

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

A. PATIENT INFORMATION			
1. Patient Identifier US3552191	2. Age at Time of Event: 66 Years or Date of Birth: (b) (6)/1953	3. Sex <input checked="" type="checkbox"/> Female <input type="checkbox"/> Male	4. Weight 164.1 lbs or 74.4 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 checked="" type="checkbox"/> Hospitalization - initial or prolonged <input 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) 09/30/2020		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) SHORTNESS OF BREATH ON EXERTION [Exertional dyspnea] BILATERAL ANKLE EDEMA [Ankle edema]  Case Description: This 66-year-old, White, female subject (US3552191) 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 shortness of breath on exertion and bilateral ankle edema.  The subject's medical history, as provided by the investigator, included breast cancer, diabetes mellitus type 2, continued in additional info section...			
6. Relevant Tests/Laboratory Data, Including Dates #1 10/09/2020 Blood albumin (continued) #2 10/09/2020 Blood creatinine (continued) #3 10/10/2020 Blood glucose (continued) #4 10/08/2020 Blood pressure measurement (continued) #5 10/09/2020 Blood pressure measurement (continued) #6 09/--/2020 Body temperature 101.6 °F 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: White #1 --/--/1987 to Ongoing Allergy, (Continued) #2 --/--/1987 to Ongoing Current Condition, (Continued) #3 --/--/1987 to Ongoing Current Condition, (Continued) continued in additional info section...			

C. SUSPECT PRODUCT(S)			
1. Name (Give labeled strength & mfr/labeler) (Regimens Continued)			
#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. 08/26/2020 to 08/26/2020	
#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 type="checkbox"/> No <input checked="" 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) CETIRIZINE (CETIRIZINE) --/--/2017 to ongoing			
2) METFORMIN (METFORMIN) 06/--/2018 to ongoing 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 #4			
9. Manufacturer Report Number (b) (6)		8. Adverse Event Term(s) Exertional dyspnea, Ankle edema	
E. INITIAL REPORTER			
1. Name and Address Dr. SHARON FREY Saint Louis University Saint Louis, MO UNITED STATES			
Phone # (b) (6)		Email Address (b) (6) @health.slu.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)**

Meniere's disease, hypercholesterolemia, obstructive sleep apnea, osteoarthritis, vitamin D deficiency, herniated disc, menopause, Achilles tendonitis, constipation, rosacea, tolmetin sodium allergy (hives), seasonal allergies, benign hypertension, disorder of vertebral column, and depression with anxiety. Concomitant medications reported included cetirizine, metformin, hydrochlorothiazide with triamterene, atorvastatin, venlafaxine, vitamin B12, gabapentin, vitamin D3, and ascorbic acid/ calcium/ minerals not otherwise specified (NOS)/ retinol/ tocopherol acetate/ vitamin B NOS/ zinc/ magnesium citrate.

The subject received the first dose of blinded intramuscular mRNA-1273 or placebo for SARS-CoV-2 vaccination on 26 Aug 2020. The subject's last dose of study drug, seven days prior to earliest event onset, was on 23 Sep 2020.

On 30 Sep 2020, the subject experienced shortness of breath on exertion.

On 06 Oct 2020, the subject experienced bilateral ankle edema.

On 07 Oct 2020, she notified the site of her shortness of breath on exertion, fatigue, and swollen ankles, which resulted in an illness visit in the patient's home, per study procedures, on 08 Oct 2020. Vital signs included temperature 98.3 degrees Fahrenheit, pulse 111 beats per minute (bpm), respiratory rate 20 breaths per minute, blood pressure 128/80 mmHg, and oxygen saturation 94%. The subject reported symptoms of mild cough, shortness of breath, fatigue, headache, and sore throat. A COVID-19 nasopharyngeal swab was collected, and the result was negative.

