

FULL EMERGENCY USE AUTHORIZATION (EUA) PRESCRIBING INFORMATION

MODERNA COVID-19 VACCINE

FULL EUA PRESCRIBING INFORMATION: CONTENTS*

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 information are not listed

Commented [A1]: SPONSOR COMMENT: Moderna has accepted the Division's changes and proposed new changes to implement the Division's requests and proposals by Moderna.

Commented [A2]: FDA COMMENT December 4, 2020: Moderna: We request that you use Section numbers as specified in the template provided by FDA on November 10, 2020. Please do not reassign section numbers to account for omitted sections

SPONSOR RESPONSE: Moderna acknowledges the Contents list provided and has updated a version in this document to reflect those section titles that would appear in the full prescribing information document once all sections are merged into one document again.

Table 1: Frequency of Solicited Local and Systemic Reactions Within 7 Days After Each Dose in Participants 18-64 Years (Solicited Safety Set, Dose 1 and Dose 2)

	<u>Moderna COVID-19 Vaccine</u>		<u>Placebo*</u>	
	<u>Dose 1</u> <u>(N=11,405)</u> <u>n (%)</u>	<u>Dose 2</u> <u>(N=10,358)</u> <u>n (%)</u>	<u>Dose 1</u> <u>(N=11,406)</u> <u>n (%)</u>	<u>Dose 2</u> <u>(N=10,321)</u> <u>n (%)</u>
<u>Local Adverse Reactions</u>				
<u>Pain</u>	<u>9,908</u> <u>(86.9)</u>	<u>9,335</u> <u>(90.1)</u>	<u>2,179</u> <u>(19.1)</u>	<u>1,942</u> <u>(18.8)</u>
<u>Pain, Grade 3^b</u>	<u>367</u> <u>(3.2)</u>	<u>479</u> <u>(4.6)</u>	<u>23</u> <u>(0.2)</u>	<u>21</u> <u>(0.2)</u>
<u>Lymphadenopathy</u>	<u>1,322</u> <u>(11.6)</u>	<u>1,654</u> <u>(16.0)</u>	<u>567</u> <u>(5.0)</u>	<u>444</u> <u>(4.3)</u>
<u>Lymphadenopathy, Grade 3^b</u>	<u>36</u> <u>(0.3)</u>	<u>45</u> <u>(0.4)</u>	<u>13</u> <u>(0.1)</u>	<u>10</u> <u>(<0.1)</u>
<u>Swelling (hardness)</u>	<u>768</u> <u>(6.7)</u>	<u>1,309</u> <u>(12.6)</u>	<u>33</u> <u>(0.3)</u>	<u>35</u> <u>(0.3)</u>
<u>Swelling (hardness), Grade 3^c</u>	<u>62</u> <u>(0.5)</u>	<u>176</u> <u>(1.7)</u>	<u>3</u> <u>(<0.1)</u>	<u>4</u> <u>(<0.1)</u>
<u>Erythema (redness)</u>	<u>345</u> <u>(3.0)</u>	<u>928</u> <u>(9.0)</u>	<u>46</u> <u>(0.4)</u>	<u>42</u> <u>(0.4)</u>
<u>Erythema (redness), Grade 3^c</u>	<u>34</u> <u>(0.3)</u>	<u>206</u> <u>(2.0)</u>	<u>11</u> <u>(<0.1)</u>	<u>12</u> <u>(0.1)</u>
<u>Systemic Adverse Reactions</u>				
<u>Fatigue</u>	<u>4,384</u> <u>(38.5)</u>	<u>7,002</u> <u>(67.6)</u>	<u>3,282</u> <u>(28.8)</u>	<u>2,530</u> <u>(24.5)</u>
<u>Fatigue, Grade 3^d</u>	<u>120</u>	<u>1,099</u>	<u>83</u>	<u>81</u>

Commented [A3]: FDA COMMENT December 5, 2020: We do not agree with the proposed revisions to Table 1 and Table 2 submitted as part of Draft-PI-sections1-8 redline_4Dec2020.docx, and continue to recommend that you present two separate tables for each age cohort (18-64 years, ≥65years). Please provide the following two separate tables:

-Table 1: Frequency of Solicited Local and Systemic Reactions Within 7 days After Each Dose, Subjects 18-64 years- Solicited Safety Sets- 1st dose, -2nd dose
 -Table 2: Frequency of Solicited Local and Systemic Reactions Within 7 days After Each Dose, Subjects 65 years and older- Solicited Safety Set-1st dose, -2nd dose
 These two separate tables stratified by age are sufficient to present the frequency of solicited adverse reactions in the PI. We recommend that the columns with 'Overall' rates be removed.

