

Mfr Report #	(b) (6)
UF/Importer Report #	
FDA Use Only	

A. PATIENT INFORMATION			
1. Patient Identifier US3742169	2. Age at Time of Event: 57 Years or Date of Birth: (b) (6)/1963	3. Sex <input type="checkbox"/> Female <input checked="" type="checkbox"/> Male	4. Weight 193.0 lbs or 87.5 kgs
In confidence			
B. ADVERSE EVENT OR PRODUCT PROBLEM			
1. <input checked="" type="checkbox"/> Adverse Event and/or <input type="checkbox"/> Product Problem (e.g., defects/malfunctions)			
2. Outcomes Attributed to Adverse Event (Check all that apply)			
<input type="checkbox"/> Death: (mm/dd/yyyy) <input type="checkbox"/> Disability or Permanent Damage			
<input type="checkbox"/> Life-threatening <input type="checkbox"/> Congenital Anomaly/Birth Defect			
<input type="checkbox"/> Hospitalization - initial or prolonged <input checked="" type="checkbox"/> Other Serious (Important Medical Events)			
<input type="checkbox"/> Required Intervention to Prevent Permanent Impairment/Damage (Devices)			
3. Date of Event (mm/dd/yyyy) 08/31/2020		4. Date of This Report (mm/dd/yyyy) 11/22/2020	
5. Describe Event or Problem Event Verbatim [LOWER LEVEL TERM] (Related symptoms if any separated by commas) RHEUMATOID ARTHRITIS [Rheumatoid arthritis]			
Case Description: This 57-year-old, American Indian or Alaskan Native, male subject (US3742169) was participating in A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older (mRNA-1273-P301), and experienced rheumatoid arthritis.			
The subject's medical history, as provided by the investigator, included gastroesophageal reflux disease, hypothyroidism, hypertension, asthma, hip pain, and environmental allergies. The subject had no medical history of continued in additional info section...			
6. Relevant Tests/Laboratory Data, Including Dates #1 09/25/2020 Anti-cyclic citrull (continued) #2 09/25/2020 Antinuclear antibody (continued) #3 09/25/2020 Blood pressure measurement (continued) #4 09/25/2020 C-reactive protein (continued) #5 09/25/2020 Complement factor C3 (continued) #6 09/25/2020 Complement factor C4 (continued) continued in additional info section...			
7. Other Relevant History, Including Preexisting Medical Conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.) Race: American Indian or Alaska Native #1 --/--/1990 to Ongoing Current Condition, (Continued) #2 --/--/1990 to Ongoing Allergy, (Continued) #3 --/--/2000 to Ongoing Current Condition, (Continued) continued in additional info section...			

C. SUSPECT PRODUCT(S)			
1. Name (Give labeled strength & mfr/labeler)			
#1. mRNA-1273 vs Placebo (Code not broken)			
#2.			
2. Dose, Frequency & Route Used		3. Therapy Dates (if unknown, give duration) from/to (or best estimate)	
#1. Blinded, Information withheld.		#1. 08/31/2020 to 08/31/2020	
#2.		#2.	
4. Diagnosis for Use (Indication)		5. Event Abated After Use Stopped or Dose Reduced?	
#1. COVID-19 (Continued)		#1. <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Doesn't Apply	
#2.		#2. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply	
6. Lot #	7. Exp. Date	8. Event Reappeared After Reintroduction?	
#1. Blinded	#1. Blinded	#1. <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Doesn't Apply	
#2.	#2.	#2. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply	
9. NDC# or Unique ID			
10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)			
1) RABEPRAZOLE (RABEPRAZOLE) --/--/2010 to ongoing			
2) LEVOTHYROXINE (LEVOTHYROXINE) --/--/1990 to continued in additional info section...			
G. ALL MANUFACTURERS			
1. Contact Office (and Manufacturing Site for Devices)		2. Phone Number	
Name ModernaTX, Inc. David Martin MD.		617-335-1804	
Address 200 Technology Square Cambridge, MA 02139 United States of America		3. Report Source (Check all that apply)	
Email Address		<input type="checkbox"/> Foreign	
		<input checked="" type="checkbox"/> Study	
		<input type="checkbox"/> Literature	
		<input type="checkbox"/> Consumer	
		<input checked="" type="checkbox"/> Health Professional	
		<input type="checkbox"/> User Facility	
		<input type="checkbox"/> Company Representative	
		<input type="checkbox"/> Distributor	
		<input type="checkbox"/> Other:	
4. Date Received by Manufacturer (mm/dd/yyyy) 11/09/2020		5. (A)NDA # IND # 019635 BLA # PMA/ 510(k) # Combination Product <input type="checkbox"/> Yes Pre-1938 <input type="checkbox"/> Yes OTC Product <input type="checkbox"/> Yes	
6. If IND, Give Protocol # mRNA-1273-P301			
7. Type of Report (Check all that apply)			
<input type="checkbox"/> 5-day <input type="checkbox"/> 30-day			
<input type="checkbox"/> 7-day <input type="checkbox"/> Periodic			
<input type="checkbox"/> 10-day <input type="checkbox"/> Initial			
<input type="checkbox"/> 15-day <input checked="" type="checkbox"/> Follow-up #3			
9. Manufacturer Report Number (b) (6)		8. Adverse Event Term(s) Rheumatoid arthritis	
E. INITIAL REPORTER			
1. Name and Address Dr. Karen Kotloff University Of Maryland School Of Medicine 685 W. BALTIMORE STREET, HSF 480 Baltimore, Maryland 21201 UNITED STATES			
Phone # (b) (6)		Email Address (b) (6) @som.umaryland.edu	
2. Health Professional? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No		3. Occupation Physician	
		4. Initial Reporter Also Sent Report to FDA <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Unk	

