

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

A. PATIENT INFORMATION			
1. Patient Identifier US3322329	2. Age at Time of Event: 51 Years or Date of Birth: (b) (6) /1968	3. Sex <input checked="" type="checkbox"/> Female <input type="checkbox"/> Male	4. Weight ____ lbs or ____ 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) 10/17/2020		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) FACIAL SWELLING [Facial swelling]			
Case Description: This 51-year-old, White, female subject (US3322329) 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 facial swelling.			
The subject's medical history, as provided by the investigator, included hysterectomy, foot surgery, cervical dysplasia, left foot tennis injury and postmenopausal. Concomitant medications reported included estradiol, testosterone and naproxen. Botox Cosmetic, Juvederm Ultra continued in additional info section...			
6. Relevant Tests/Laboratory Data, Including Dates #1 10/15/2020 Physical examination (continued)			
7. Other Relevant History, Including Preexisting Medical Conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.) Race: White #1 --/--/2007 to --/--/2007, Historical Condition, Hysterectomy #2 --/--/2007 to --/--/2007, Historical Condition, Cervical dysplasia #3 --/--/2014 to Ongoing, Current Condition, Postmenopause 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. BOTOX COSMETIC (BOTULINUM TOXIN TYPE A)			
2. Dose, Frequency & Route Used		3. Therapy Dates (if unknown, give duration) from/to (or best estimate)	
#1. Blinded, Information withheld.		#1. 09/12/2020 to 09/12/2020	
#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. Cosmetic procedure (Continued)		#2. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply	
6. Lot #	7. Exp. Date		
#1. Blinded	#1. Blinded		
#2.	#2.		
9. NDC# or Unique ID			
10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)			
1) NAPROXEN (NAPROXEN) 09/16/2020 to 09/16/2020			
2) ESTRADIOL (ESTRADIOL) Pellet --/--/2014 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) 11/06/2020	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) Facial swelling		
E. INITIAL REPORTER			
1. Name and Address continued in additional info section Dr. VERONICA FRAGOSO DM Clinical Research - Texas Center For Drug Development 6550 MAPLERIDGE STREET HOUSTON, TX 77081			
Phone # (b) (6)	Email Address (b) (6) @tcddresearch.com		
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

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## C. SUSPECT PRODUCT(S)

1. <b>Name</b> (Give labeled strength & mfr/labeler)	
#3. JUVEDERM ULTRA PLUS XC (HYALURONIC ACID, (Continued)	
#4. JUVEDERM VOLUMA XC (HYALURONIC ACID, LIDOCAINE)	
2. <b>Dose, Frequency &amp; Route Used</b>	3. <b>Therapy Dates</b> (if unknown, give duration from/to (or best estimate)
#3.	#3.
#4.	#4.
4. <b>Diagnosis for Use</b> (Indication)	5. <b>Event Abated After Use Stopped or Dose Reduced?</b>
#3. Cosmetic procedure (Continued)	#3. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
#4. Cosmetic procedure (Continued)	#4. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
6. <b>Lot #</b>	7. <b>Exp. Date</b>
#3.	#3.
#4.	#4.
9. <b>NDC# or Unique ID</b>	8. <b>Event Reappeared After Reintroduction?</b>
NA	#3. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
	#4. <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply
10. <b>Concomitant Medical Products and Therapy Dates</b> (Exclude treatment of event)	

**ADDITIONAL INFORMATION****B5. EVENT DESCRIPTION (Continued)**

Plus XC and Juvederm Voluma subcutaneous were reported by the Investigator as co-suspect products.

The subject received the first dose of blinded mRNA-1273 or placebo for SARS-CoV-2 vaccination on 12 Sep 2020 and her second, final dose of study drug two days prior to event onset, on 15 Oct 2020.

On 02 Oct 2020, the subject had cosmetic injections in her cheeks. She was injected with a Botox/Filler combination consisting of 60 units of BOTOX Cosmetic, 1 unit of Juvederm Ultra Plus XC, and 3 units of Juvederm Voluma subcutaneous.

On 15 Oct 2020, the subject presented to the site for her Dose 2 visit and her physical examination was normal, including a skin assessment.

On 17 Oct 2020, the subject developed injection site swelling/ hardness measuring 125 mm with mild deltoid tenderness at the site of study drug administration, but denied trouble moving the affected arm. That night, she experienced bilateral facial swelling, which was greater on the left side than the right. The subject contacted the doctor that performed the cosmetic procedure concerning her moderate facial swelling and was prescribed a five-day course of oral prednisolone (initial dose of 25 mg, followed by 40 mg daily) as treatment.

On 18 Oct 2020, the area of study drug injection site swelling/hardness had reduced to 55 mm.

On 20 Oct 2020, the subject reported that her facial swelling was almost completely resolved, with minimal swelling remaining under the left eye.

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

The event, facial swelling, was considered resolved on 22 Oct 2020.