SPONSOR RESPONSE: Moderna has updated the tables per the Division's email request on December 5, 2020, and included them in this document in response.

Commented [A4]: Sources: IND 19745 SN0080
 Table 14.3.1.1.4 Summary of Subjects with Solicited Adverse Reactions Within 7 Days After First Injection by Age Group and Grade First Injection Solicited Safety Set
 Table 14.3.1.1.5 Summary of Subjects with Solicited Adverse Reactions Within 7 Days After Second Injection by Age Group and Grade Second Injection Solicited Safety Set

	(1.1)	(10.6)	(0.7)	(0.8)
Fatigue, Grade 4 ^e	1 (<0.1)	0 (0)	0 (0)	0 (0)
Headache	4,031 (35.4)	6,500 (62.8)	3,303 (29.0)	2,617 (25.4)
Headache, Grade 3 ^f	219 (1.9)	515 (5.0)	162 (1.4)	124 (1.2)
Myalgia	2,698 (23.7)	6,353 (61.3)	1,626 (14.3)	1,312 (12.7)
Myalgia, Grade 3 ^d	73 (0.6)	1,032 (10.0)	38 (0.3)	39 (0.4)
Arthralgia	1,892 (16.6)	4,685 (45.2)	1,327 (11.6)	1,087 (10.5)
Arthralgia, Grade 3 ^d	47 (0.4)	603 (5.8)	29 (0.3)	36 (0.3)
Arthralgia, Grade 4 ^e	1 (<0.1)	0 (0)	0 (0)	0 (0)
Chills	1,051 (9.2)	5,001 (48.3)	730 (6.4)	611 (5.9)
Chills, Grade 3 ^g	17 (0.1)	151 (1.5)	8 (<0.1)	14 (0.1)
Gastrointestinal Symptoms ^h	1,069 (9.4)	2,209 (21.3)	908 (8.0)	754 (7.3)
Gastrointestinal symptoms, Grade 3 ^{h,i}	6 (<0.1)	8 (<0.1)	8 (<0.1)	8 (<0.1)
Fever	105 (0.9)	1,806 (17.4)	39 (0.3)	38 (0.4)
Fever, Grade 3 ^j	10 (<0.1)	168 (1.6)	1 (<0.1)	1 (<0.1)
Fever, Grade 4 ^k	4 (<0.1)	10 (<0.1)	4 (<0.1)	2 (<0.1)

* 7 days included day of vaccination and the subsequent 6 days.

^a Placebo was a saline solution.

^b Grade 3 pain and lymphadenopathy: Defined as any use of prescription pain reliever; prevents daily activity.

^c Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.

^d Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.

^e Grade 4 fatigue, arthralgia: Defined as requires emergency room visit or hospitalization.

^f Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.

^g Grade 3 chills: Defined as prevents daily activity and requires medical intervention.

^h Gastrointestinal symptoms = nausea, vomiting, diarrhea, and/or abdominal pain.

ⁱ Grade 3 gastrointestinal symptoms: Defined as prevents daily activity, requires outpatient intravenous hydration.

^j Grade 3 fever: Defined as $\geq 39.0 - <40.0^{\circ}\text{C}$ / $\geq 102.1 - <104.0^{\circ}\text{F}$.

^k Grade 4 fever: Defined as $>40.0^{\circ}\text{C}$ / $>104.0^{\circ}\text{F}$.

