claims

Reports of residual DNA in the mRNA COVID-19 vaccines and its purported dangers spread further after a Sept. 12 South Carolina Senate committee listening session. One speaker, molecular biologist and cancer geneticist Phillip Buckhaults from the University of South Carolina, shared his own findings that DNA pieces were present in leftover vaccine in the bottom of used Pfizer/BioNTech vials.

In his presentation, which was shared widely online, he said that DNA "can and likely will" integrate into the genomes of people's cells, and he shared concerns about various potential health impacts, including cancer. As we've said, other experts and regulatory agencies disagree that residual DNA is likely to integrate into a person's own DNA.

"It was surprising to me to see any DNA in this product, and I am a bit concerned about the theoretical possibility of genome modification," Buckhaults told us in an email. "I want the scientific community to help find out if this is a real hazard or not a problem."

He also said that he did not intend for his comments "to be widely circulated in the public and compromising people's confidence in vaccines."

Another widely posted clip from the listening session was of Janci Lindsay, who runs a toxicology consulting firm and has a history of sharing incorrect information about vaccines and COVID-19. She also spoke about unsubstantiated cancer risks and told the lawmakers that she believes the SV40 DNA sequences were included in the vaccines with "nefarious intent." The idea that the presence of these sequences is nefarious is a conspiracy theory with no basis in reality.

Lindsay goes on to reference hydroxychloroquine and ivermectin, falsely concluding, "We never needed these vaccines. We had treatments that worked." This is incorrect. The COVID-19 vaccines saved many lives, and randomized controlled trials have shown that hydroxychloroquine and ivermectin do not help people recover from COVID-19.

FactCheck.org obtained a copy of an Oct. 16 letter sent to the Senate committee by Pfizer. In the letter, Pfizer disagrees with comments made during the session, saying that statements are incorrect that "the vaccine contains plasmid DNA that could potentially impact a person's DNA and be a theoretical cancer risk." The letter continues, "There is no evidence to support these claims and they provide the risk of being misconstrued by either Committee members and/or the public at large."

The letter also states that "no signs of DNA mutation or COVID-19 vaccine-induced cancer have been reported to date" related to the Pfizer/BioNTech COVID-19 vaccine.

DNA in Vaccines Is Not Inherently Dangerous

Research into residual DNA in vaccines dates back decades. Anti-vaccine fear-mongering about residual DNA or other substances in vaccines is also not a new phenomenon.

Many currently available vaccines are made using cells. Some vaccines, such as the one against chickenpox, rely on weakened virus that is grown in cells. For other vaccines, such as for hepatitis A, viruses are grown in cell culture and then inactivated. Cells also can be used to produce protein-based vaccines. One example is the COVID-19 vaccine from Novavax, which is grown in moth cells.

In all of these cases, the active ingredients for the vaccines are purified, but the vaccines can still contain small amounts of residual DNA from the cells used to make them. The FDA and other regulatory agencies have offered guidance on limiting the quantity and size of residual DNA left over from cells used to make vaccines.

The limits are based on the theoretical concern that residual DNA — specifically from mammalian cell lines — could cause cancer or a viral infection, particularly if there were a cancer-causing gene or certain viral DNA present in the cell line. But Dr. Paul Offit, director of the Vaccine Education Center at Children's Hospital of Philadelphia, told us that regulatory limits on residual DNA in vaccines are set conservatively.

Pfizer's letter to the South Carolina Senate committee refers to a quality control process that ensures that residual DNA levels in its mRNA vaccine for COVID-19 are within regulatory limits.

"The validated method for assessment of residual DNA has shown that the Pfizer-BioNTech COVID-19 vaccine meets the requirements of the World Health Organization (WHO) and the FDA for biological products," the letter states. "Vaccine batches are only certified and released if the criteria, during quality control testing, are met using the validated and approved method."

Photo by Christophe Gateau/picture alliance via Getty Images.

The EMA spokesperson added that in the European Union, these results must be checked by an independent laboratory. "As a result, we are confident that the DNA levels in the vaccine are consistently below the approved/safe level," the spokesperson said.