The investigator assessed the event, facial swelling, as related to study drug and not related to study procedure. The investigator noted that facial swelling was a known potential side effect of Voluma dermal filler injections and stated that she believed the injection of dermal filler was a contributing factor to the subject's development of facial swelling. However, since the subject developed facial swelling almost two weeks after the dermal filler injections and only two days after administration of study drug, the investigator concluded that the temporal relationship provided a reasonable probability of a causal relationship between the subject's facial swelling and receipt of investigational product.

Follow-up received on 30 Oct 2020 and 03 Nov 2020 included updated medical history and end date.

Follow-up received on 06 Nov 2020 and 13 Nov 2020 included medical records which provided cosmetic injection details and event outcome.

Analysis of Similar Events: On 26-Oct-2020, the safety database was searched for events similar to facial swelling using the following search criteria: PT: Facial swelling; SMQ: Angioedema.

As of 26-Oct-2020 under IND 019745 for mRNA-1273, 5 similar events were retrieved, including the current index case. None of the cases retrieved were previously submitted as IND Safety Reports. There were 4 cases reporting the following events, summarized below: Swelling face (1) (b) (6), Oedema peripheral (1) (b) (6), Angioedema (1) (b) (6), Laryngeal oedema (1) (b) (6).

(b) (6): An event of swelling face was reported in a subject with swelling to the right side of the face/jaw after a recent dental history of root canal on the same side. The facial swelling occurred 7 days after blinded study vaccine administration and 14 days after root canal. A consultant ENT suggested the event may be due to an odontogenic infection.

(b) (6): An event of bilateral ankle edema (and concurrent dyspnea on exertion) was reported in a 66-year-old subject with medical history of breast cancer, diabetes mellitus type 2, and hypertension. The event of bilateral ankle edema occurred 1 month 8 days after the first administration of blinded study vaccine and 11 days after the last vaccine administration.

(b) (6): An event of angioedema was reported in a subject taking concomitant lisinopril for hypertension. The event occurred 21 days after the first dose of the study medication. The event resolved 2 days after discontinuation of lisinopril. The event  
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is more likely explained by the subject's concomitant use of lisinopril known to cause angioedema.

(b) (6): An event of laryngeal edema was reported in a subject with medical history of sulfa allergy (hives) and concomitant use of lisinopril. The event occurred 4 days after the second dose of blinded study medication administration. The event of laryngeal edema was likely associated with lisinopril therapy which was discontinued due to adverse event.

As of 13 Nov 2020, one additional report was received of "Facial swelling" (b) (6), in which a 46-year-old, white, female subject who received bilateral Voluma (hyaluronic acid) cheek injections in May 2020 without incident and subsequently experienced the unexpected event of cheek swelling, bilateral six months after Voluma injections and 2 days after the second dose of blinded study drug administration. The event was considered related to the study vaccine in agreement with the Investigator's assessment and will be submitted as an additional IND Safety Report.

The review of the cases of one-sided facial edema possibly due to a dental etiology, one event of bilateral edema of the ankles and two events of angioedema and laryngeal edema likely due to lisinopril did not identify other clinically similar adverse events to the current IND safety report, (b) (6). However, there was another case of facial swelling with a temporal relationship to study drug administration. In both cases, the subjects had a history of bilateral cheek dermal filler injections with Voluma prior to receiving study drug (6 months, 13 days respectively); for which the relevance to the event is unknown.

The Sponsor cannot rule out a possible cause and effect relationship between administration of blinded study vaccine and the occurrence facial swelling. 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:

Company Comment: This case concerns a 51-year-old, White, female subject with recent dermal filler cosmetic injection in her cheeks, who experienced an unexpected event of facial swelling. The event occurred 1 month 6 days after the first dose of blinded study vaccine administration and 2 days after the last dose administration. The event was considered related to the study vaccine in agreement with the Investigator's assessment. Contributing factors may include subjects Botox/Filler combination.

## B6. LABORATORY DATA

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	10/15/2020	Physical examination  Normal including skin	OTHER	

## B7. OTHER RELEVANT HISTORY

#	Start/Stop Date	Condition Type / Condition	Notes
4	--/--/2018 --/--/2018	Historical Condition Foot operation	
5	--/--/2018 --/--/2018	Historical Condition Limb injury	Tennis injury; left

## C1. NAME (Continued)

Suspect Medication #3: JUVEDERM ULTRA PLUS XC(HYALURONIC ACID, LIDOCAINE HYDROCHLORIDE)

## C4. DIAGNOSIS FOR USE (Continued)

- #1:COVID-19 vaccination (COVID-19 immunisation)
- #2:Cosmetic procedure (Skin cosmetic procedure)
- #3:Cosmetic procedure (Skin cosmetic procedure)
- #4:Cosmetic procedure (Skin cosmetic procedure)

## C10. CONCOMITANT MEDICAL PRODUCTS (Continued)

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ongoing

3) TESTOSTERONE (TESTOSTERONE) Pellet --/--/2014 to ongoing

E1. NAME AND ADDRESS (Continued)

Dr. VERONICA FRAGOSO

DM Clinical Research - Texas Center For Drug Development

6550 MAPLERIDGE STREET HOUSTON, TX 77081 UNITED STATES

## 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.	10/15/2020 to 10/15/2020	Blinded	Blinded