Table 2: Frequency of Solicited Local and Systemic Reactions Within 7 Days After Each Dose in Participants 65 Years and Older (Solicited Safety Set, Dose 1 and Dose 2)

	Moderna COVID-19 Vaccine		Placebo ^a	
	Dose 1 (N=3,762) n (%)	Dose 2 (N=3,589) n (%)	Dose 1 (N=3,748) n (%)	Dose 2 (N=3,549) n (%)

Commented [A5]: Sources: IND 19745 SN0080
Table 14.3.1.1.4 Summary of Subjects with Solicited Adverse Reactions Within 7 Days After First Injection by Age Group and Grade First Injection Solicited Safety Set
Table 14.3.1.1.5 Summary of Subjects with Solicited Adverse Reactions Within 7 Days After Second Injection by Age Group and Grade Second Injection Solicited Safety Set

Local Adverse Reactions				
Pain	<u>2,782</u> (74.0)	<u>2,990</u> (83.4)	<u>481</u> (12.8)	<u>421</u> (11.9)
Pain, Grade 3 ^b	<u>50</u> (1.3)	<u>96</u> (2.7)	<u>32</u> (0.9)	<u>17</u> (0.5)
Lymphadenopathy	<u>231</u> (6.1)	<u>302</u> (8.4)	<u>155</u> (4.1)	<u>90</u> (2.5)
Lymphadenopathy, Grade 3 ^b	<u>12</u> (0.3)	<u>21</u> (0.6)	<u>14</u> (0.4)	<u>8</u> (0.2)
Swelling (hardness)	<u>166</u> (4.4)	<u>386</u> (10.8)	<u>19</u> (0.5)	<u>13</u> (0.4)
Swelling (hardness), Grade 3 ^c	<u>20</u> (0.5)	<u>69</u> (1.9)	<u>3</u> (<0.1)	<u>7</u> (0.2)
Erythema (redness)	<u>86</u> (2.3)	<u>265</u> (7.4)	<u>19</u> (0.5)	<u>13</u> (0.4)
Erythema (redness), Grade 3 ^c	<u>8</u> (0.2)	<u>75</u> (2.1)	<u>2</u> (<0.1)	<u>3</u> (<0.1)
Systemic Adverse Reactions				
Fatigue	<u>1,251</u> (33.3)	<u>2,094</u> (58.4)	<u>851</u> (22.7)	<u>695</u> (19.6)
Fatigue, Grade 3 ^d	<u>30</u> (0.8)	<u>248</u> (6.9)	<u>23</u> (0.6)	<u>20</u> (0.6)
Headache	<u>921</u> (24.5)	<u>1,665</u> (46.4)	<u>724</u> (19.3)	<u>635</u> (17.9)
Headache, Grade 3 ^c	<u>52</u> (1.4)	<u>107</u> (3.0)	<u>34</u> (0.9)	<u>32</u> (0.9)
Myalgia	<u>743</u> (19.8)	<u>1,683</u> (46.9)	<u>443</u> (11.8)	<u>385</u> (10.8)
Myalgia, Grade 3 ^d	<u>17</u> (0.5)	<u>201</u> (5.6)	<u>9</u> (0.2)	<u>10</u> (0.3)
Arthralgia	<u>618</u> (16.4)	<u>1,252</u> (34.9)	<u>456</u> (12.2)	<u>381</u> (10.7)
Arthralgia, Grade 3 ^d	<u>13</u> (0.3)	<u>122</u> (3.4)	<u>8</u> (0.2)	<u>7</u> (0.2)
Chills	<u>202</u> (5.4)	<u>1,099</u> (30.6)	<u>148</u> (4.0)	<u>144</u> (4.1)
Chills, Grade 3 ^f	<u>7</u> (0.2)	<u>27</u> (0.8)	<u>6</u> (0.2)	<u>2</u> (<0.1)
Gastrointestinal symptoms ^g	<u>194</u> (5.2)	<u>425</u> (11.8)	<u>166</u> (4.4)	<u>129</u> (3.6)
Gastrointestinal symptoms, Grade 3 ^{g,h}	<u>4</u> (0.1)	<u>10</u> (0.3)	<u>4</u> (0.1)	<u>3</u> (<0.1)
Gastrointestinal symptoms, Grade 4 ^{g,i}	<u>0</u> (0)	<u>1</u> (<0.1)	<u>0</u> (0)	<u>0</u> (0)
Fever	<u>10</u> (0.3)	<u>366</u> (10.2)	<u>7</u> (0.2)	<u>5</u> (0.1)
Fever, Grade 3 ^j	<u>1</u> (<0.1)	<u>18</u> (0.5)	<u>1</u> (<0.1)	<u>0</u> (0)
Fever, Grade 4 ^k	<u>0</u> (0)	<u>1</u> (<0.1)	<u>2</u> (<0.1)	<u>1</u> (<0.1)

* 7 days included day of vaccination and the subsequent 6 days.