On 09 Oct 2020, the subject's primary care provider recommended that she go to the hospital Emergency Department after reporting that she could not talk much without feeling winded. Presenting vital signs included temperature 35.6 degrees Celsius temporal and 36.8 degrees Celsius oral, pulse rate 74 bpm, respiratory rate 18 breaths per minute, blood pressure 128/62 mmHg, and oxygen saturation 99%. The subject reported moderate shortness of breath, exacerbated by exertion, for the previous two weeks. Relieving factors included rest and sitting upright. She denied chest pain, fever, cough, nausea, vomiting, sweating, a previous history of shortness of breath, lung problems, pulmonary embolism, or other complaints. She reported that she felt horrible after the last dose of study drug, with fever up to 101.6 degrees Fahrenheit, myalgias, chills, and sweats lasting one day, but that she continued to experience shortness of breath, particularly with exertion, as well as fatigue. She began to feel a little better about one week ago, but she began to have dyspnea on exertion around her house and was unable to walk around her yard without shortness of breath. Over the last few days, she noticed increased swelling in her legs and feet bilaterally. Relevant findings on physical examination included tachycardia, breath sounds were clear and equal bilaterally, +2 bipedal edema with further evaluation noting intact neurovascular status, brisk capillary refill, palpable and equal pulses bilaterally, negative calf girth discrepancy, negative Homan's sign, strength 5/5, and deep tendon reflexes 2/4 in both patellar and Achilles distribution. An electrocardiogram showed sinus tachycardia with no evidence of injury pattern. A chest x-ray revealed no active disease, noting clear lungs and a cardiac silhouette within normal limits showing no evidence of failure. A computerized tomogram of the chest showed no evidence of pulmonary embolism, clear lungs, and mild cardiomegaly. Relevant laboratory test results included D-dimer 610.0 ng/mL (0.0-400.0), brain natriuretic peptide 69 pg/mL (15-50), white blood cell count 3.2 x10E3/uL (4.0-11.0), red blood cell count 3.55 x10E6/uL (4.00-6.00), hemoglobin 10.7 g/dL (12.0-18.0), hematocrit 31.4% (36.0-54.0), total protein 5.7 g/dL (6.4-8.3), albumin 3.3 g/dL (3.5-5.0), and troponin I <0.020 ng/mL (0.020-0.034). She was admitted overnight. Treatment included a single dose of intravenous furosemide.

On 10 Oct 2020, the subject stated that she felt a little improved. Her ankle swelling improved and she denied chest pain, nausea, vomiting, abdominal pain, and change in bowel or bladder. Relevant laboratory test results included troponin I <0.020 ng/mL. Vital signs prior to discharge included temperature range of 36.8 degrees Celsius, blood pressure range of 125/59 mmHg, respiratory rate 18 breaths per minute, and oxygen saturation 95% on room air. She was discharged from the hospital with instructions for follow-up echocardiogram, per cardiology's recommendation.

On 12 Oct 2020, per cardiologist's office, echocardiogram was negative.

Action taken with study drug was not applicable, as the subject had already received both scheduled doses per protocol.

The events, bilateral ankle edema and shortness of breath on exertion was considered resolving.

The Investigator assessed the events, shortness of breath on exertion and bilateral ankle edema, as related to study drug and not related to study procedure. The Investigator's rationale provided for assessing the events as being related to study drug was that there was no identified alternate etiology and because the subject's history wasn't consistent with the symptoms that evolved in the weeks following administration of the second dose of study drug. The Investigator noted that the subject's multiple underlying comorbidities, including diabetes, negative cardiac work-up, and low hemoglobin were confounding factors in her assessment.

Follow-up received on 21 Oct 2020 included upgrading severity of both events to grade 4 (previously grade 3), laboratory and diagnostic test, and investigator's rationale for relatedness.

Follow-up received on 28 Oct 2020 and 30 Oct 2020 included the start date for the event of shortness of breath on exertion and updated concomitant medications.

Follow-up received on 09 Nov 2020 and 11 Nov 2020 included updated concomitant medication and updated outcome for event of shortness of breath on exertion.

Case Comment/Sender's Comment:

Company Comment: This case concerns a 66 year old, White, female subject who experienced an unexpected events of shortness of breath on exertion and bilateral ankle edema. The event bilateral ankle edema occurred 1 month 8 days after the blinded study vaccine and 11 days after the last vaccine administration. The event shortness of breath on exertion occurred 1 month 5 days after the study vaccine and 8 days after the last dose administration. The events were considered unrelated to the study vaccine as the event might be explained by the subject's medical history of breast cancer and pre-existing diabetes mellitus type 2 and hypertension.

B6. LABORATORY DATA

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	10/09/2020	Blood albumin Low	3.3 g/dL	5.0 3.5
2	10/09/2020	Blood creatinine Low	0.5 mg/dl	1.3 0.6
3	10/10/2020	Blood glucose High 140	119 mg/dl	100 70
4	10/08/2020	Blood pressure measurement	128/80 mmHg	
5	10/09/2020	Blood pressure measurement	128/62 mmHg	
7	10/08/2020	Body temperature	98.3 °F	
8	10/09/2020	Body temperature Low Temporal  36.8 Oral	35.6 degree Celsius	
9	10/09/2020	Brain natriuretic peptide  Slightly elevated	69 pg/ml	50 15
10	10/09/2020	Chest X-ray  Showed no significant or acute findings and no active disease.		
11	10/09/2020	Computerised tomogram thorax  No evidence of pulmonary embolism, clear lungs, and mild cardiomegaly.		
12	10/12/2020	Echocardiogram Negative Per cardiologist's office, echocardiogram was negative.		
13	09/--/2020	Ejection fraction  Unremarkable		