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event

ADDITIONAL INFORMATION

B5. EVENT DESCRIPTION (Continued)

joint pain/swelling. Concomitant medications included rabeprazole, levothyroxine, enalapril, fluticasone furoate/vilanterol trifenatate, salbutamol, levocetirizine, and montelukast.

Additional information regarding the subject's medical history of hypothyroidism was provided in response to queries. Hypothyroidism was diagnosed around the early 1990's and the subject reported that a possible cause considered was exposure to iodine radioisotopes (I-125); however, a definitive cause was not identified. He did not recall whether an autoimmune work-up was pursued at that time.

The subject received their first, and only, dose of blinded study drug on 31 Aug 2020. Later that same day, through 06 Sep 2020, the subject reported muscle and joint aches/pain (Vaccine Toxicity Scale Grades 1 to 2 in severity) in the e-diary. The subject also experienced tinnitus, insomnia and constipation post-vaccination.

During the time period starting around 10 Sep 2020 through the last week of Sep 2020, the subject experienced recurrent muscle joint aches/pain. The quality of the pain was different than the joint aches/pain previously reported, with the left knee and right shoulder bothering him the most. It was constant regardless of rest or activity and was not worse at any particular time of the day. The subject also experienced joint stiffness in the mornings, which improved with a shower and movement. He denied joint swelling. The subject treated his symptoms with paracetamol and diclofenac, which reduced his pain. Diclofenac use lasted only a few days, at the peak of pain.

On 25 Sep 2020, relevant laboratory results included complement component 3 of 194 (high), rheumatoid factor 62.5 IU/mL (0-13), cyclic citrullinated peptide (CCP) antibody >250 units (<20), complement component 4 of 32, antinuclear antibody test was negative, erythrocyte sedimentation rate 4 mm/hr, and C-reactive protein <0.1.

On 29 Sep 2020, the Rheumatology provider noted that the subject reported ongoing mild pain in the left elbow with lifting objects, in the right shoulder, and in the right knee. He reported feeling a little weak at the peak of his pain and denied shortness of breath, chest pain, rash, and fevers during his arthralgias. The subject also felt his heart rate was higher than usual; in the 80s, when it was typically in the 50s-60s. Vital signs during the visit included blood pressure 124/71 mmHg, heart rate 70 per minute, body mass index 29.78, and pain score of 6.5. The subject's review of systems was positive for weight gain, weakness, hearing loss, tinnitus, wheezing, constipation, nausea, headache, insomnia, joint pain, and muscle weakness. Physical examination findings included 5/5 strength in bilateral upper and lower extremities, mild left elbow discomfort with extreme flexion and with lifting a box of surgical gloves, tenderness to bilateral elbows at the lateral epicondyles, and no other findings of musculoskeletal tenderness, swelling, effusion, or limitations to range of motion. The Rheumatology provider's initial assessment was that the subject had reactive arthritis based on mild symptoms and tenderness over lateral epicondyles. However, after reviewing the laboratory results, the provider was concerned about the possibility of rheumatoid arthritis due to the high level of CCP antibody and rheumatoid factor. Diagnoses included rheumatoid arthritis and lateral epicondylitis, and no new medications or treatment was prescribed. The provider noted that he was suspicious of a positive causal relationship to study drug due to the subject's lack of symptoms prior to study drug administration. The plan was to follow-up with rheumatology in two weeks for re-evaluation.

On 20 Oct 2020, the subject began treatment with oral meloxicam.

Study drug was withdrawn in response to the event.

The event, rheumatoid arthritis, was considered not resolved. The event was not expected to resolve.

The investigator assessed the event, rheumatoid arthritis, as related to study drug and not related to study procedure.