^a Placebo was a saline solution.

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Draft December 6, 2020

^b Grade 3 pain and lymphadenopathy: Defined as any use of prescription pain reliever; prevents daily activity.

^c Grade 3 swelling and erythema: Defined as >100 mm / >10 cm.

^d Grade 3 fatigue, myalgia, arthralgia: Defined as significant; prevents daily activity.

^e Grade 3 headache: Defined as significant; any use of prescription pain reliever or prevents daily activity.

^f Grade 3 chills: Defined as prevents daily activity and requires medical intervention.

^g Gastrointestinal symptoms = nausea, vomiting, diarrhea, and/or abdominal pain.

^h Grade 3 gastrointestinal symptoms: Defined as prevents daily activity, requires outpatient intravenous hydration.

ⁱ Grade 4 gastrointestinal symptoms: Defined as requires emergency room visit or hospitalization for hypotensive shock.

^j Grade 3 fever: Defined as $\geq 39.0 - < 40.0^{\circ}\text{C}$ / $\geq 102.1 - < 104.0^{\circ}\text{F}$.

^k Grade 4 fever: Defined as $> 40.0^{\circ}\text{C}$ / $> 104.0^{\circ}\text{F}$.

11 USE IN SPECIFIC POPULATIONS

11.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Moderna COVID-19 Vaccine during pregnancy. Women who are vaccinated with Moderna COVID-19 Vaccine during pregnancy are encouraged to enroll in the registry by calling 1-866-MODERNA (1-866-663-3762).

Risk Summary

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Available data on Moderna COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy. Therefore, use of Moderna COVID-19 Vaccine is not recommended in pregnant women.

11.2 Lactation

Risk Summary

Data are not available to assess the effects of Moderna COVID-19 Vaccine on the breastfed infant or on milk production/excretion.

11.3 Pediatric Use

Safety and effectiveness have not been assessed in persons less than 18 years of age. Emergency Use Authorization of Moderna COVID-19 Vaccine does not include use in individuals younger than 18 years of age.

11.4 Geriatric Use

Clinical studies of Moderna COVID-19 Vaccine included participants 65 years of age and older receiving vaccine or placebo, and their data contributes to the overall assessment of safety and efficacy. In an ongoing Phase 3 clinical study, xx24.8% (n=xxxx7,520) of participants were 65 years of age and older and xx4.6% (n=xxxxx1,400) of participants were 75 years of age and older. In an interim analysis, no overall differences in safety or effectiveness were observed between these subjects-participants 65 years of age and older and younger subjects-participants.

Commented [A6]: SPONSOR COMMENT: It is Moderna's position that this sentence should be retained. Insufficient data are available regarding use in pregnancy and we would prefer to be clear in the labeling that use in this population is not recommended.

Commented [A7]: SPONSOR COMMENT: It is Moderna's position that this sentence should be retained to be clear in the labeling that the vaccine has not been studied in this population.

Commented [A8]: FDA COMMENT December 4, 2020: Moderna, please insert percentages and number of subjects for these 2 age groups.

SPONSOR RESPONSE: Moderna has added the requested percentages and numbers for the two age groups. Additional changes are proposed in this section to clarify the population. Also, Moderna has separated the statement about efficacy and safety into two statements to accurately reflect the differences observed.

Commented [A9]: Source: EUA 27073 SN0001 Table 14.1.3.2.2 Baseline Demographics and Characteristics by Age Group Safety Set

Commented [A10]: Source: EUA 27073 SN0001 Table 14.1.3.2.2 Baseline Demographics and Characteristics by Age Group Safety Set

18-64 years of age [see Clinical Trial Results and Supporting Data for EUA (18)]. Participants 65 years of age and older reported solicited local and systemic adverse reactions at a lower rate than participants 18-64 years of age. [see Clinical Trials Experience (6.1)].~~Clinical Trial Results and Supporting Data for EUA (13)].~~

13 DESCRIPTION

Moderna COVID-19 Vaccine is a lipid nanoparticle (LNP) suspension for intramuscular injection comprised of a synthetic messenger ribonucleic acid (mRNA) encoding the pre-fusion stabilized Spike glycoprotein (S) of SARS-CoV-2 virus and four lipids. The synthetic mRNA is manufactured in a cell-free, in vitro transcription reaction and formulated with SM-102 (a proprietary ionizable lipid), PEG2000-DMG, cholesterol, and 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) to form the mRNA/lipid nanoparticles.