A spokesperson from the Therapeutic Goods Administration, which regulates medical products in Australia, told us that the agency has been monitoring batches of Moderna and Pfizer/BioNTech mRNA COVID-19 vaccines. "This includes independent testing performed by the TGA laboratories to confirm that residual DNA impurity levels are below the acceptable limit," the spokesperson told us in an email. "To date all batches of COVID-19 vaccines supplied in Australia have met all quality specifications."

Research on experimental DNA vaccines, which contain DNA as their active ingredient, also supports the idea that DNA in vaccines is unlikely to integrate into a person's DNA. Stephen M. Kaminsky, a professor of research in genetic medicine at Weill Cornell Medical College, told us via email that "there is little concern of integration from DNA vaccines that are delivered in much greater quantities" than any residual DNA that might be found in one of the mRNA vaccines for COVID-19.

"Since amounts of DNA vaccines in the milligram range have been approved for clinical evaluation, it is difficult to imagine that the smaller quantities of residual cell-substrate DNA present in viral vaccines would pose a significant risk due to integration," FDA scientists also concluded in one paper.

The FDA scientists went on to state that they consider the primary cancer-related concern with DNA in vaccines to be the introduction of an activated version of a cancer-causing gene to a cell — not just any DNA integrating into the genome at the wrong place.

Offit added that we are constantly exposed to DNA, including in the food we eat and from viruses that don't cause cancer.

Cancer Theory Relies on Improbable Sequence of Events

Experts told us that theories for how residual DNA would cause cancer rely on an entire series of events, many of them unlikely.

As we've discussed above, changing a person's DNA is not easy. The residual DNA would first need to get into a cell. This could happen if the DNA was inside one of the fatty bubbles called lipid nanoparticles used to package the mRNA in the vaccines, Veldhoen, the immunologist in Portugal, said. But even if this happened, the DNA would only end up in the

cytoplasm, the region of a cell outside the nucleus.

Next, any residual DNA that made it into a cell would need to get access to a person's DNA in the nucleus and insert itself. In general, a cell needs to be in the process of dividing for foreign DNA to integrate into the cell's own DNA.

The mRNA vaccines are injected into the muscles, where the bulk of the vaccine remains. Muscle cells "do not divide rapidly and have lots of cytoplasm compared to the size of their nuclei," Milavetz, the molecular biologist at the University of North Dakota, said. This means that it is "very unlikely" that any residual DNA from a vaccine introduced to the cytoplasm of a cell will make it into the nucleus and insert itself into the DNA there in the first place, he added.

"Even if it enters the nucleus, which it probably can't, it would still have to be integrated into DNA, which requires an integrase, which it also doesn't have," Offit said. An integrase is an enzyme some viruses use to insert themselves into cellular DNA.

In the event that some residual DNA did manage to insert into a person's DNA, it would need to be exactly the wrong kind of DNA, land in exactly the wrong place or a combination of the two.

And then, if this entire sequence of events occurred in one of a person's trillions of cells, the cell would need to avoid destruction by the immune system, divide and give rise to other cells, which would need to continue along the path toward becoming cancerous.

In reality, the immune system can detect when cells take up foreign DNA or mRNA, Veldhoen said. In the end, cells that had taken up residual DNA would not survive, he said, and the DNA bits would be "broken down, its individual parts recycled."

SV40 Sequence Unlikely to Cause Cancer

As we've said, social media posts misleadingly refer to the presence of "SV40, a cancer causing sequence." This brings to mind past concerns, which were not borne out, that contamination of polio vaccines with the entire SV40 virus could cause cancer. Researchers discovered in 1960 that monkey kidney cells that had been used to produce some polio vaccines were contaminated with SV40, which was found to cause cancer in rodents. But the virus has not been shown to cause cancer in humans, and the contamination did not ultimately lead to more cancer in children who received the contaminated vaccines compared with those who didn't.

The small amount of SV40 DNA in the DNA template for the Pfizer/BioNTech vaccine does not encode the entire virus. SV40 "is a naturally occurring virus and the virus itself is not included in either starting materials, plasmid DNA, or in the final product of the Pfizer-BioNTech COVID-19 vaccine," the Pfizer spokesperson said.

McKernan's original preprint did not indicate the presence of the whole virus or any DNA encoding viral proteins, but rather highlighted regulatory DNA. Regulatory DNA, including a type of sequence called a promoter, helps control which genes in a cell are turned on.