14	10/09/2020	Electrocardiogram		
		No evidence of injury pattern. Sinus tachycardia with possible left atrial enlargement.		
15	10/09/2020	Fibrin D dimer	610.0 ng/mL	400.0 0.0
		Elevated		
16	10/09/2020	Haematocrit	31.4 percent	54.0 36.0
		Low		
17	10/09/2020	Haemoglobin	10.7 g/dL	18.0 12.0
		Low		
18	10/08/2020	Heart rate	111 heart beats per minute	
19	10/09/2020	Heart rate	74 heart beats per minute	
20	10/08/2020	Oxygen saturation	94 percent	
21	10/09/2020	Oxygen saturation	99 percent	
22	10/09/2020	Protein total	5.7 g/dL	8.3 6.4
		Low		
23	10/09/2020	Red blood cell count	3.55 10 <sup>12</sup> /L	6.00 4.00
		Low		
24	10/08/2020	Respiratory rate	20 breaths per minute	
25	10/09/2020	Respiratory rate	18 breaths per minute	
26	10/08/2020	SARS-CoV-2 test Negative Nasopharyngeal swab		
27	10/09/2020	Troponin I	<0.020 ng/mL	0.034 0.020
		Low		
28	10/10/2020	Troponin I	<0.020 ng/mL	0.034 0.020
		Low		
29	10/09/2020	White blood cell count	3.2 10 <sup>9</sup> /L	
		Low		

## B7. OTHER RELEVANT HISTORY

#	Start/Stop Date	Condition Type / Condition	Notes
1	--/--/1987 Ongoing	Allergy Drug hypersensitivity	
2	--/--/1987 Ongoing	Current Condition Intervertebral disc protrusion	
3	--/--/1987 Ongoing	Current Condition Osteoarthritis	

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4	--/--/1990 Ongoing	Current Condition Depression	
5	--/--/1990 Ongoing	Current Condition Rosacea	
6	--/--/2000 Ongoing	Current Condition Hypercholesterolaemia	
7	--/--/2003 Ongoing	Current Condition Menopause	
8	01/--/2007 01/--/2012	Historical Condition Breast cancer	
9	--/--/2012 Ongoing	Current Condition Vitamin D deficiency	
10	--/--/2015 Ongoing	Current Condition Meniere's disease	
11	--/--/2017 Ongoing	Allergy Seasonal allergy	
12	06/--/2018 Ongoing	Current Condition Type 2 diabetes mellitus	
13	--/--/2019 Ongoing	Current Condition Constipation	
14	03/--/2020 Ongoing	Current Condition Tendonitis	
15	Ongoing	Current Condition Sleep apnoea syndrome	On continuous positive airway pressure.
16	Ongoing	Current Condition Hypertensive heart disease	
17	Ongoing	Current Condition Spinal disorder	Vertebral column
18	Ongoing	Current Condition Depression	

#### C4. DIAGNOSIS FOR USE (Continued)

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

#### C10. CONCOMITANT MEDICAL PRODUCTS (Continued)

3) HYDROCHLOROTHIAZIDE WITH TRIAMTERENE (HYDROCHLOROTHIAZIDE, TRIAMTERENE) --/--/2015 to ongoing

4) ATORVASTATIN (ATORVASTATIN) --/--/2010 to ongoing

5) VENLAFAXINE (VENLAFAXINE) --/--/1990 to ongoing

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- 6) VITAMIN B12 NOS (VITAMIN B12 NOS) 06/--/2018 to ongoing
- 7) GABAPENTIN (GABAPENTIN) --/--/2016 to ongoing
- 8) VITAMIN D3 (COLECALCIFEROL) --/--/2012 to ongoing
- 9) CENTRUM SILVER [ASCORBIC ACID;CALCIUM;MINERALS NOS;RETINOL;TOCOPHERYL ACETATE;VITAMIN B NOS;VITAMINS NOS;ZINC] (ASCORBIC ACID, CALCIUM, MINERALS NOS, RETINOL, TOCOPHERYL ACETATE, VITAMIN B NOS, VITAMINS NOS, ZINC) --/--/2014 to ongoing
- 10) MAGNESIUM CITRATE (MAGNESIUM CITRATE) --/--/2019 to ongoing

## Block C - Additional Dosage Regimens

Suspect Product	2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration)	6. Lot #	7. Exp. date
#1 mRNA-1273 vs Placebo Regimen # 2	Blinded, Information withheld.	09/23/2020 to 09/23/2020	Blinded	Blinded