Moderna COVID-19 Vaccine is provided as a suspension for intramuscular injection and is white to off-white in appearance. Each 0.5 mL dose contains 100 mcg RNA and a total lipid content of 1.93 mg in tris buffer (0.31 mg tromethamine, 1.18 mg tromethamine hydrochloride), 0.043 mg acetic acid, 0.12 mg sodium acetate, and 43.5 mg sucrose.

Moderna COVID-19 Vaccine does not contain any preservatives, antibiotics, adjuvants, or human- or animal-derived materials. The vial stopper does not contain natural rubber latex.

14 CLINICAL PHARMACOLOGY

14.1 Mechanism of Action

The mRNA in the Moderna COVID-19 Vaccine is formulated-encapsulated in lipid nanoparticles, which enable delivery of the mRNA into host cells to allow expression of the SARS-CoV-2 S antigen. The vaccine elicits both neutralizing antibody and cellular immune responses to the S antigen, which may contribute to protection against COVID-19.

18 **CLINICAL TRIAL RESULTS AND SUPPORTING DATA FOR EUA**

A Phase 3 randomized, placebo-controlled, observer-blind clinical trial to evaluate the efficacy, safety, and immunogenicity of the Moderna COVID-19 Vaccine in participants 18 years of age and older is ongoing conducted in the United States (NCT04470427). Randomization was stratified by age and health risk: 18 to <65 years of age without comorbidities (not at risk for progression to severe COVID-19), 18 to <65 years of age with comorbidities (and at risk for progression to severe COVID-19), and 65 years of age and older with or without comorbidities. Participants who were immunocompromised and those with a known history of SARS-CoV-2 infection were excluded from the study. Participants with no known history of SARS-CoV-2 infection but with positive laboratory results indicative of infection at study entry were included. The study allowed for the inclusion of participants with stable pre-existing medical conditions, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 3 months before enrollment, as well as participants with stable human immunodeficiency virus (HIV) infection. A total of 30,418 participants 18 years of age and older were randomized -equally to receive 2 doses of the Moderna COVID-19 Vaccine or saline placebo 1 month apart. The efficacy analyses included participants who received their second

Commented [A11]: SPONSOR COMMENT: It is Moderna's position that this information should be retained in the label. The sponsor has received numerous requests to verify this information from CDC, healthcare professionals, and the public. Providing it in the labeling will help readers find the information directly.

Commented [A12]: SPONSOR COMMENT: Moderna has provided additional changes in the text portion of this section to further clarify the age and health risk stratification and the SARS-CoV-2 history at study entry. Additionally, a sentence has been added regarding the day range when Dose 2 was given to provide context to the 1-month timeframe.

dose within 21 to 42 days after the first dose. Participants will be followed for efficacy and safety until 24 months after the second dose.

The primary efficacy analysis population (referred to as the Per-Protocol Set), included 27,817 subjects-participants who received two doses (at 0 and 1 month) of either Moderna COVID-19 Vaccine (n=13,934) or placebo (n=13,883), and had a negative baseline SARS-CoV-2 status, and did not develop confirmed COVID-19 within 14 days after the second dose. In the Per-Protocol Set, 47.4% were female, 20% were Hispanic or Latino; 79.4% were white, 9.7% were African American, 4.7% were Asian, and 3.1% other races. The median age of subjects-participants was 53 years (range 18-95) and 25.3% of participants were 65 years of age and older. Of the study participants in the Per Protocol Set, 22.3% were at increased risk of severe COVID-19 due to at least one pre-existing medical condition (chronic lung disease, significant cardiac disease, severe obesity, diabetes, liver disease, or HIV infection) regardless of age. There were no notable differences in demographics or pre-existing medical conditions between participants who received Moderna COVID-19 Vaccine or placebo.