Milavetz said that the portion of SV40 shown to have the potential for causing cancer in the lab — encoding a protein called T-antigen — is not among the sequences McKernan identified in the vaccine.

It is unclear why the Pfizer/BioNTech DNA template would include SV40 regulatory DNA. The EMA told us that "the sequence is not directly relevant" for producing copies of the DNA template or for producing mRNA for the vaccine, "so it is considered to be a non-functional part of the structure of the source plasmid."

McKernan has suggested that a piece of SV40 regulatory DNA could cause cancer by integrating into a person's DNA and turning on a cancer-causing gene. In response to criticisms that it's difficult for DNA to get into the nucleus, McKernan points to research showing a role for part of that sequence in helping to bring DNA into the cell nucleus.

But it's hardly clear that any nuclear entry mechanism would be at play in human cells exposed to residual DNA fragments. And as we have previously explained, there are multiple reasons why residual DNA is unlikely to integrate into a person's DNA.

"Fragments of the SV40 sequence may only be present as residual impurities at very low levels that are routinely controlled," the EMA spokesperson said. "There is no scientific evidence that any of these SV40 fragments can act as insertional mutagens," the spokesperson said, meaning there is no evidence the fragments would integrate into a person's DNA.

Buckhaults, who also found SV40 regulatory DNA in Pfizer/BioNTech vaccine vials, told us the bits of SV40 DNA aren't "any more dangerous than all the other bits" of DNA he found in the vaccine vials.

Milavetz pointed out the improbability of the SV40 regulatory sequence causing cancer, even if it did somehow integrate into a person's DNA.

He said that any residual DNA present would be unlikely to contain only the SV40 sequence needed to turn on a gene. There would likely be extra chunks of DNA that would prevent it from functioning.

"For this to be a viable problem only critical portions of the promoter would have to be introduced into the regulatory region of only a very small subset of genes in a human in a very specific way," he said. "In my opinion there are too many things that would have to occur perfectly for the promoter to be integrated into one of these critical human genes."

'No Meaningful Difference' from Manufacturing Process Change

Various posts also reference a change in the DNA template used to produce the Pfizer/BioNTech vaccine between the clinical trials and the rollout of the vaccine to the general public. To make the vaccine supply that was primarily used in the clinical trials, manufacturers produced copies of the DNA template using a process called PCR, in which DNA is amplified in a lab without the help of biological organisms. To help scale up production, manufacturers enlisted bacteria to make many copies of a plasmid, a circular piece of DNA. The bacteria divide rapidly and can make large quantities of DNA.

Based on this process change, social media posts have said that the "Pfizer covid vaccine approved the for emergency use was not the same one used on the public!" or posted the "BREAKING" news that "Pfizer's COVID vaccine that was approved for emergency use was not the same one they injected into billions of arms."

To be clear, the fact there was a process change has long been publicly available information. It is mentioned in the Pfizer clinical trial protocol, the emergency use authorization from the FDA and an EMA public assessment report first published in December 2020. The EMA spokesperson confirmed that vaccine batches produced by both processes were tested in clinical studies, adding that the manufacturer provided test results and other information to show the comparability of the product resulting from both processes. "This assessment of comparability confirmed there was no meaningful difference in the quality of material from process 1 and process 2 that could impact the safety and/or efficacy of the vaccine," the EMA spokesperson said.

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December 14, 2023

Joseph A. Ladapo, MD, PhD
State Surgeon General
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4052 Bald Cypress Way, Bin A-00
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Dear Dr. Ladapo,

This is in response to your letter of December 6, 2023, regarding the mRNA COVID-19 vaccines. In your letter, you raise the concern that SV40 promoter/enhancer DNA is present in these vaccines and that this raises safety concerns.[1] **We would like to make clear that based on a thorough assessment of the entire manufacturing process, FDA is confident in the quality, safety, and effectiveness of the COVID-19 vaccines.** The agency's benefit-risk assessment and ongoing safety surveillance demonstrate that the benefits of their use outweigh their risks. Additionally, with over a billion doses of the mRNA vaccines administered, no safety concerns related to residual DNA have been identified. Responses to each of your three specific questions follow below:

1. **In response to the question regarding potential genotoxicity of the mRNA COVID-19 vaccines:** No SV40 proteins are encoded for or are present in the vaccines. On first principle, it is quite implausible that the residual small DNA fragments located in the cytosol could find their way into the nucleus through the nuclear membrane present in intact cells and then be incorporated into chromosomal DNA.[2] Additionally, studies have been conducted in animals using the modified mRNA and lipid nanoparticle together that constitute the vaccine, including the minute quantities of residual DNA fragments left over after DNAse treatment during manufacturing, and demonstrate no evidence for genotoxicity from the vaccine.[3] Pharmacovigilance data in hundreds of millions of individuals also indicate no evidence indicative of genotoxicity.

2. **Regarding whether FDA considers the lipid nanoparticle delivery system in setting the safe levels of DNA in the mRNA vaccine:** The agency has taken into account the totality of the mRNA COVID-19 vaccine product, including the lipid nanoparticles, as it reviewed the manufacturers' specifications for residual DNA fragments present. Any contamination with residual DNA fragments is monitored routinely as a product specification.

3. **Regarding concern for possible integration of the residual DNA fragments into reproductive cells:** Please see the response to the first question above regarding the implausibility that the minute amounts of small DNA fragments present could find their way into the nucleus of these cells. Additionally, reproductive toxicology studies have been conducted to evaluate the mRNA COVID-19 vaccines and have found no concerns.

[1] In your letter, you raise questions, citing to the 2007 Guidance for Industry: Considerations for Plasmid DNA Vaccines for Infectious Disease Indications. This guidance was developed for DNA vaccines themselves, not for DNA as a contaminant in other vaccines, and is not applicable to the mRNA COVID-19 vaccines.

[2] The Nuclear Envelope and Traffic between the Nucleus and Cytoplasm - The Cell - NCBI Bookshelf (nih.gov);

[3] https://www.fda.gov/media/151733/download?attachment; https://www.fda.gov/media/155931/download?attachment

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Perpetuating references to this information about residual DNA without placing it within the context of the manufacturing process is misleading. Therefore, we hope the following general explanation of the manufacturing process for these vaccines will be helpful.

The starting material for the manufacture of the mRNA portion is a DNA template. As part of the purification process during production, the mRNA is treated with DNAse to digest residual DNA. There are internationally agreed upon recommendations for the quantity of residual DNA present in all biological products, including the mRNA vaccines.[4] The specification for the COVID-19 mRNA vaccines for residual DNA following DNAse treatment results in the presence of DNA fragments at a quantity that is less than three orders of magnitude lower than the quantity of the RNA dose by weight. This has been determined (and continues to be determined during production of lots) with a validated quantitative PCR assay.

No SV40 proteins are encoded by the nucleotide sequences present in the mRNA vaccines. The treatment of the products with DNAase also fragments any residual DNA template that might be present after other manufacturing steps. Thus, as noted above, following manufacture of the mRNA COVID-19 vaccines, no DNA encoding SV40 proteins is present in the residual DNA remaining in the products.

Additionally, animal studies with the mRNA delivery technology done over the past decade show no evidence of genotoxicity. Moreover, we now have access to global surveillance data on over one billion doses of the mRNA vaccines that have been given, and there is nothing to indicate harm to the genome, such as increased rates of cancers.

FDA takes its responsibility for ensuring the safety, effectiveness and manufacturing quality of all vaccines licensed in the U.S., including the mRNA COVID-19 vaccines, very seriously. We stand firmly behind our regulatory decision making with the authorizations and approvals of the COVID-19 vaccines, which have a highly favorable safety profile, and which have saved, and continue to save, many lives.

The challenge we continue to face is the ongoing proliferation of misinformation and disinformation about these vaccines which results in vaccine hesitancy that lowers vaccine uptake. Given the dramatic reduction in the risk of death, hospitalization and serious illness afforded by the vaccines, lower vaccine uptake is contributing to the continued death and serious illness toll of COVID-19.

We hope the information provided addresses your concerns and those of your constituents.