Follow-up information received on 14 Oct 2020, 15 Oct 2020, 16 Oct 2020 included updated medical history, concomitant and treatment medications, and onset of the event. A consultation note was also received which included assessment, vitals, and laboratory results.

Follow-up received on 28 Oct 2020 included no new information.

Follow-up received on 09 Nov 2020 included information regarding outcome and treatment medications.

Analysis of Similar Events: On 23-Oct-2020, the safety database was searched for events similar to rheumatoid arthritis and immune-mediated/autoimmune disorders using the following search criteria: PT: Rheumatoid arthritis, HLGT: Immune disorders NEC, FDA-CBER-2022-1614-4434494

HLGT: Autoimmune disorders, HLGT: Connective tissue disorders (excl congenital) and SMQ: Arthritis.

As of 23-Oct-2020 under IND 019745 for mRNA-1273 vs Placebo, 1 IND safety report of similar adverse events had been previously submitted. The case reporting the following event was submitted as IND Safety Report: possible polymyalgia rheumatica:

(b) (6)

There were five events that were non-IND Safety Reports (unexpected and unrelated to the IMP) reporting the following events: worsening right knee pain (b) (6), left hip osteoarthritis (b) (6), left total shoulder arthroplasty related to osteoarthritis (b) (6), gout exacerbation in right knee (b) (6) and left hip arthroplasty (b) (6).

Based on review of available data, the Sponsor cannot rule out a possible cause and effect relationship between administration of mRNA-1273 / blinded IMP and the occurrence of rheumatoid arthritis.

After review of the clinical details and investigator comments pertaining to this adverse event, and based upon experience to date, the Sponsor does not believe that changes to the conduct of this clinical trial are warranted. The Company will continue to monitor these and other serious adverse events reported in association with the IMP and will communicate any relevant changes to the protocol, Informed Consent Form, Investigator's Brochure, and/or Core Safety Information.

Case Comment/Sender's Comment:

This case concerns a 57-year-old, American Indian or Alaskan Native, male subject with medical history of hypertension, hypothyroidism, asthma, and environmental allergies, who experienced an unexpected event of rheumatoid arthritis. The event occurred 14 days after the first, and only, study vaccine. The event was considered related to the study vaccine in agreement with the Investigator's assessment; however, the subject's medical history of hypertension and hypothyroidism may potentially indicate pre-existing autoimmune disease. Study vaccine was withdrawn.

B6. LABORATORY DATA

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	09/25/2020	Anti-cyclic citrullinated peptide antibody	>250 unit	<20
2	09/25/2020	Antinuclear antibody Negative		
3	09/25/2020	Blood pressure measurement	124/71 mmHg	
4	09/25/2020	C-reactive protein	<0.1 OTHER	
5	09/25/2020	Complement factor C3 High	194 OTHER	
6	09/25/2020	Complement factor C4	32 OTHER	
7	--/--/2020	Heart rate 80s	/min	60s 50s
8	09/25/2020	Heart rate	70 /min	60s 50s
9	09/25/2020	Physical examination weight gain, weakness, hearing loss, tinnitus, wheezing, constipation, nausea, headache, insomnia, joint pain, muscle weakness, lateral epicondyle tenderness of right, and lateral epicondyle tenderness of left elbow		
10	09/25/2020	Red blood cell sedimentation rate mm/hr	4 OTHER	
11	09/25/2020	Rheumatoid factor	62.5 international unit per millilitre	13 FDA-CBER-2022-1614-4434495

B7. OTHER RELEVANT HISTORY

#	Start/Stop Date	Condition Type / Condition	Notes
1	--/--/1990 Ongoing	Current Condition Hypothyroidism	reason could have been exposure to iodine radioisotopes I-125 but no exact reason identified.
2	--/--/1990 Ongoing	Allergy Hypersensitivity	
3	--/--/2000 Ongoing	Current Condition Asthma	
4	--/--/2010 Ongoing	Current Condition Gastroesophageal reflux disease	
5	--/--/2018 Ongoing	Current Condition Hypertension	
6	01/--/2020 Ongoing	Current Condition Arthralgia	

C4. DIAGNOSIS FOR USE (Continued)

#1:COVID-19 vaccination (COVID-19 immunisation)

C10. CONCOMITANT MEDICAL PRODUCTS (Continued)

ongoing

3) ENALAPRIL (ENALAPRIL) --/--/2018 to ongoing

4) BREO ELLIPTA (FLUTICASONE FUROATE, VILANTEROL TRIFENATATE) 08/--/2020 to ongoing

5) ALBUTEROL [SALBUTAMOL] (ALBUTEROL [SALBUTAMOL]) --/--/2000 to ongoing

6) LEVOCETIRIZINE (LEVOCETIRIZINE) --/--/2018 to ongoing

7) MONTELUKAST (MONTELUKAST) --/--/1990 to ongoing