Efficacy Against COVID-19

COVID-19 was defined based on the following criteria: The participant must have experienced at least two of the following systemic symptoms: fever ($\geq 38^{\circ}\text{C}$), chills, myalgia, headache, sore throat, new olfactory and taste disorder(s); or the participant must have experienced at least one of the following respiratory signs/symptoms: cough, shortness of breath or difficulty breathing, or clinical or radiographical evidence of pneumonia; and the participant must have at least one NP swab, nasal swab, or saliva sample (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR. COVID-19 cases were adjudicated by a Clinical Adjudication Committee.

At the time of the interim analysis, the median length of follow up for efficacy for participants in the study was 7 weeks post dose-Dose 2. There were 5 COVID-19 cases in the Moderna COVID-19 Vaccine group and 90 cases in the placebo group, with a vaccine efficacy of 94.5% (95% confidence interval of 86.5% to 97.8%).

Table 23: Interim Primary Efficacy Analysis: COVID-19* in Participants 18 Years of Age and Older Starting 14 Days After Dose 2 per Adjudication Committee Assessments – Per-Protocol Set

Moderna COVID-19 Vaccine			Placebo			% Vaccine Efficacy (95% CI) [†]
Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	
13,934	5	1.840	13,883	90	33.365	94.5 (86.5, 97.8) (p<0.0001) [‡]

Commented [A13]: FDA COMMENT December 4, 2020: Moderna: Please move age groups down to the table that presents analyses of efficacy by subgroups.

SPONSOR RESPONSE: Moderna has moved the age groups to Table 4 as requested and removed the age column at the far left as it is no longer necessary. Additionally, the p value has been added to the Vaccine Efficacy column with the appropriate footnote.

Age-Group- (Years)	Subjects (N)	COVID-19 Cases (n)	Incidence- Rate-of- COVID-19 per 1,000 Person- Years	Subjects (N)	COVID-19 Cases (n)	Incidence- Rate-of- COVID-19 per 1,000 Person- Years	% Vaccine Efficacy- (95% CI)†
Overall- (≥18)	13,934	5	1.840	13,883	90	33.365	94.5 (86.5, 97.8)‡
18 to <65	10,407	5	2.504	10,384	75	37.788	93.4 (83.7, 97.3)
≥65	3,527	0	—	3,499	15	21.046	100

* COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom. Cases starting 14 days after Dose 2.

† VE and 95% CI from the stratified Cox proportional hazard model

‡ The one-sided p-value is <0.0001 from the stratified Cox proportional hazard model to test the null hypothesis of VE ≤30%, achieving the pre-specified efficacy boundary: the one-sided nominal alpha of 0.0049 based on 95 cases using the Lan-DeMets O'Brien-Fleming spending function.

The subgroup analyses of vaccine efficacy are presented in Table 3.

Table 34: Interim Subgroup Analyses of Vaccine Efficacy: COVID-19* Cases Starting 14 Days After Dose 2 per Adjudication Committee Assessments – Per- Protocol Set

Subgroup	Moderna COVID-19 Vaccine			Placebo			% Vaccine Efficacy (95% CI)*
	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person- Years	Participants (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person- Years	
18 to <65	10,407	5	2.504	10,384	75	37.788	93.4 (83.7, 97.3)
≥65	3,527	0	—	3,499	15	21.046	100

Subgroup	Moderna COVID-19 Vaccine			Placebo			% Vaccine Efficacy- (95% CI)†
	Subjects (N)	COVID-19 Cases (n)	Incidence- Rate of COVID-19 per 1,000 Person- Years	Subjects (N)	COVID-19 Cases (n)	Incidence- Rate of COVID-19 per 1,000 Person- Years	
Overall- high- risk‡	3,116	1	1.604	3,075	24	39.177	95.9 (69.7, 99.4)
High risk‡ 18 to <65	2,098	1	2.428	2,061	18	44.673	94.6 (59.4, 99.3)
Not high risk‡ 18 to <65	8,309	4	2.524	8,323	57	36.034	93.0 (80.8, 97.5)

EUA Full EUA Prescribing Information (AR Tables, Sections 11-21)
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Draft December 6, 2020

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Commented [A14]: FDA COMMENT December 4, 2020:
Moderna please include only analyses of age groups 18-65
and 65 and above and delete the other information.