Sincerely,

Peter Marks

Peter Marks, M.D., Ph.D.
Director
Center for Biologics Evaluation and Research

[4] WHO (World Health Organization) Meeting Report Study group on cell substrates for production of biologicals. June 11 and 12, 2007; 1–30; FDA Guidance for Industry: Characterization and Qualification of Cell Substrates and Other Biological Materials Used in the Production of Viral Vaccines for Infectious Disease Indications | FDA. U.S. Department of Health and Human Services, Food and Drug Administration Center for Biologics Evaluation and Research, February, 2010.

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Federal Institute for Vaccines and Biomedicines

Paul-Ehrlich-Institut

Langen, 22.12.2023

Information for Healthcare Professionals

TESTING OF COVID-19 mRNA VACCINES

Methodology for Testing COVID-19 mRNA Vaccines for Alleged Contaminants

Due to a large number of inquiries from healthcare professionals, the Paul-Ehrlich-Institut would like to provide information on the current developments regarding alleged contaminants in vaccines. This information should also serve to inform both unsettled patients and those willing to vaccinate.

A large share of the data and studies on suspected contamination of COVID-19 mRNA vaccines circulating in the public are based on methodological deficiencies. There is also the issue of potentially improper storage of the vaccine doses tested. Experimental determinations, e.g. to test for residual third-party DNA in vaccine doses available on the market, must meet the following criteria in order to produce scientifically valid results:
(i) They must not be taken using samples from expired (expiration date exceeded) vaccine vials or from opened or improperly stored vaccine vials.
(ii) The methodology used to determine the amount of residual DNA must be demonstrably suitable and comprehensible – in particular, test interference should be ruled out by the presence of lipid nanoparticles in the vaccine vials (which cannot be guaranteed when tested on the final vaccine vial).
(iii) The method used must be validated to provide reliable and verifiable results.

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In the frequently cited preprint publications by McKernan et al. (April 2023)[1] and Speicher et al. (October 2023)[2], there is a lack of sufficient information as to whether the aforementioned conditions have been met, as well as information on the comprehensibility of the chosen methodology. Method validation is essential to ensure that reliable and reproducible results are achieved at all times with the implementation of the method used, regardless of the person performing it, and that the method is suitable for its intended purpose. Manufacturers comply with the above-mentioned conditions for obtaining scientifically tenable measurement results in residual DNA determinations.

Part of the plasmid DNA serves as a template for the production of the COVID-19 mRNA vaccines. After transcribing the relevant DNA sequence into mRNA, the plasmid DNA is then comminuted by means of enzymatic digestion with DNase and depleted via the purification process to obtain the active substance (mRNA). However, a residual amount of plasmid DNA is present in small amounts that are considered harmless below a threshold specified in the marketing authorisation. To date, there is no evidence to suggest that any adverse events could be associated with residual DNA levels in authorised COVID-19 mRNA vaccines.

The Paul-Ehrlich-Institut would like to explicitly state that no DNA from cells of animal origin is used in the production of COVID-19 mRNA vaccines. Exclusively plasmid DNA of bacterial origin is used in the production process. Possible risks that could arise from residual animal cell DNA are a potential tumourigenicity due to the transmission of proto-oncogenes and potential DNA infectivity due to the transmission of completely functional viral genes. These risks are not present with DNA of bacterial origin. In this context, the WHO guideline "Recommendations for the evaluation of animal cell cultures as substrates for the manufacture of biological medicinal products and for the characterization of cell banks" and the US FDA guideline "Characterization and Qualification of Cell Substrates and Other Biological Materials Used in the Production of Viral Vaccines for Infectious Disease Indications" are not used for the production of mRNA vaccines. This is due to the fact that both guidelines explicitly refer to cells of animal origin, not to

[1] McKernan Kevin, Helbert Yvonne, Kane Liam T, McLaughlin Stephen (April 2023): Sequencing of bivalent Moderna and Pfizer mRNA vaccines reveals nanogram to microgram quantities of expression vector dsDNA per dose.
[2] Speicher David J, Rose Jessica, Gutschi L. Maria, Wiseman David M, McKernan Kevin (October 2023): DNA fragments detected in monovalent and bivalent Pfizer/BioNTech and Moderna modRNA COVID-19 vaccines from Ontario, Canada: Exploratory dose response relationship with serious adverse events.

bacterial cell substrates. Bacterial cells are expressly excluded from the guidelines.