SPONSOR RESPONSE: Moderna has updated the table as
requested.

Females	6,661	2	2,271	6,514	45	34,991	93.5 (79.2, 98.0)
Males	7,273	2	1,433	7,369	45	31,883	95.5 (81.5, 98.9)

* * COVID-19: symptomatic COVID-19 requiring positive RT-PCR result and at least two systemic symptoms or one respiratory symptom. Cases starting 14 days after Dose 2. Subjects at increased risk of severe COVID-19 due to at least one pre-existing medical condition (chronic lung disease, significant cardiac disease, severe obesity, diabetes, liver disease, or HIV infection), regardless of age

† VE and 95% CI from the stratified Cox proportional hazard model

Severe COVID-19 was defined based on confirmed COVID-19 as per the primary efficacy endpoint case definition, plus any of the following: Clinical signs indicative of severe systemic illness, respiratory rate ≥ 30 per minute, heart rate ≥ 125 beats per minute, SpO₂ $\leq 93\%$ on room air at sea level or PaO₂/FIO₂ < 300 mm Hg; or respiratory failure or ARDS, (defined as needing high-flow oxygen, non-invasive or mechanical ventilation, or ECMO), evidence of shock (systolic blood pressure < 90 mmHg, diastolic BP < 60 mmHg or requiring vasopressors); or significant acute renal, hepatic, or neurologic dysfunction; or admission to an intensive care unit or death.

Among all subjects-participants in the Per-Protocol Set interim analysis, no cases of severe COVID-19 were reported in the Moderna COVID-19 Vaccine group compared with 11 cases reported in the placebo group (incidence rate 4.072 per 1,000 person-years).

Additional Efficacy Analyses

An interim subgroup analysis was conducted on confirmed COVID-19 cases starting 14 days after Dose 2 of Moderna COVID-19 Vaccine or placebo in high-risk subjects, females, and males (HYPERLINK \l "_bookmark16" Table 3).

Table 3: Interim Subgroup Analyses of Vaccine Efficacy: COVID-19 Cases 14 Days After Dose 2 per Adjudication Committee Assessments (Primary Efficacy Analysis Set) Per Protocol Set

Subgroup	Moderna COVID-19 Vaccine			Placebo			% Vaccine Efficacy (95% CI)†
	Subjects (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	Subjects (N)	COVID-19 Cases (n)	Incidence Rate of COVID-19 per 1,000 Person-Years	
Overall high-risk ^a	3,116	1	1.604	3,075	24	39.177	95.9 (69.7, 99.4)
High risk ^a 18 to < 65	2,098	1	2.428	2,061	18	44.673	94.6 (59.4, 99.3)
Not high risk ^a 18 to < 65	8,309	4	2.524	8,323	57	36.034	93.0 (80.8, 97.5)

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Females	6,661	3	2,271	6,514	45	34,991	93.5 (79.2, 98.0)
Males	7,273	2	1,433	7,369	45	31,883	95.5 (81.5, 98.9)

* Subjects at increased risk of severe COVID-19 due to at least one pre-existing medical condition (chronic lung disease, significant cardiac disease, severe obesity, diabetes, liver disease, or HIV infection), regardless of age

† VE and 95% CI from the stratified Cox proportional hazard model

19 HOW SUPPLIED/STORAGE AND HANDLING

Moderna COVID-19 Vaccine is supplied as a multiple-dose vial containing 10 doses of 0.5 mL each.

Each carton of Moderna COVID-19 Vaccine contains 10 multiple-dose vials (NDC 80777-273-99).

Store frozen between -25° to -15°C (-13° to 5°F). Store in the original carton to protect from light. Do not store on dry ice or below -40°C (-40°F).

Vials can be stored refrigerated between 2° to 8°C (36° to 46°F) for up to 30 days prior to first use. Do not refreeze.

Unopened vials may be stored between 8° to 25°C (46° to 77°F) for up to 12 hours. Do not refreeze.

After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F). Discard vial after 6 hours. Do not refreeze.

20 PATIENT COUNSELING INFORMATION

Advise the recipient or caregiver to read the Fact Sheet for Recipients and Caregivers.

21 CONTACT INFORMATION

If you have questions, please contact: Moderna
1-866-MODERNA (1-866-663-3762)
medinfo@modernatx.com

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