Irrespective of this, the regulatory principle applies that as few contaminants as possible should be present in a vaccine and even theoretical risks should be reduced as far as possible. Therefore, very conservative limits for residual DNA have been set for the authorised COVID-19 mRNA vaccines and they may not be exceeded. Both residual bacterial genomic DNA and residual plasmid DNA are tested in the course of the production process. The fragmentation of plasmid DNA via DNase treatment of the mRNA, as it is done in the authorised COVID-19 mRNA vaccine products, provides additional safety, because even if complete and functional genes were contained, they would be almost completely degraded by DNase digestion during production and thus rendered harmless. This is because small DNA fragments are considered harmless as they cannot code for functional proteins (FDA Guidance for Industry (2010): "Characterization and Qualification of Cell Substrates and Other Biological Materials Used in the Production of Viral Vaccines for Infectious Disease Indications").

The testing for residual DNA is not part of the official experimental OMCL (Official Medicines Control Laboratory) testing for batch release. Experimental OMCL testing of samples of each authorised vaccine batch includes the product-specific laboratory efficacy (potency) and safety parameters identified as relevant based on the evaluation of the vaccines in the authorisation process. The decision regarding the parameters to be reviewed is made in parallel with and based on the content of the benefit-risk assessment of each vaccine candidate as part of the authorisation process. This decision is the responsibility of the OCABR (Official Control Authority Batch Release) network and is based on a scientific consensus of the official experts. They identify and determine within an official procedure the product-specific critical test procedures, test parameters, and release criteria to be reviewed in the laboratory that are relevant to the efficacy and safety of an authorised vaccine product. The decision is evidence-based and scientifically substantiated as it is based on data and findings collected as part of the development process and reviewed in the authorisation process.

In addition to the experimental testing of the specified efficacy and safety parameters by the official testing laboratories (OMCL), testing of the manufacturing documentation (Lot Release Protocol, LRP) is also part of the scope of the official batch release. The OMCL checks the results of the experimental batch tests carried out by the manufacturer with regard to whether all

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critical parameters specified in the marketing authorisation and their thresholds (specifications) have been complied with. The analytical methods used by manufacturers to determine residual amounts of DNA in COVID-19 mRNA active substances are described in the authorisation dossiers of the authorised mRNA vaccine products. Their validity is checked in accordance with guidelines from ICH (International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use) and proven on the basis of the data provided. Each batch of the vaccine product Comirnaty is tested for residual DNA and the results are part of the manufacturer's batch release protocol, which is independently assessed by the authorities as part of the official batch testing process (OCABR). When it comes to federal batch release in Germany, the test data collected by the manufacturer using a defined and validated method are cross-checked by the Paul-Ehrlich-Institut before the Institute carries out a federal batch release for Germany.

Residual plasmid DNA quantities are deliberately tested on the active substance of the COVID-19 mRNA vaccines (drug substance) and not on the final product (drug product). This is the only way to rule out possible test interference by lipid nanoparticles (LNPs), which are only present in the final product. In the production steps between the production of the active ingredient and the production of the final product, no more DNA can enter the process or the product. This means that no increase in the DNA content per vaccine dose is possible during the production of the final vaccine doses from the active ingredient. Testing the residual DNA on the active substance is therefore more sensitive and representative of the DNA content of the final vaccine product.

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ICH Q2(R2) Validation of analytical procedures - Scientific guideline

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This guideline presents a discussion of elements for consideration during the validation of *analytical procedures* included as part of registration applications submitted within the ICH member regulatory authorities. It provides guidance and recommendations on how to derive and evaluate the various *validation tests* for each analytical procedureand serves as a collection of terms, and their definitions. This guideline applies to new or revised analytical procedures used for release and stability testing of commercial drug substances and products (chemical and biological/biotechnological). The guideline can also be applied to other analytical procedures used as part of the control strategy following a risk-based approach. The guideline is directed to the most common purposes of analytical procedures, such as assay/potency, purity, impurities), identity and other quantitative or qualitative measurements.

Keywords: Validation, analytical procedures, accuracy, precision, specificity, detection limit, quantitation limit, linearity, range

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